EVERYDAY DOCTORING

A New Approach to the Logic and Reasoning of Neurology and Medicine



by Sheldon Margulies, M.D.

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of Neurology and Medicine

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DEDICATION

ONE OF NATURE'S GREAT IRONIES IS THAT NEW LIFE SHOULD sprout, indeed flourish, amidst the ruins of decay and misfortune. I dedicate this book to my mentally retarded older sister, Deborah, whose handicap has shaped and encouraged my career in medicine and neurology.

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FOREWORD

In this book I've tried to set out the rules of anatomic localization (with obvious emphasis on the nervous system) and also how to gather the necessary signs on physical examination to apply to those rules. Obviously there are exceptions to almost every rule of anatomic localization. Aphasia may occasionally result from a thalamic or other subcortical insult,[1] some patients may recall events during absence status,[2] akinetic mutism may indicate a hypothalamic lesion,[3] asterixis may result from a focal brain lesion,[4] decerebrate posturing may occur during sedative overdose,[5] downbeat nystagmus may result from a supratentorial lesion,[6] a sensory level may occur with parietal lobe lesions,[7] the Romberg sign may be positive in cerebellar[8] or vestibular disease,[9] botulism may have sensory findings,[10] proximal weakness may be neurogenic,[11] distal weakness may be myopathic,[12] and muscle hypertrophy may, rarely, be due to neurogenic lesions.[13]

Exceptions cannot be minimized, but, after all, they are exceptions and do not invalidate the rules. The best will always be the enemy of the good. The point of this manual is not to highlight each and every exception, but to give you some insight into the fundamental logic and reasoning underlying the steps in medical and neurologic diagnosis. Besides, once you understand the rules, the exceptions will be easier to remember.

In many fields of neurology—speech and higher cortical function especially—conflicting data, insufficient data, different ways of interpreting the data, and a technical vocabulary combine to cloud the issues. In such circumstances I have chosen what I think are logical frameworks that fit the data in a straightforward manner. Admittedly, new clinical observations will change these frameworks, but in the meantime they provide clinically useful approaches. As such, many of the statements in this manual are opinions. Unless references are cited to support a particular point of view, take these statements as opinions only. Same on the ward—opinions are opinions; they are not a substitute for scientific investigation. Only radiologists are allowed to say "Well, we see that." The rest of us must be prepared to substantiate our opinionated statements with references to the medical literature.

The top of each page contains the text, and the bottom of the page contains definitions and asides that help clarify the text.

PREFACE TO FRESHMAN MEDICAL STUDENTS

I THINK IT IS IMPORTANT FOR DOCTORS IN THE TRENCHES to explain how they do it. The craft of medicine is an apprenticeship not easily learned from textbooks. Sure, you can learn anatomy and physiology, but it's a big jump from the classroom to the clinic. You need to translate anatomy and physiology into symptoms and signs, and then you need to translate those symptoms and signs into simple English, the kind of English *patients* understand.

At some point in medical school you have to evolve from a go-fer—continually asking your interns and residents "What should I do now?"—into a doer—stating that "I think this and this should be done," and defending that opinion. The moment you realize that *you* are directing the patient's tests and therapy, that *you* are the one the patient turns to for help, that *you* are responsible for that patient's welfare, all of this doctoring business will become a lot more immediate. But finally when you realize that you *can* competently look after patients, you're on your way. Getting you there is the hard part. You need to master a large body of facts, then learn how to draw conclusions based on those facts, and finally, how to draw conclusions when you don't have all the necessary facts.

It is very easy to become entangled in all the historical facts, physical signs, and laboratory data. There are too many diseases, too much scut work, not enough guidance, and too many people ready to jump down your throat if you make a mistake. It is simply too easy to lose track of where you are headed in a case. You need a systematic approach, one that you can always refer to when you get lost.

I hope the approach outlined in this manual will help you feel comfortable talking to patients and sorting out their medical problems. Once you understand how doctors reason, you can really start thinking about the diseases themselves—their pathophysiology, complications, prognosis, and treatment. And the sooner you start thinking seriously about diseases, the sooner we'll all find new ways to do something about them.

ACKNOWLEDGMENT

I WOULD LIKE TO ACKNOWLEDGE THE GENEROUS HELP AND GUIDANCE of my many teachers during and following medical school and residency, most notably Dr. Robert Fishman and Dr. James Halsey, both of whom championed doctoring at the bedside first and foremost.

I would also like to thank the Staff of the Royal Victoria Hospital at McGill University in Montreal, Quebec for instilling an appreciation of physical diagnosis as a scientific art.

I am sincerely indebted to Helen Corless Mabry for the time, effort, and exacting care in preparing the illustrations, and to Dr. Ann Cross for her many helpful suggestions.

INTRODUCTION

DURING MEDICAL SCHOOL, I RECALL LEARNING A WHOLE NEW VOCABULARY and a vast number of facts and figures, but I never really learned how doctors reason out medical problems. Even during the last two years of medical school when I learned how to elicit the present illness, the past medical history, social history, and review of systems, and how to perform a complete physical exam, I never learned how to think, only how to memorize. Later, during my internship and residency when days and nights on call consisted of admitting two or three (or more) critically ill patients while simultaneously attending to a ward full sick patients and putting out brush fires in the emergency room, I could no longer rely on reflex memory alone to get me through morning report. I had no logical way to keep straight all those histories, physicals, laboratory tests, differential diagnoses, and treatments. I was simply forced to develop a systematic and efficient method of thinking about patients' problems. The approach that evolved from these pressures not only helped streamline my history-taking and physical examination, but also helped me remember each patient's history and physical, helped me organize a comprehensive differential diagnosis, and even aided my understanding of disease processes. No doubt there are many other ways of approaching medical problems which are just as efficient and handy as the one outlined in this manual, but I have found this framework of thinking very useful in times of fatigue, panic, and just everyday doctoring.

To solve any complex problem, especially one like physical diagnosis, you first have to reduce all the seemingly unorganized, but potentially related bits of information down to some comprehensible size. This is accomplished by paring off all the unnecessary information, and then hammering the remaining essentials into a few pivotal questions. Applied to physical diagnosis, this means consciously guiding the patient along a systematic line of reasoning so that you can focus on and answer those few pivotal questions. I have tried in this manual to lead you through what I think are the logical steps in physical diagnosis, the specific questions that systematically lead to a well thought-out differential diagnosis.

Neurology takes a lot of heat from other specialties because all it seems we care about is "Where is the lesion?" Anatomic localization *is* of utmost concern in neurology, but no more than in any other speciality—it's just easier in other specialities. For example, when someone presents with microscopic hematuria, your first goal is anatomic localization—where is the exact site of bleeding: bladder, ureter, renal pelvis, glomerulus, or renal parenchyma? Only after you've decided where the bleeding site is can you rationally consider specific causes.

Anatomic localization in neurology is so much harder than in internal medicine that a great deal more time and emphasis *is* given to neurologic localization. As a result, so much of our time is spent on simply localizing the lesion that little time is left for in-depth discussions about the pathogenesis of neurologic diseases. By organizing the neurologic exam and mapping out the rules of anatomic localization, I hope this manual will help free up your time to study what is the most fascinating question in all of medicine and physiology: How in the world *does* the brain work?

Neuroanatomic localization is not unlike a lot of three-step logic problems. First you begin with a set of rules stating how to localize lesions to each area of the nervous system. Then you find the patient's neurologic signs on exam, and finally, you apply the neurologic signs to the rules of neuroanatomic localization. Of the three steps, the hardest is finding the neurologic signs. The rules of neuroanatomic localization may tell you which signs to look for, but *you* have to decide whether that sign is present. When do you decide a person is aphasic? What kind of aphasia does he have? Is his difficulty walking due to weakness, stiffness, slowness, or incoordination—which signs did you find? Did you find any atrophy? Did you even look for atrophy? How about fasciculations?

In order to apply the neurologic signs to the rules of neuroanatomic localization, you do have to know the rules. The rules governing each area of the nervous system are composed of elements, A, B, C, D, etc. For example, the elements for the pyramidal tract are: spasticity, weakness, slowing of rapid alternating movements, hyperreflexia, and a Babinski sign. What makes neuroanatomic localization so difficult is that not *every* element of the rule needs to be satisfied. In other words, the lesion may still be in the area of the nervous system governed by that rule even if all the elements are not satisfied. Finding all five signs of the pyramidal tract would obviously confirm a pyramidal tract lesion, but so would these combinations: spasticity and weakness, weakness and hyperreflexia, slowing of rapid alternating movements and hyperreflexia, or even a Babinski sign alone. This becomes very important as patients present earlier and earlier in their disease with only a few, and often subtle, signs. If you decide to wait until all the elements appear before making an anatomic diagnosis, you've waited too long.

What's the point, you may ask, of worrying about the physical exam when we have sensitive tests like the CAT scan, nuclear magnetic resonance, electroencephalography, and electromyography to localize the lesion for us? No question, these tests *are* indispensable, but they should only be ordered after you know what you're looking for. Putting aside the argument that you didn't enter medical school to become a body mechanic, it would simply be too expensive for the country to allow every physician to order these costly tests indiscriminately. Through insurance, we all end up paying for everyone else's doctor bills. Moreover, many of the tests carry risks. If the test wasn't necessary and the patient suffers a complication from the test, who's going to defend you?

Another reason for not ordering sensitive laboratory tests too early is that many people walking the streets have all sorts of subclinical abnormalities, undetectable by exam but detectable by laboratory tests. Uncovering everyone's asymptomatic "illness" would quickly overwhelm the medical system. And finally, before you correct the abnormality discovered by a laboratory test, you better be sure that that abnormality adequately explains your patient's symptoms, or else you'll be back to square one when the treatment fails. Only the physical exam can connect your patient's complaints to the abnormal laboratory test.

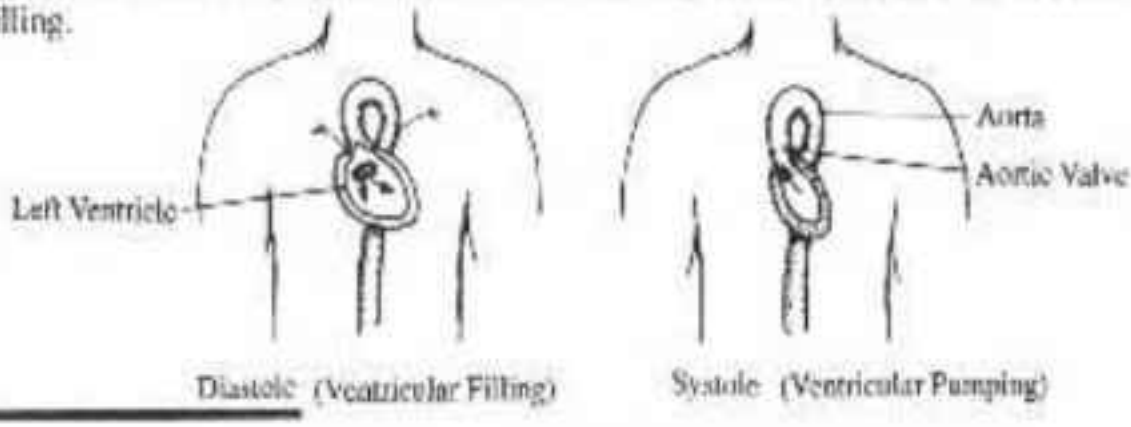
THE ORGAN SYSTEMS

THE ART OF MEDICAL DIAGNOSIS is a two-step procedure. The first step is to establish a physical, or anatomic diagnosis and the second step is to establish an etiologic, or causative diagnosis: *where* is the lesion*? and what's *causing* it? Though all doctors eventually learn anatomic diagnosis, the mastery of anatomic localization takes longer than it should because physical diagnosis is taught the same way anatomy is—that the body is anatomically divided into the geographical areas of head, neck, chest, abdomen, and extremities. This is simply the wrong way to think of the body because the body neither works geographically nor becomes ill geographically. Instead, the body works, like any machine, by the cooperation of separate organ systems. In a car these would be the fuel system, electrical system, cooling system, transmission, exhaust system, etc. The human body contains sixteen such systems which are most easily remembered by grouping them as follows: **systemic, skin, neuromuscular; eyes, ears, endocrine; respiratory, cardiac, gastrointestinal; reticuloendothelial, urologic, genital; vascular, hematologic, bone, coverings-and-connective tissue.**

SYSTEMIC

Blood pressure, pulse, respiration, and temperature—the "vital signs."

Blood pressure: Each heart beat pumps about a third of a cup of blood from the heart's main pumping chamber, the left ventricle*, through an aortic valve into the aorta (trunk of the arterial* tree). During this contraction phase, called systole*, arterial blood pressure rises to its systolic height. After blood is pumped out of the left ventricle, the aortic valve closes and diastole* begins—the period of left ventricular filling.



Lesion: Any abnormality; usually means a structural abnormality, not a chemical one.

Ventricle: Belly in Latin.

Arterial: Arteries carry blood away from the heart; veins carry it back. The more general term, blood vessel, or the prefix vaso, refers to any artery or vein.

Systole: Latin: to contract.

Diastole: Latin: to dilate.

In the aorta, meanwhile, blood runs off into peripheral arterial twigs. To prevent intra-arterial* pressure from dropping to zero, the elastic arteries constrict, maintaining some pressure in the arterial system at all times. The level to which the blood pressure drops is the diastolic pressure. A normal blood pressure is 120 mm* systolic and 80 mm diastolic, written 120/80. Above about 140/90 is called hypertension*; too low a blood pressure is hypotension*. Life-threateningly low blood pressure (below about 80 mm systolic) is called shock*.

Pulse: Crucial features of the pulse are its rate (beats per minute) and its rhythm (regular or irregular). A normal rate at rest is around 60–80 beats per minute. Too slow a heart rate is called bradycardia*; too fast, tachycardia.

Respiration: Both rate and depth determine the adequacy of respiration. A normal rate is about 12–16 breaths per minute. Depth is measured in cc's* per usual relaxed breath ('tidal volume') or in cc's comfortably breathed per minute ('minute volume'). A patient's respiratory reserve is measured in cc's per *deep* breath: 'vital capacity.' A vital capacity below 500cc (you and I are capable of 4000cc) usually requires assistance by a mechanical respirator.

Temperature: Normal oral temperature is 98.6 degrees (written 98.6°) Fahrenheit, or 37° Centigrade; rectally, a degree higher: 99.6°F (37.6°C). 40°C is equivalent to 104°F.

SKIN

Includes an outer, superficial layer—the epidermis*—and a deeper layer, the dermis, containing the blood vessels and fat. Between skin and muscle is a space (which is easy to demonstrate by pinching up the skin) called the subcutaneous* space. Skin also includes the nails, hair, eyebrows, and sweat glands.

NEUROMUSCULAR

Every nerve cell (neuron), whether in brain, spinal cord, or peripheral nerve, is made up of the same components: dendrites, cell body, and axon.

Intra-arterial: Intra = within; inter = between.

mm: The height, in millimeters, of a column of mercury.

Hypertension: Hyper means too much; hypo means too little.

Hypotension: In general, the lower the blood pressure, the better (less strain on the heart and vascular systems). Hypotension is diagnosed when problems arise *because* of the low blood pressure, that is, when there is inadequate pressure to pump enough blood to the internal organs. This usually occurs when the systolic pressure drops below about 80–85 mm.

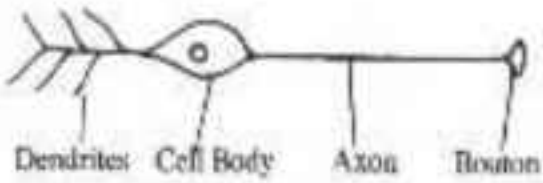
Shock: Strictly speaking, shock exists whenever the blood pressure is not high enough to meet the needs of the internal organs. Fever increases the chemical activity of all organs, and with it, the demand for oxygen. So, febrile patients may occasionally be in shock even with a relatively normal blood pressure.[1]

Bradycardia: Brady in Greek means slow; tachy means fast.

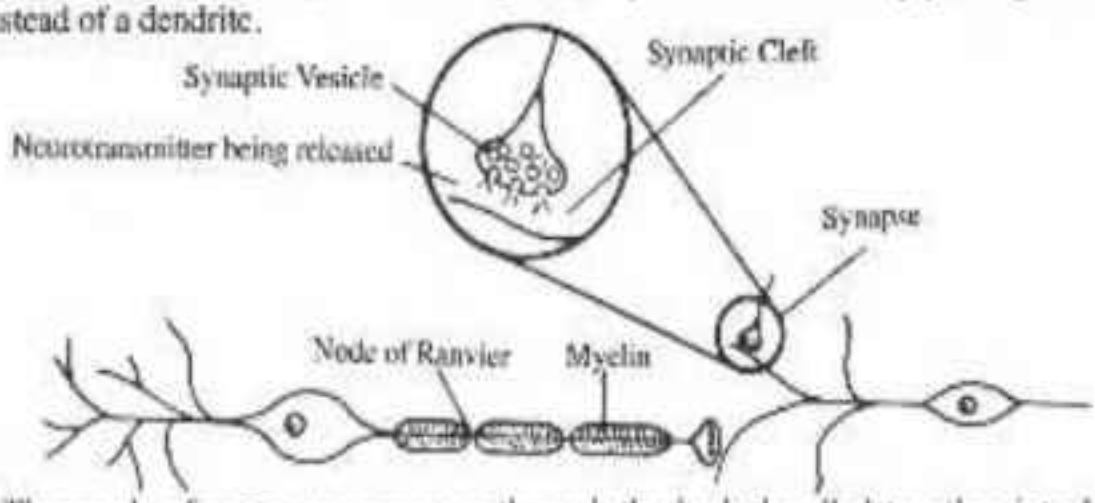
cc's: Cubic centimeters. One teaspoon is 5cc's; a tablespoon, 15cc's.

Epidermis: Epi (upon) dermis (skin): the outer, superficial layer.

Subcutaneous: Sub (under) cutaneous (skin), from Latin (cutis = skin).



Neurons communicate with each other by sending a small jolt of electricity down an axon* into a terminal bouton* which, goosed by the electrical jolt, sprays a chemical neurotransmitter* across the synaptic cleft to stimulate the next neuron's dendrites*. The electrical impulse then makes its way along those dendrites toward headquarters in the cell body, which waits until it has received enough dendritic impulses before firing its own axon. If an axon is used to stimulate a muscle, then the synaptic cleft is called a neuromuscular junction, the post-synaptic membrane simply being a muscle instead of a dendrite.



Thousands of nerve axons course through the body bundled together into large, individual peripheral nerves. Many axons within each peripheral nerve are, like individual wires in a telephone cable, insulated from one another with a fatty jacket called myelin*. Myelin prevents electrical impulses from spreading into neighboring axons, and also speeds electrical transmission along those axons carrying critical sensory information to, and vital motor instructions from, the brain.

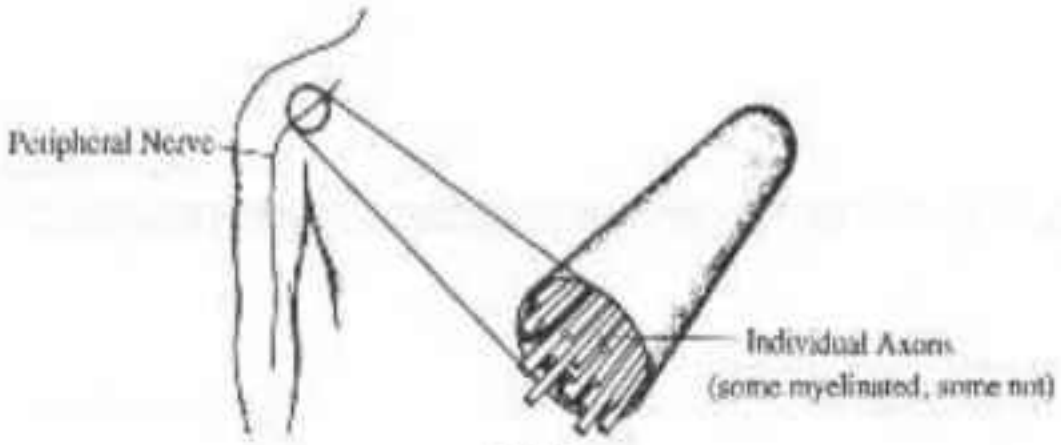
Axon: Axis in Greek.

Bouton: French: knob, bud.

Neurotransmitter: It took until 1921 before anyone proved that neurons release neurotransmitters. In that year Dr. Otto Loewi dreamt the definitive experiment: bathe a spontaneously beating frog heart—with its nerves still attached—in a salt solution, and then stimulate the vagus nerve, the nerve that slows the heart. Then take that solution and dip another spontaneously beating heart into it—this time without any attached nerves. If the heart slows, as it did for Dr. Loewi, then the vagus must have released a neurotransmitter into the bathing solution. The neurotransmitter was later identified as acetylcholine, a popular neurotransmitter among neurons.

Dendrites: From Greek meaning tree-shaped.

Myelin: Derived from an old Greek term for spinal cord: myelos.



EYE

The wall of the ocular globe is made of a tough, white coat called the sclera*, which is kept distended by vitreous* humor*, a clear, jelly-like substance inside the globe. Blood vessels in the white of the eye travel within the conjunctiva*, a thin transparent membrane overlying the sclera and extending up underneath the eyelid. Also tucked up under the upper eyelid is the lacrimal (tear) gland. Tears are drained from the eye through a lacrimal duct* into the nose.[1] A bead of goo normally collects overnight at the entrance of the lacrimal duct.



Surrounding the central black pupil* is a variably colored, life-saver shaped iris*, a muscle which opens and closes the pupil to keep light intensity at a moderate level. The iris also improves close-up vision by constricting the pupil*, a reflex you can verify by looking at someone's pupil when he glances from a distant target to a very close one. Light enters the globe through the cornea*, passes through the iris, and is focused by a lens onto the retina where rods and cones convert light into electricity.

Sclera: Tough. (Greek)

Vitreous: As clear as glass. (Latin)

Humor: Liquid. The ancient Greeks thought that everything was made up of four elements: Earth, Fire, Water, and Air. From these were derived the four corresponding humors that govern the human body and temperament: Black Bile, Yellow Bile, Phlegm, and Blood.

Conjunctiva: From the Latin word, conjungere—to join together, which the conjunctiva does to the eyelid and eyeball.

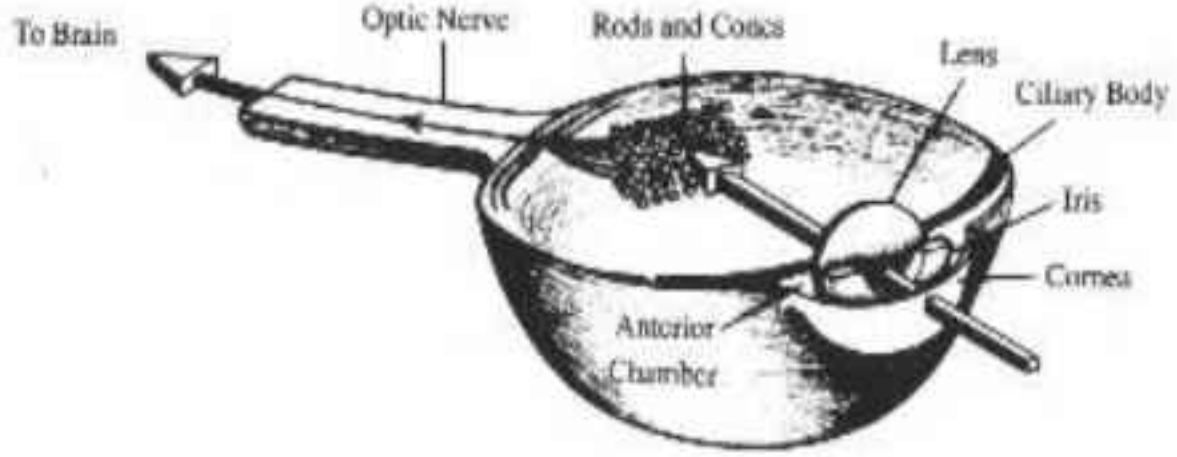
Duct: Any tube conducting fluid from one place to another.

Pupil: Little girl or doll (what you see reflected back from the pupil).

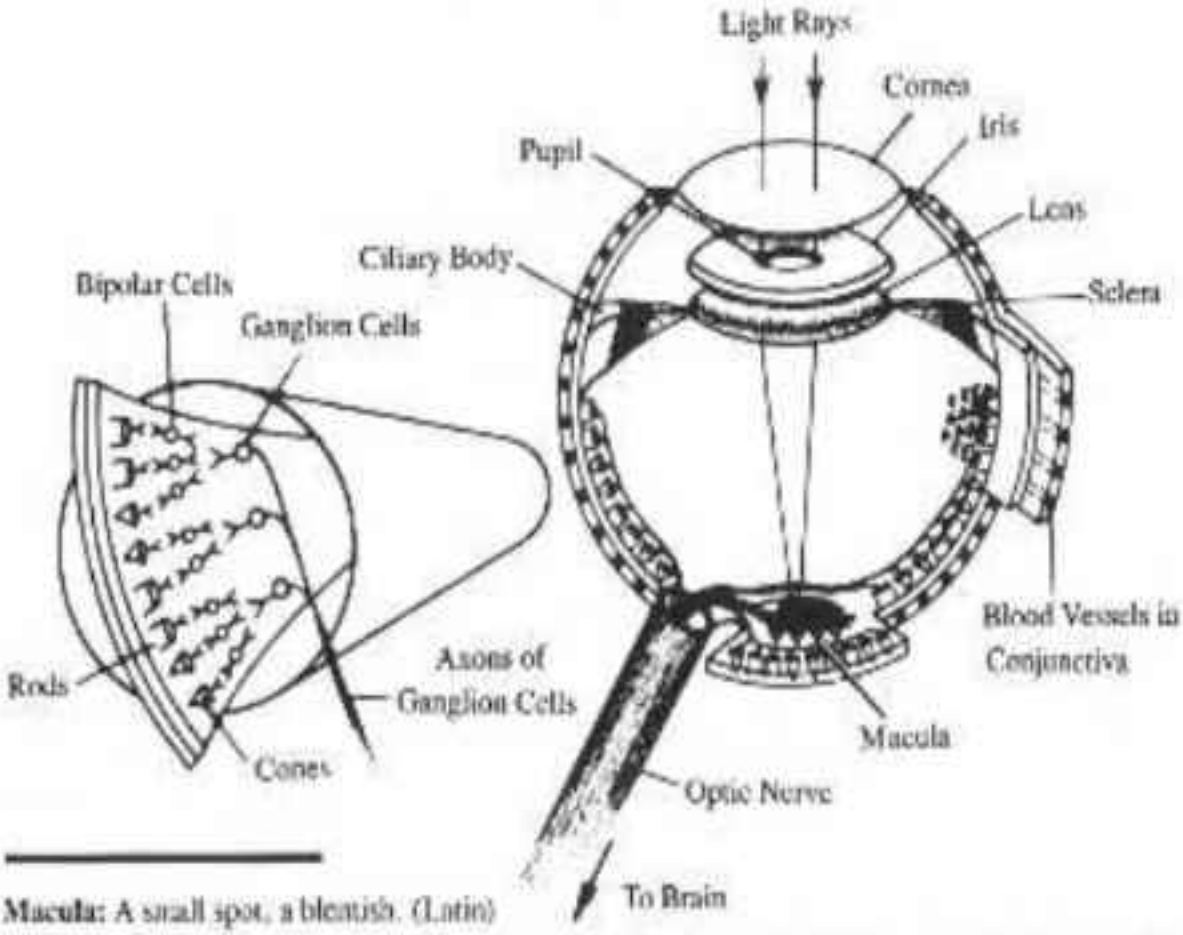
Iris: Rainbow. (Greek)

Constricting the Pupil: You can verify that iris constriction improves resolution by noting how much clearer objects are when viewed through a pinhole. In fact, a pinhole will suffice for a camera lens if you're willing to wait for enough light to strike the film.

Cornea: From Latin cornu (horn), hence corn on a toe.



Our highest resolution, 'central fixation,' is mediated by the macula*, a dense concentration of cones (no rods). Cones are very sensitive to color and relatively insensitive to light. Rods, in contrast, being exquisitely sensitive to light (but not color), allow us to see at night. In bright daylight the rods shut down, but then require a few minutes to reactivate when the lights go out* (which is obvious to anyone groping for a seat in a darkened movie theater). The electrical impulses generated by rods and cones are carried along the retinal surface by long nerve cells—ganglion* cells—to the optic nerve head through which visual information enters the brain.



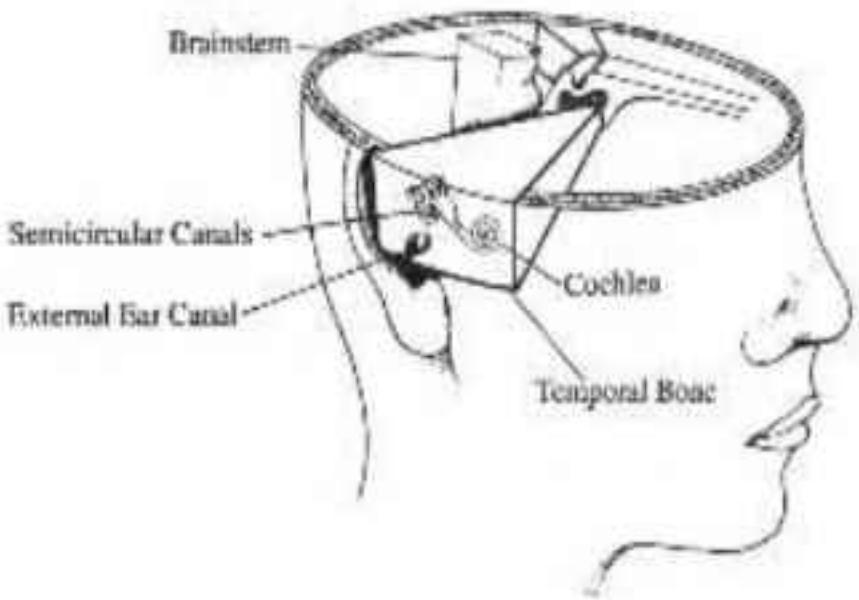
Macula: A small spot, a blemish. (Latin)

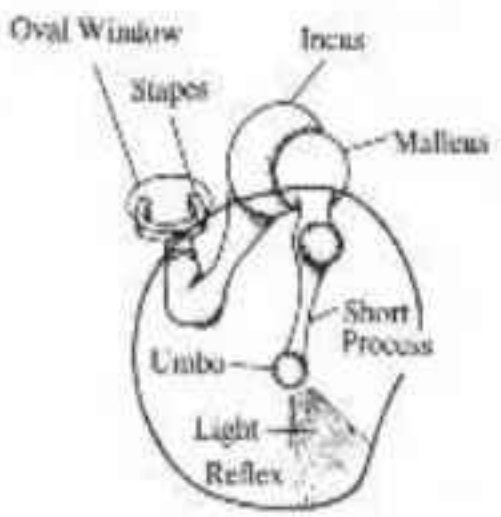
When the Lights Go Out: During World War II night pilots adapted their rods for nighttime flight while still remaining in room light by wearing red goggles, a color that rods cannot see. Zookeepers also capitalize on this handicap by using red lights to spy on nocturnal creatures whose eyes contain only rods.

Ganglion: Originally meant a nodule under the skin; now used for any collection of nerve cell bodies.

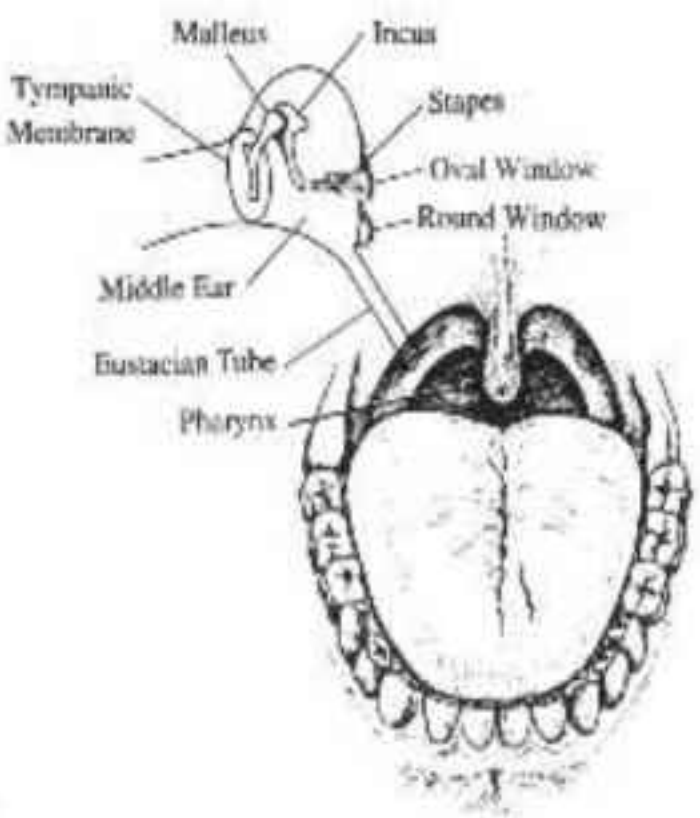
EARS

Sounds collected through the external ear canal vibrate the tympanic* membrane (ear drum) which conducts this mechanical energy via three middle ear bones—malleus*, incus*, and stapes*—to the oval window, entryway to the inner ear. Pressure is kept equal on both sides of the tympanic membrane by venting the middle ear to the mouth through the Eustacian tube*.





Right Tympanic Membrane
(as viewed through an otoscope)



Tympanic: A tympanum is a Greek kettle drum.

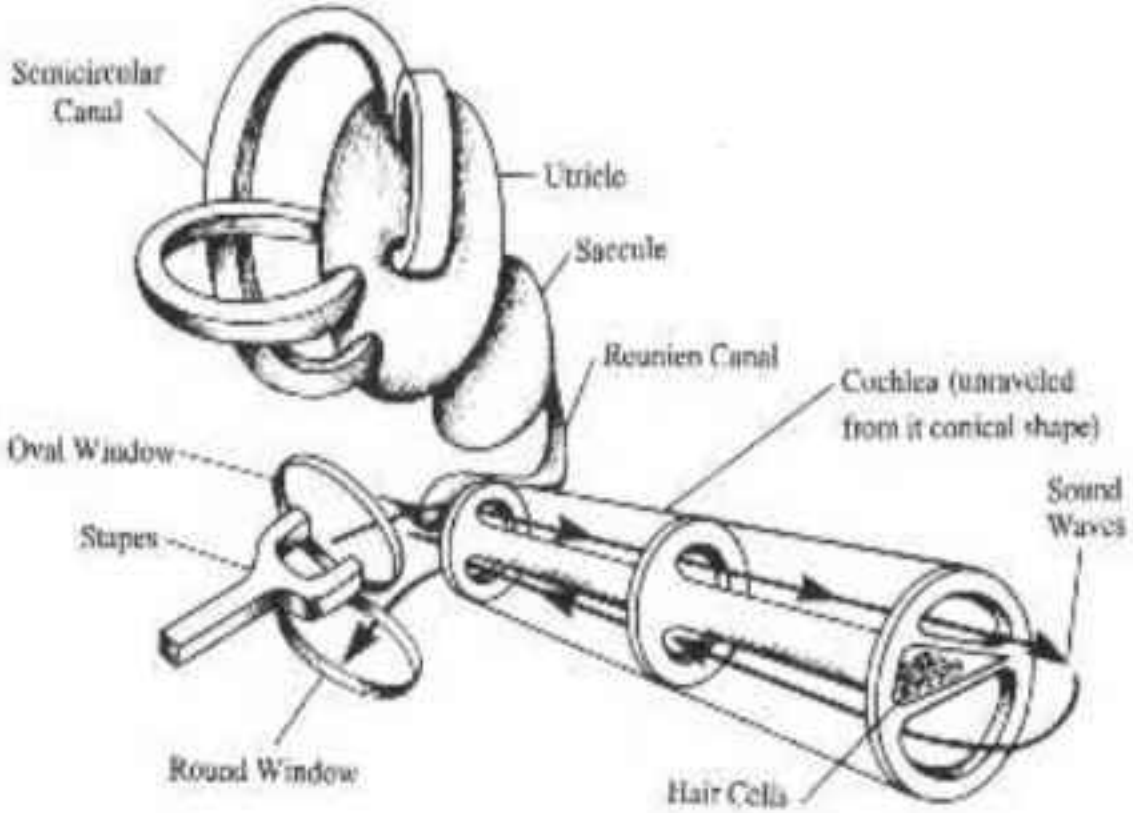
Malleus: Hammer.

Incus: Anvil.

Stapes: Stirrup.

Eustacian Tube: You can blow open your Eustacian tube by pinching your nose, closing your lips, and blowing hard.

Within the inner ear the cochlea*, shaped like a spiral conch shell, converts mechanical energy into electrical energy. Inside the cochlea thousands of special hairs at varying distances from the oval window—each hair sensitive to a particular pitch—discharge electrical impulses when selectively vibrated by differently pitched sounds.[3]



Adjacent to this hearing apparatus, carved into the temporal* bone is the labyrinth*, the balance-sensing organ. The labyrinth consists of an ingenious set of three fluid-filled loops (semicircular canals), one for each dimension of space. When the head turns, fluid within these canals moves, stimulating sensitive hairs lining the canals. By computing which hair cells in which semicircular canal were stimulated, the brain can sense the direction and speed of head turning.

The three semicircular canals join at their base into a common chamber, the utricle*, which abuts another small chamber, the saccule*. Together, the utricle and saccule tell the brain what position the head is in when it's still. A chip of calcium weighing against sensitive hair cells inside each utricular and saccular chamber announces whether the head is up, down, or tilted. And when the head accelerates straight ahead (without turning), like accelerating from a stop sign, those calcium chips are suddenly forced up against the utricular and saccular walls; the amount of force signals how fast you're accelerating.[4]

Cochlea: Snail in Latin.

Temporal: Related to the word time (tempo). Being thin, the temporal bone was vulnerable during battle ("time's up"). Also, the first sign of aging (time) is graying temples.

Labyrinth: So named because of its involved shape.

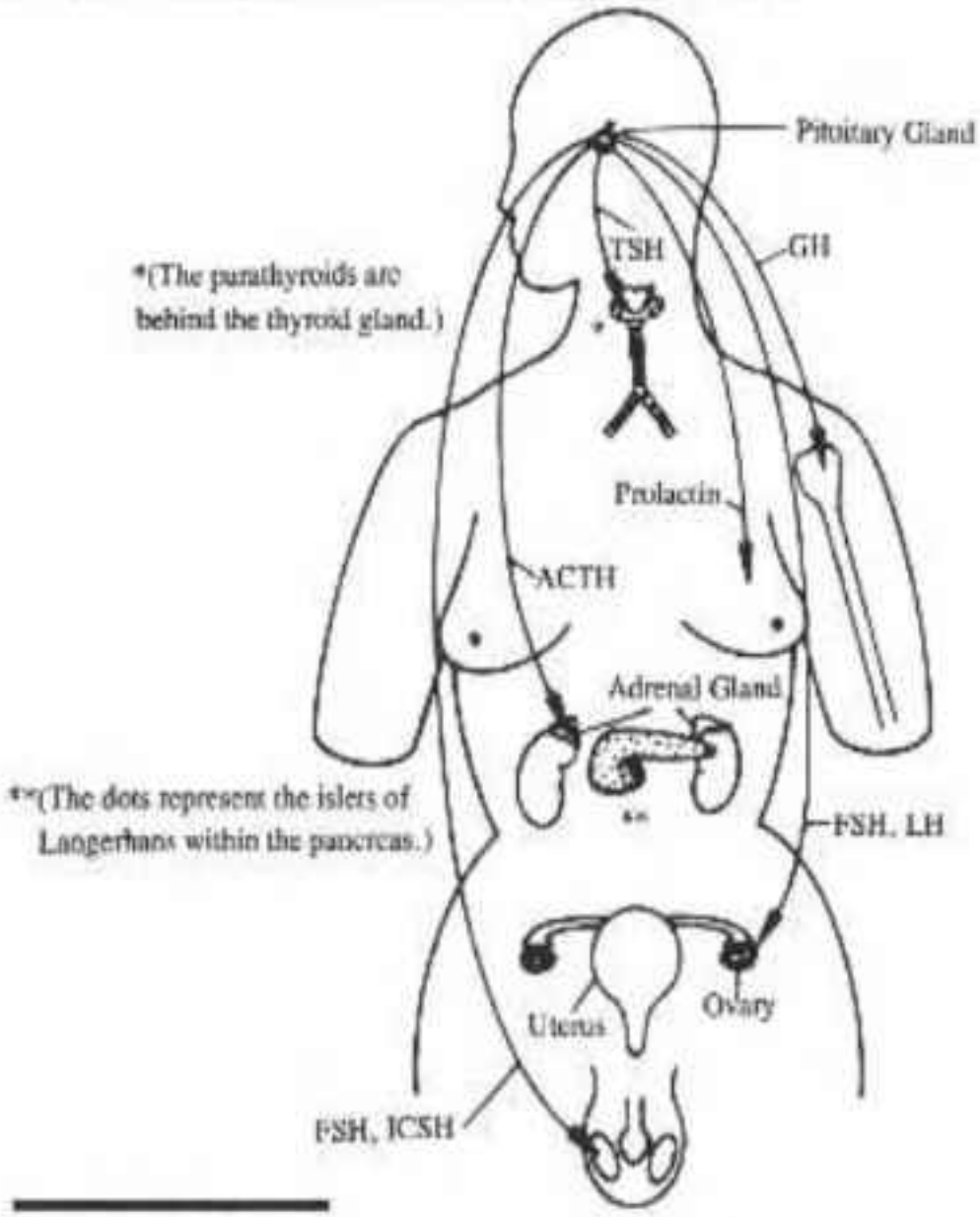
Utricle: A small wine sac. Same origin for uterus.

Saccule: Small sac.

ENDOCRINE

Glands* were originally designed to produce chemicals for specific jobs, but because the job sites were often distant from the site of synthesis, Mother Nature had to devise some way to deliver the chemicals. Two routes evolved: via ducts and via the bloodstream. Those glands which secrete* their chemicals into ducts in the form of juices are called *exocrine* glands—the lacrimal glands, salivary glands, pancreas*, sweat glands, and breast.

Each exocrine gland produces a chemical that performs only one or two limited tasks within a relatively confined space. For more widespread effects, Mother Nature devised six *endocrine** glands which secrete their hormones* directly into the bloodstream. Each endocrine gland secretes specific hormones:



Glands: Endocrine glands are not to be confused with lymph glands located in the neck and groin. As part of the reticuloendothelial system (page 28), lymph glands enlarge during infections to produce antibodies and white cells.

Secrete: To export from a cell or gland.

Pancreas: Pan = all; kreas = flesh.

Endocrine: Endo (within) emphasizes that endocrine glands secrete into the body; exocrine glands secrete their juices outside the body (exo = outside).

Hormone: From Greek, to set in motion.

This hormone:	Secreted by this endocrine gland:	Performs this function:
Follicle* Stimulating Hormone (FSH)	Pituitary*	Together FSH and LH stimulate egg and sperm development.
Luteinizing* Hormone (LH)	Pituitary	
Prolactin*	Pituitary	Stimulates breast milk production*.
Growth Hormone	Pituitary	Increases body growth.
Oxytocin*	Pituitary	Contracts the uterus during labor.
Antidiuretic Hormone*	Pituitary	Tells the kidney to save water.
Thyroxin	Thyroid*	Speeds up all the body's chemical reactions.
Parathormone	Parathyroid*	Raises the calcium level* in the blood.

Follicle: Small bag. (Pertaining to the small capsule around each egg in the ovary.)

Pituitary: Pituita is a mucous secretion; the Greeks thought the pituitary gland secreted mucus into the nose.

Luteinizing: Luteus means yellow, the color of the corpus luteum, a progesterone-secreting structure left after the egg is released into the Fallopian tube.

Prolactin: *Pro*motes *lac*tation (secretion of milk).

Milk Production: Prolactin's role in males is still unsolved.

Oxytocin: Oxy – rapid, tocin – birth.

Antidiuretic Hormone (ADH): A diuretic is anything that stimulates urine production. The reason you urinate so much at bars is that alcohol inhibits the release of antidiuretic hormone. Another name for antidiuretic hormone is vasopressin because antidiuretic hormone also constricts blood vessels.

Thyroid: A shield. The old Greek war shields were notched at the top to allow for the chin, a shape resembling the thyroid gland.

Parathyroid: Para means next to. The parathyroid glands are actually embedded within the thyroid gland.

Raises Calcium Level: By dissolving the body's great reservoir of calcium: bone. Parathormone also increases the blood calcium by improving calcium absorption from the gut and by impairing calcium excretion from the kidneys. Another hormone, calcitonin (secreted by C cells also embedded in the thyroid), plays an ill- defined role in *lowering* blood calcium.[5]

This hormone:	Secreted by this endocrine gland:	Performs this function:
Cortisol	Adrenal Cortex*	Regulates the balance of fat, protein, and carbohydrates* in every cell of the body. Also inhibits inflammation*.
Aldosterone	Adrenal Cortex	Regulates the balance of sodium*, potassium, water, and acid in the blood. Works via the kidney.
Epinephrine*	Adrenal Medulla*	Prepares the body for stress by speeding up the heart, raising the blood pressure, dilating the bronchial tubes*, dilating the pupils*, heightening vigilance, raising the blood sugar, and mobilizing fat for additional energy.

Adrenal Cortex: Ad (to) renal (kidney). Cortex means outer shell, rind.

Carbohydrates: The building blocks of carbohydrates are single sugar molecules called monosaccharides: glucose, galactose, and fructose (also mannose and xylose). Table sugar, sucrose, is a disaccharide of glucose-fructose linked together. Mother's milk contains another disaccharide, lactose: glucose-galactose. Starch, glycogen, and cellulose are simply longer, more complex chains of polysaccharides (poly = many).

Inflammation: Whenever something foreign penetrates the body's front line defenses in direct contact with the outside world—the skin, eye, mouth, gut, vagina—the reticuloendothelial system reacts with inflammation. First, blood vessels dilate (making the area *red* and *warm*) to bring in troops of white blood cells for the inflammatory attack. Fluid and white cells pouring through the dilated, porous blood vessels *swell* the area. The white cells release deadly chemicals that destroy the foreigner, and other chemicals that cause the *pain*.

Cortisol inhibits every step of the inflammatory process.[b] Corticosteroids—any drug that looks and acts like cortisol—are commonly injected into athletes' joints to reduce inflammatory pain.

Sodium: Sodium chloride (NaCl) is common table salt. Salt substitute is potassium chloride (KCl).

Epinephrine: The chemical secreted from the adrenal gland sitting epi (upon) nephrine (nephron, Greek for kidney). Another name for epinephrine is adrenalin.

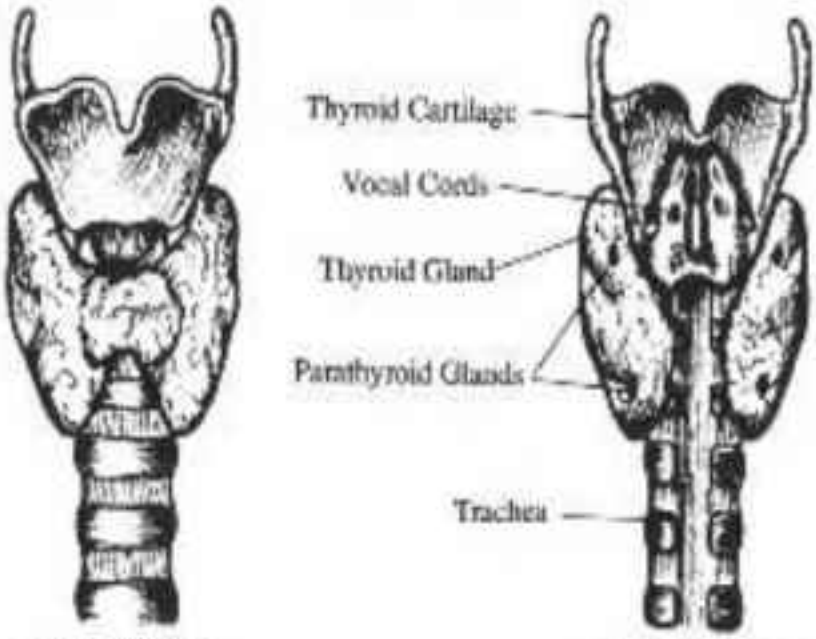
Medulla: Middle.

Bronchial Tubes: Tubes carrying air into the lungs.

Dilating the Pupils: To allow better night vision.

This hormone:	Secreted by this endocrine gland:	Performs this function:
Insulin*	Islets of Langerhans	Lowers blood sugar by facilitating glucose transport into all cells (except the brain which admits glucose freely).
Glucagon	Islets of Langerhans	Raises blood sugar*.
Estrogen/Testosterone*	Ovary/Testes	Makes you look like a man or woman.
Progesterone*	Ovary	During each menstrual cycle progesterone prepares the uterus for pregnancy.

The continuous question each endocrine gland must decide is *when* to secrete its hormone into the bloodstream. The **parathyroid gland** and **islets of Langerhans** do this without supervision by directly monitoring calcium and glucose levels in the blood. The parathyroid consists of four nubbins (two on each side of the trachea*) abutting the back of the thyroid gland; the islets of Langerhans consist of thousands of identical islands scattered throughout the pancreas. The parathyroids and islets of Langerhans are the only two glands which have independent control over their own secretions.



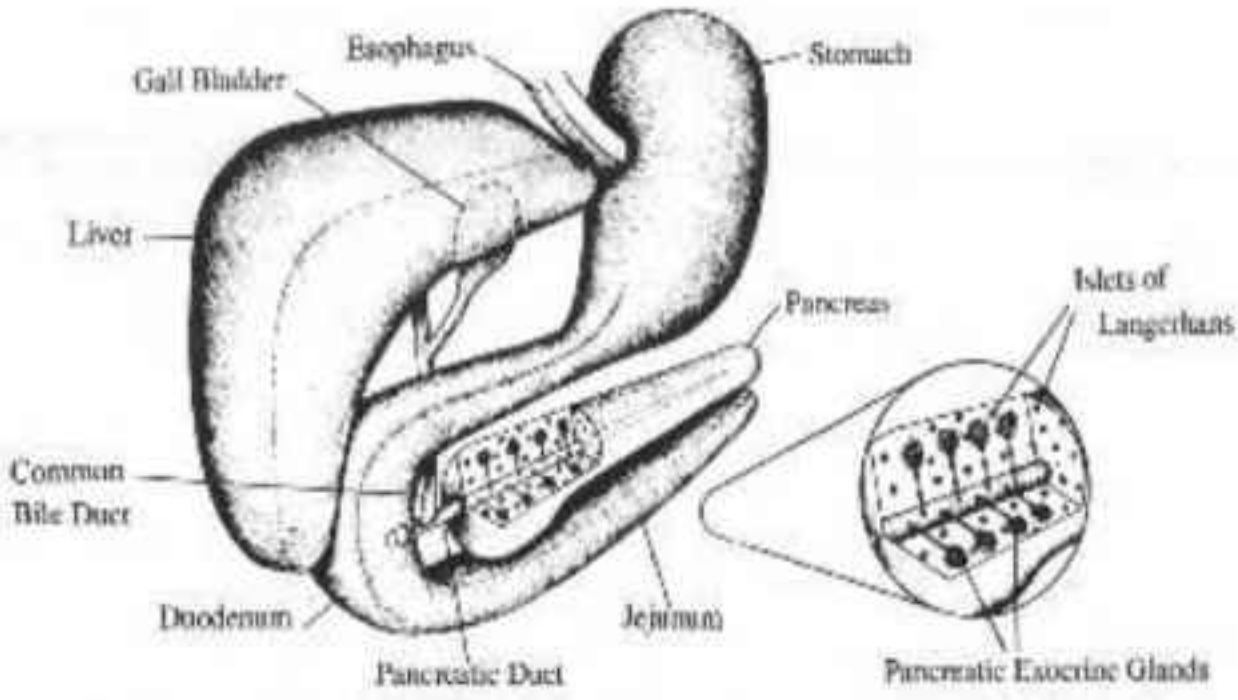
Insulin: Insula means island. Islet (as in Langerhans) is a small island.

Raises Blood Sugar: Like epinephrine, glucagon stimulates the liver to release its stores of glucose.[7]

Testosterone: Small amounts of testosterone are also made in the adrenal cortex.

Progesterone: Pro (before) gestation (growth of a fertilized egg in the uterus). After each mid-cycle ovulation, remnants of the ovum (egg) form into a corpus luteum which secretes progesterone for another two weeks to prepare the uterus for implantation by a fertilized ovum. If no implantation occurs, the prepared uterine wall is shed as menstruation (mensis – month).

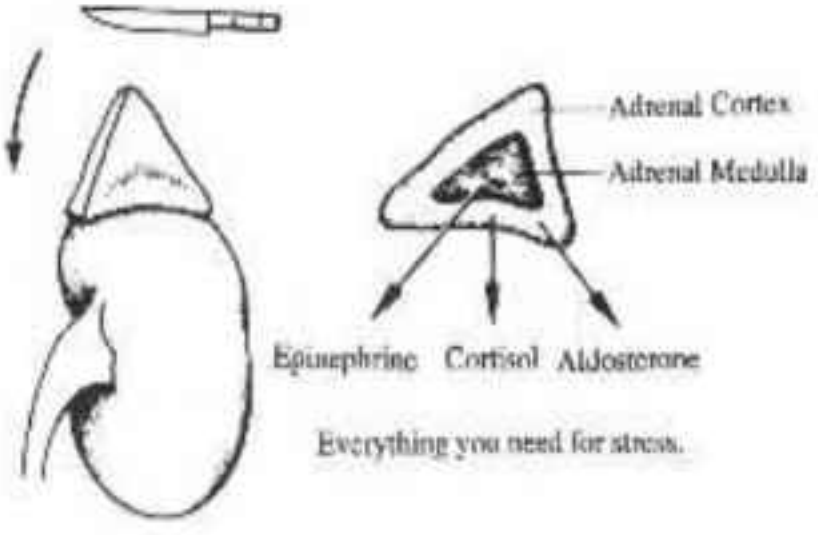
Trachea: Your windpipe. (Means 'rough' in Greek.)



The adrenal cortex secretes aldosterone in response to a complicated chain of instructions from the kidney whenever the kidney senses a drop in blood pressure.



The adrenal medulla releases epinephrine by direct stimulation from sympathetic nerves, part of the unconscious (autonomic) nervous system*.



Autonomic Nervous System: Controls the body's involuntary responses to environmental changes or internal emotions by blushing, sweating, having an erection, ejaculating, moving the gut, or by adjusting the heart rate, blood pressure, and pupillary size.

The **thyroid, gonads***, and cortisol-secreting cells in the **adrenal cortex** secrete their hormones on instructions from the pituitary, which sends specific 'MESSENGER' hormones—follicle stimulating hormone (FSH), interstitial* cell stimulating hormone (ICSH*), thyroid stimulating hormone (TSH), or adrenocortical stimulating hormone (ACTH)—into the bloodstream to dictate to the gonads, thyroid, or adrenal glands when to secrete additional hormone.

Besides instructing other endocrine glands to secrete their hormones, the pituitary also acts like any other peripheral endocrine gland, directly secreting hormones that perform primary endocrine functions. These 'PRIMARY' hormones are secreted from all three pituitary lobes*: anterior, intermediate, and posterior. The posterior lobe secretes antidiuretic hormone and oxytoxcin; the intermediate lobe, melanocyte* stimulating hormone; and the anterior lobe, follicle stimulating hormone (FSH), luteinizing hormone* (LH), prolactin, growth hormone, adrenocortical stimulating hormone, and thyroid stimulating hormone. All the anterior pituitary hormones together—primary and messenger—are colloquially known as 'FAT **PIG**': **F**SH, **A**CTH, **T**SH, **P**rolactin, **I**CSH, **G**H. (See chart page 14.)

How does the pituitary know when to secrete each of its nine different hormones? Alas, despite its supremacy in the endocrine system, the pituitary, like everyone, receives instructions from higher up through the soft underbelly of the brain—the hypothalamus.

The hypo(below)thalamus* is a mysterious jungle of impossibly sensitive cells which maintain the body's internal environment by regulating hunger, thirst, temperature, and growth, and by masterminding the response of the endocrine and autonomic nervous systems to emotions: fear, hate, love, and happiness, and also to stresses: bleeding, infection, and burns.

The hypothalamus controls the endocrine system by directing the pituitary in two ways: 1) via 'releasing factors' secreted into an ingeniously private bloodstream (the portal* hypophyseal* system) flowing non-stop to the *anterior* pituitary, and 2) via special nerves extending all the way from the hypothalamus directly into the *posterior* pituitary where these nerves release either oxytocin or antidiuretic hormone from their nerve tips right into the body's bloodstream.

Gonads: Ovaries and testes.

Interstitial: The interstitial space is the thin no-man's-land between cells.

ICSH: Interstitial Cell Stimulating Hormone in males is identical to Luteinizing Hormone (LH) in females.

Lobes: A lobe, like your earlobe, is any smooth, rounded section. A lobule is a small lobe.

Melanocyte: A cell in the skin that manufactures melanin, a black chemical which filters sunlight. Although it stands to reason that MSH should control skin pigmentation, Ostjes, Walton, and Ney maintain that there's not enough circulating MSH to account for melanocyte stimulation.[3] The true role of MSH is still unclear.

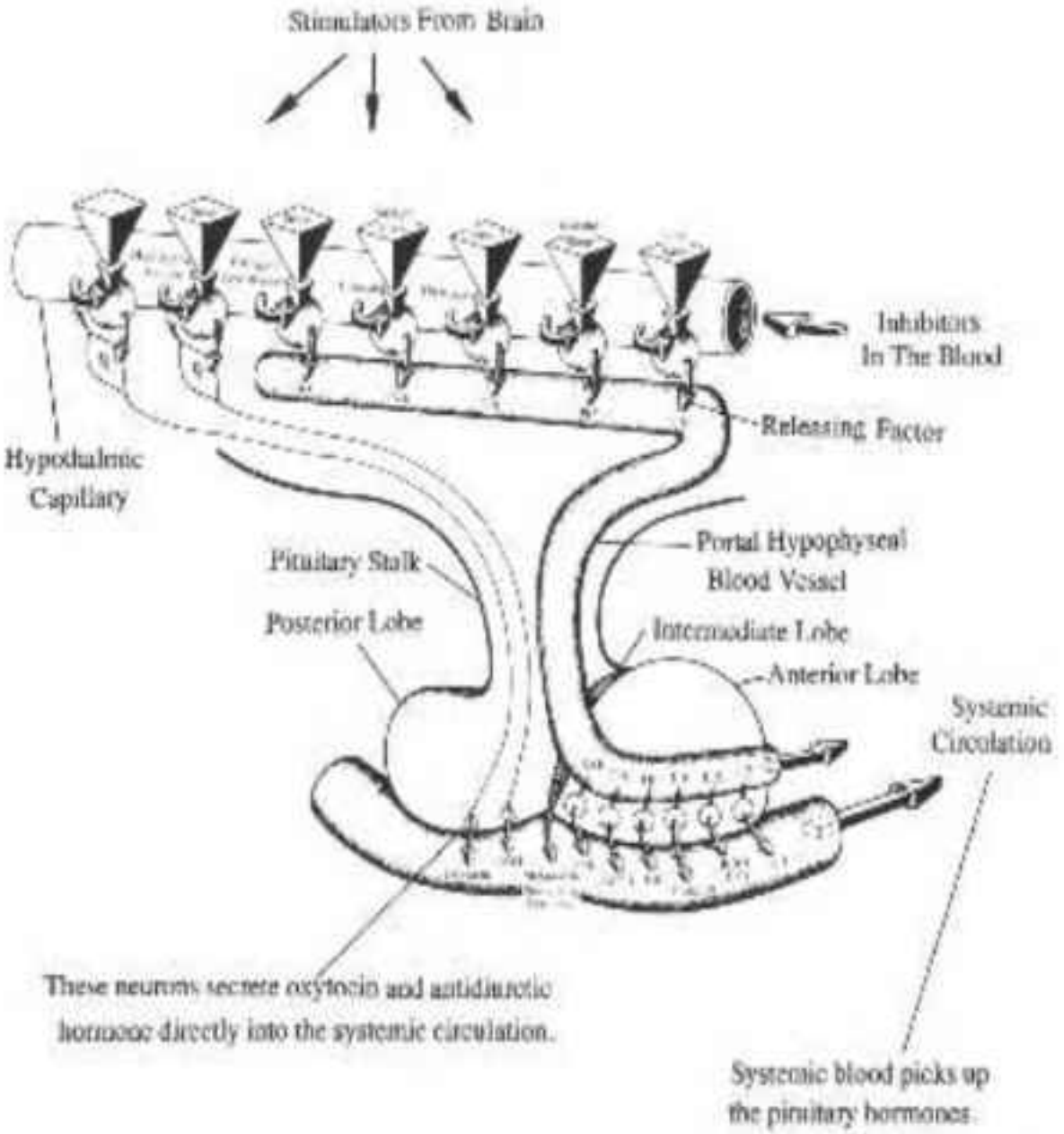
Luteinizing Hormone: FSH and LH pay dual roles. As messengers they instruct the testes to make testosterone, or the ovaries to make estrogen. As primary hormones they stimulate development of eggs and sperm.

Thalamus: Chamber, room. (Greek)

Portal: Gateway.

Hypophyseal: The hypophysis is another name for the pituitary: hypo(below) physis(growing).

PRIMARY FUNCTION:			MESSENGER FUNCTION:	
DO THIS	MAKES THIS ORGAN	THIS PITUITARY HORMONE	TELLS THIS ORGAN	TO MAKE THIS HORMONE
Mature the egg	Ovary (Follicle)	*F*SH (Follicle Stimulating Hormone)	Ovary (Follicle)	Estrogen
Mature the sperm	Testes			
		*A*CTH (Adrenocortical Stimulating Hormone)	Adrenal Cortex	Cortisol, some Aldosterone
		*T*SH (Thyroid Stimulating Hormone)	Thyroid	Thyroxine
Synthesize Milk	Breast	*P*rolactin		
Ovulate	Ovary (Follicle)	*I*CSH (Interstitial Cell Stimulating Hormone in males; Luteinizing Hormone in females)	Ovary (Corpus Luteum) Testes (Interstitial Cell)	Progesterone Testosterone
Grow	Body	*G*H (Growth Hormone)	← Anterior Lobe	
Conserve Water	Kidney (Distal Tubule)	Antidiuretic Hormone	← Posterior Lobe	
Release Milk	Breast	Oxytocin		
Darken Skin	Skin Melanocyte	Melanocyte Stimulating Hormone	← Intermediate Lobe	

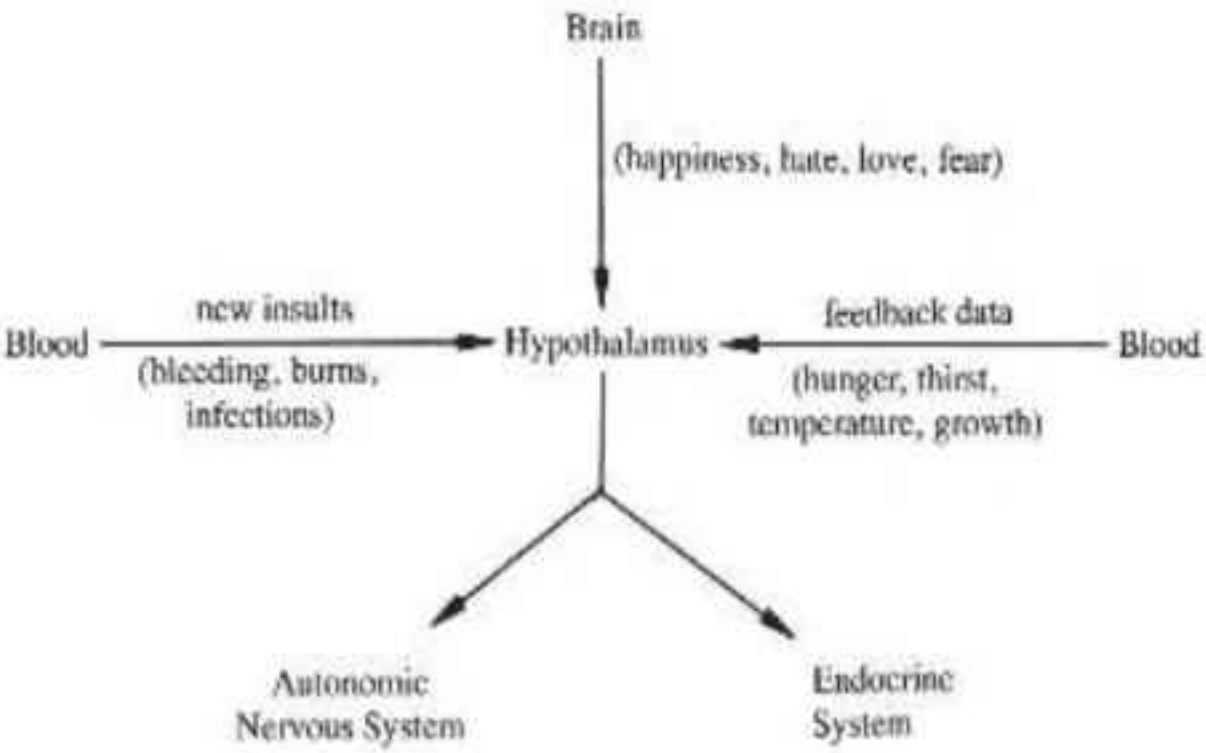


Below are the hypothalamic releasing factors secreted into portal hypophyseal blood vessels to instruct the *anterior* pituitary:[9]

This releasing factor*:	Does this in the pituitary:
LHRH (Luteinizing Hormone Releasing Hormone)	Stimulates FSH *and* LH (ICSH) release
CRF (Corticotropin Releasing Factor)	Stimulates ACTH release
TRH (Thyroid Releasing Hormone)	Stimulates TSH release
PIF (Prolactin Inhibiting Factor)	*Inhibits* Prolactin release
GRF (Growth Hormone Releasing Hormone)	Stimulates GH release

Releasing Factor: More than likely there's an inhibitory factor for every releasing factor, though this has only been confirmed for prolactin and growth hormone.

If the endocrine organs (except for the parathyroid and islets of Langerhans) are governed by the pituitary, and the pituitary is governed by the hypothalamus, what governs the hypothalamus? The hypothalamus *does* reign over the endocrine system by monitoring the blood's osmolarity* and the blood levels of cortisol, thyroxine, estrogen, testosterone, and growth hormone. But before sending its releasing hormones into the portal hypophyseal system, the hypothalamus also takes into consideration all sorts of other internal and external stimuli being experienced by the brain, like fear, anger, sadness, love, happiness, sexual arousal, daylight, suckling, impending childbirth . . . and the list goes on.



RESPIRATORY

Air inhaled through the nose is heated and moisturized by turbinates* in the nasopharynx*. Air is then sucked across the pharynx, past an open epiglottis* and larynx (Adam's apple), down the trachea (windpipe) into bronchi and bronchioles, finally terminating in alveoli* where oxygen diffuses into the bloodstream.

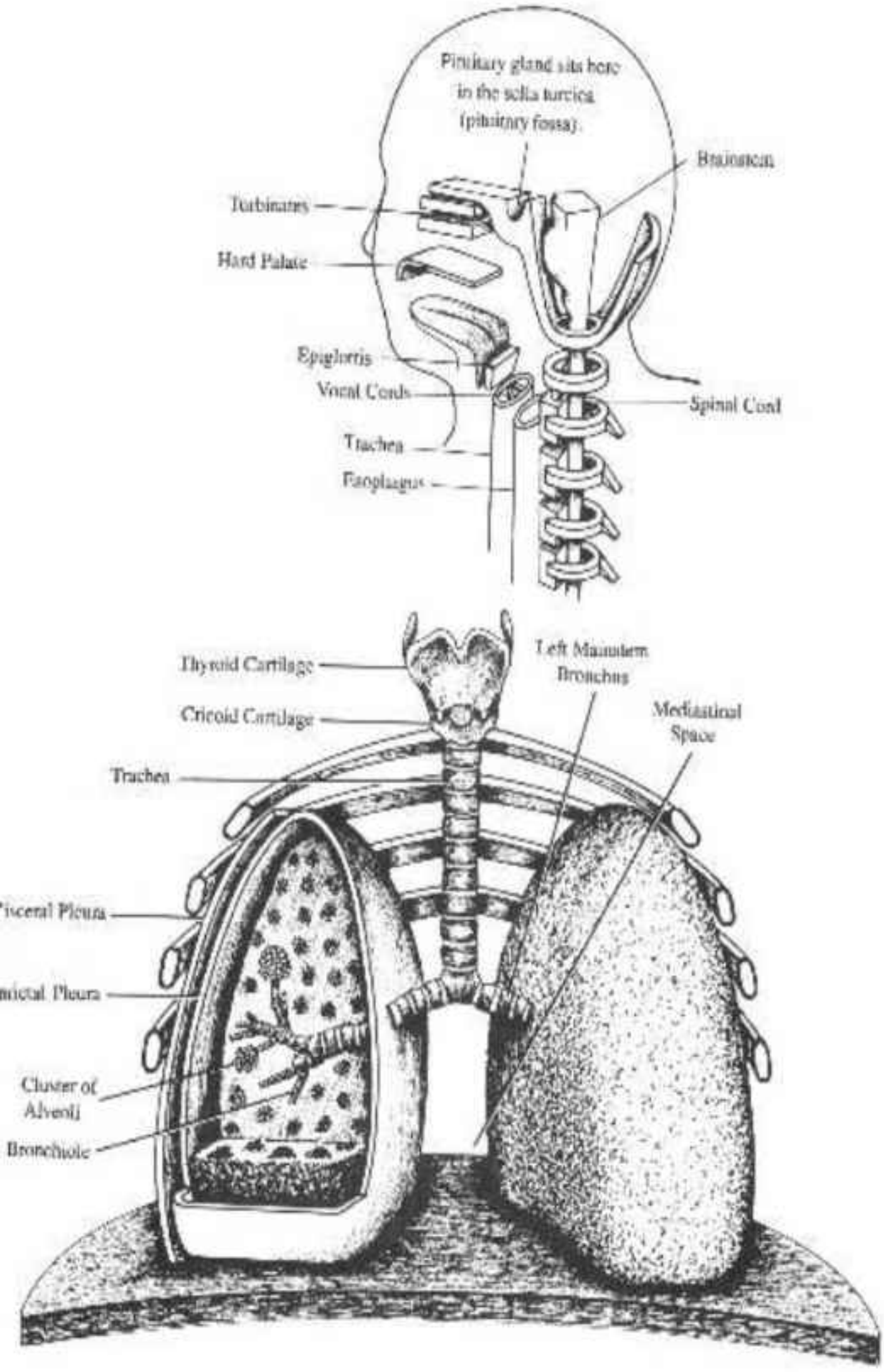
Osmolarity: The number of molecules—sodium, potassium, chloride, glucose, etc.—dissolved in a given volume (usually 100cc) of blood. If the blood is too concentrated, the hypothalamus sends antidiuretic hormone to the kidneys to retain water.

Turbinates: Like a turbine engine, the nasal turbinates spin inhaled air to thrust dust particles against the sticky nasal mucosa lining the nasopharynx. Mucosa is that wonderfully soft, warm, moist, pink lining of the mouth, nose, gut, eye, vagina, and urethra (urinary duct from the bladder to the outside world).

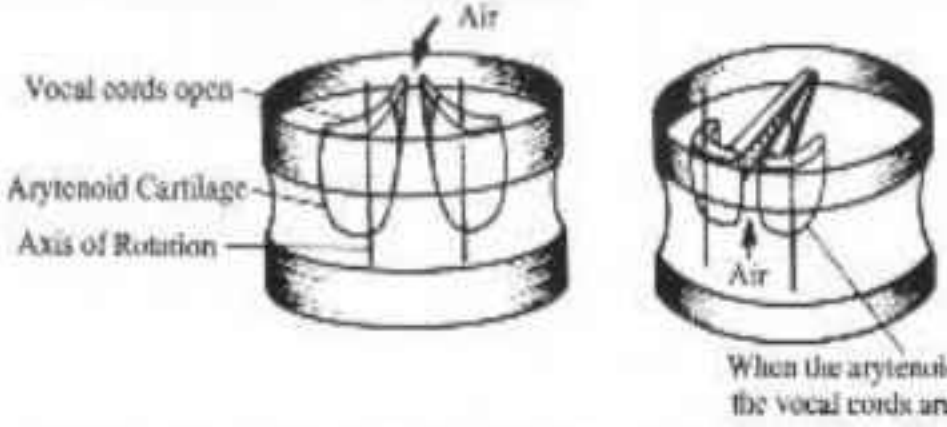
Nasopharynx: Naso (nose) pharynx (throat)

Epiglottis: Epi (above) glottis (entrance to the trachea)

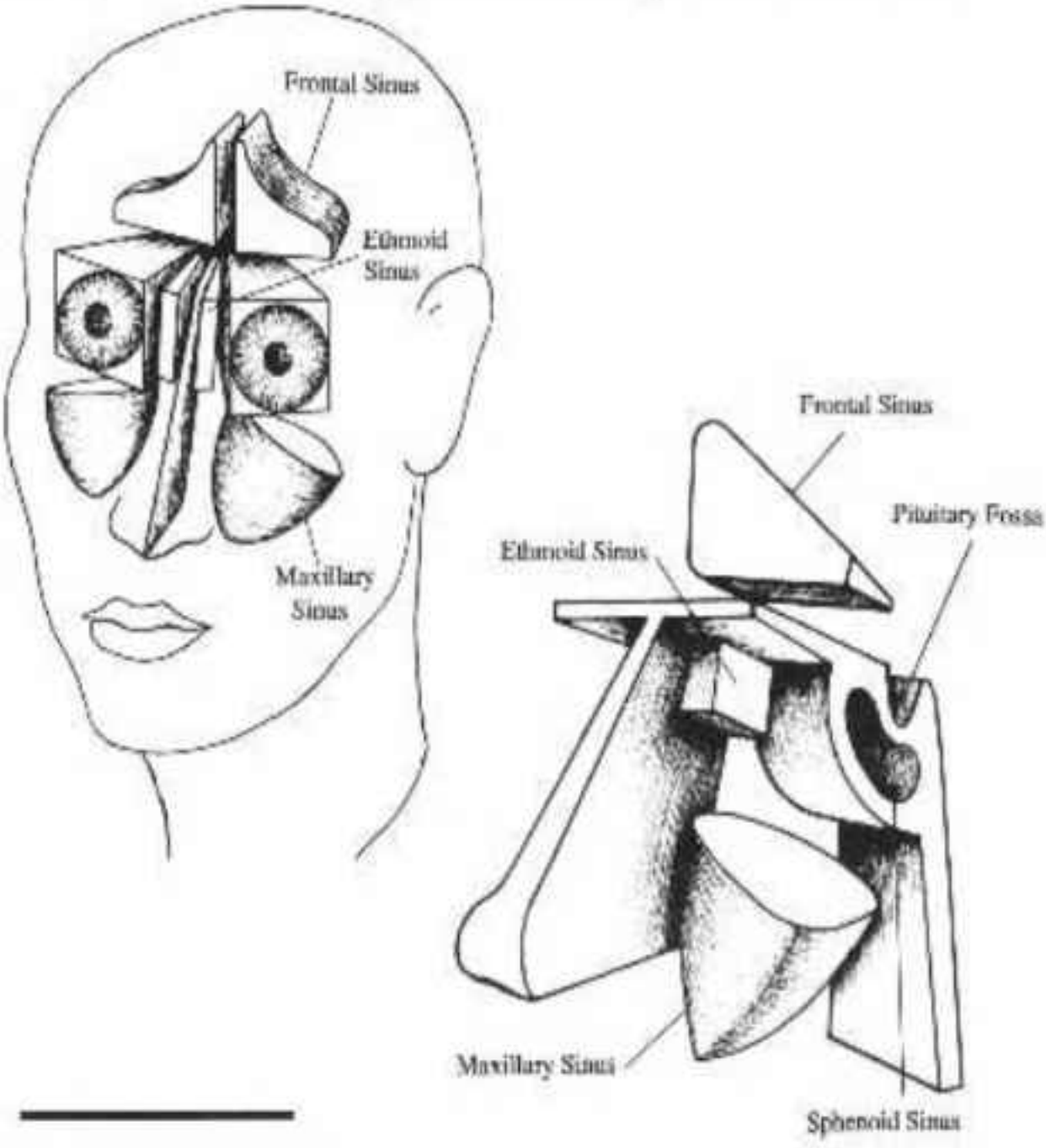
Alveoli: Alveus is Latin for hollow. Alveolus is a small hollow structure.


Pituitary gland sits here
in the sella turcica
(pituitary fossa).
Brainstem
Turbinates
Hard Palate
Epiglottis
Vocal Cords
Spinal Cord
Trachea
Esophagus
Thyroid Cartilage
Left Mainstem
Bronchus
Cricoid Cartilage
Mediastinal
Space
Trachea
Visceral Pleura
Parietal Pleura
Cluster of
Alveoli
Bronchiole

To speak, two vocal cords in the larynx jut together, occluding the entire trachea except for a slit between them. Air rushing upward through this slit vibrates the cords, and the vibrations are articulated into speech by the pharynx, nasopharynx, tongue, cheeks, and lips.



Connected to the nasopharynx and pharynx are hollow chambers within the facial bones, called sinuses*, which lighten the skull and help mold our facial features.



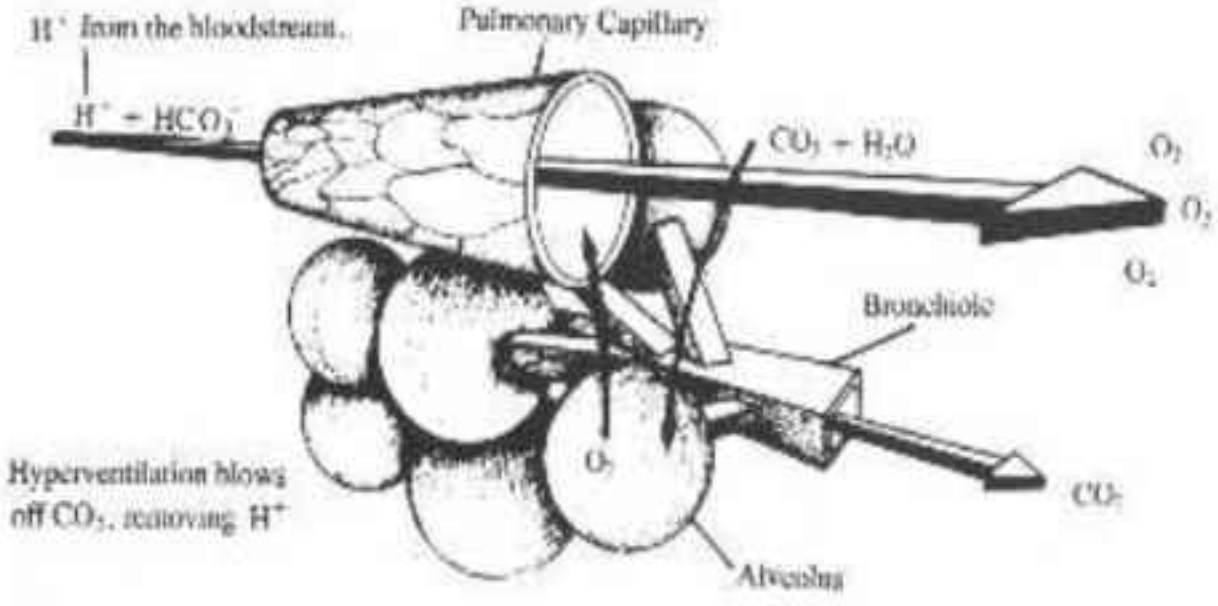
Sinus: A cavity or hollow space.

Lungs perform three functions: oxygenate the blood, rid the body of carbon dioxide (CO_2), and together with the kidneys help regulate acid-base balance (pH) of the blood. Normal oxygen pressure in arterial blood, written pO_2 (p=pressure, O_2=oxygen), is between 85 and 100 mm*. Normal arterial pCO_2 is 40 mm. Normal pH is 7.40.

Since CO_2 diffuses extremely rapidly from the blood into alveoli, all that's needed to rid the body of CO_2 is to move a little air in and out of the lungs. Therefore, a rise in arterial pCO_2 above 40 mm is a sensitive indicator that the patient is physically not moving adequate air in and out of the lungs. As excess CO_2 accumulates in the blood, the CO_2 combines with water to form H_2CO_3 which ionizes into H^+ and HCO_3^-*. The acidic hydrogen ion lowers the blood pH from its normal 7.40*, creating a 'respiratory acidosis.'

Hyperventilation, in contrast, rids the body of CO_2 which drives up the blood pH (above 7.40), called 'respiratory alkalosis.' This time the kidneys respond by dumping bicarbonate into the urine to help lower the blood pH back to 7.40.

Any alteration of blood pH is strongly resisted by the body. Sensitive respiratory centers in the brainstem (the most primitive area of the brain) respond to this acid challenge by making you feel short of breath. The more breaths you take, the more CO_2 is removed from the blood restoring the blood to a normal pH. The kidneys also help rid the body of excess acid by conserving HCO_3^- to buffer the blood's excess acid.



100mm: Total atmospheric pressure at sea level is 760mm of mercury. Oxygen constitutes only 20%, nitrogen the other 80% (minus a bit for carbon dioxide, and water vapor). Though 20% of 760mm is 152mm, arterial pO_2 is only 100mm because the lungs do not completely empty with each breath. Instead, the lungs leave some 'old' air (pO_2 45mm)—called dead space—to mix with fresh incoming air, a design which keeps alveolar (and therefore arterial) pO_2 constant. If the lungs had two sets of bronchial tubes to segregate inhaled from exhaled air, arterial pO_2 would fluctuate too much during each breath (albeit reaching a higher peak pO_2).

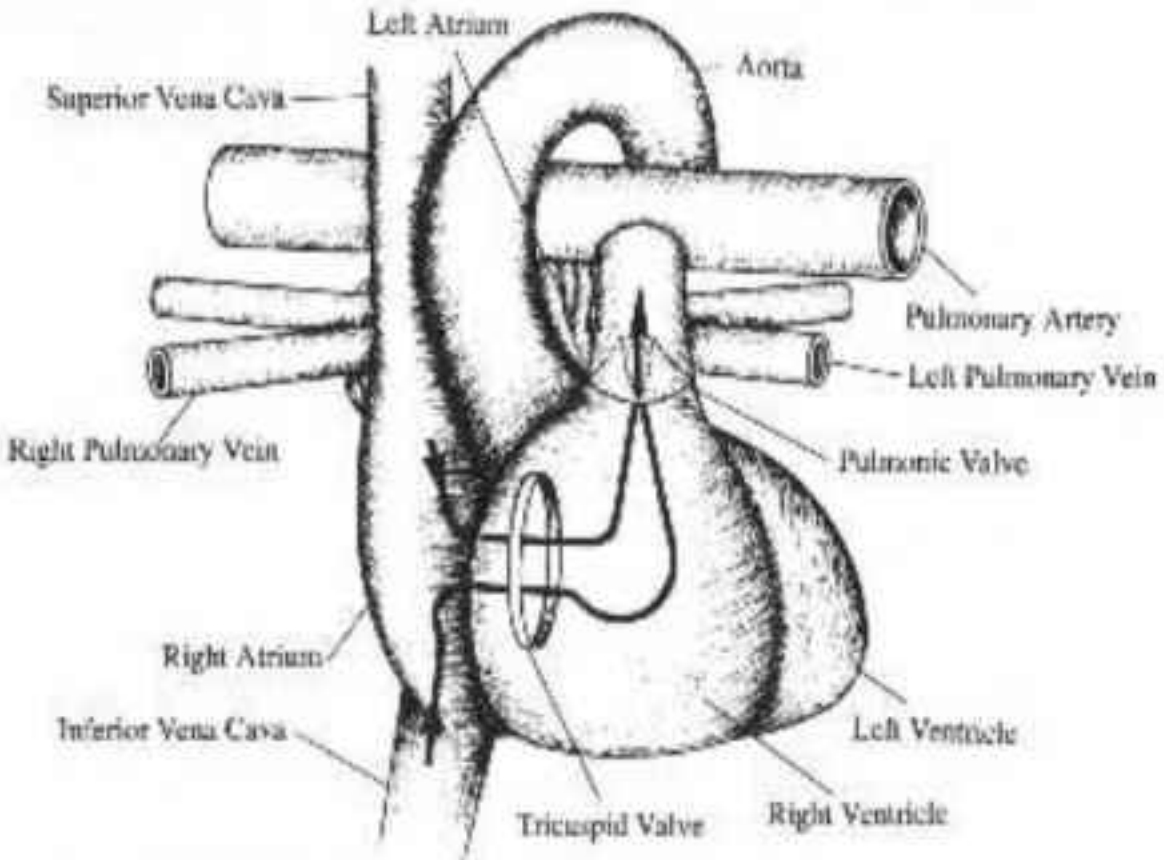
HCO_3: Bicarbonate ion. Sodium bicarbonate ($NaHCO_3$), baking soda, buffers excess stomach acid.

7.40: Even though each H^+ ion is electrically balanced by a negative HCO_3^- ion, the pH drops if H^+ ions are allowed to float free in the bloodstream. pH depends only on the H^+ ion concentration, not on the net electrical charge.

Life-threatening acidosis is below about 7.20. Below 6.90 you should be dead.

CARDIAC

Venous blood returning to the heart—via the superior vena cava from the upper torso and via the inferior vena cava from the lower torso—enters the heart through the right atrium*. As soon as the pulmonic valve closes, the tricuspid* valve opens to allow right atrial blood into the right ventricle. After diastole (ventricular filling) the ventricles contract, ejecting right ventricular blood across the pulmonic valve into the pulmonary artery (and simultaneously, left ventricular blood into the aorta).



After picking up oxygen in the lungs, right ventricular blood returns to the left atrium via the pulmonary veins. When the aortic valve closes after left ventricular contraction, left atrial blood plunges past the mitral* valve into the left ventricle at the same time that right atrial blood is filling the right ventricle. At the start of systole, the left ventricle begins contracting against a closed aortic valve; the amount of left ventricular pressure needed to open the aortic valve depends on both the aortic pressure* (hypertension makes the heart work harder) and the size of the aortic valve (a stenotic* aortic valve also makes the heart work harder).

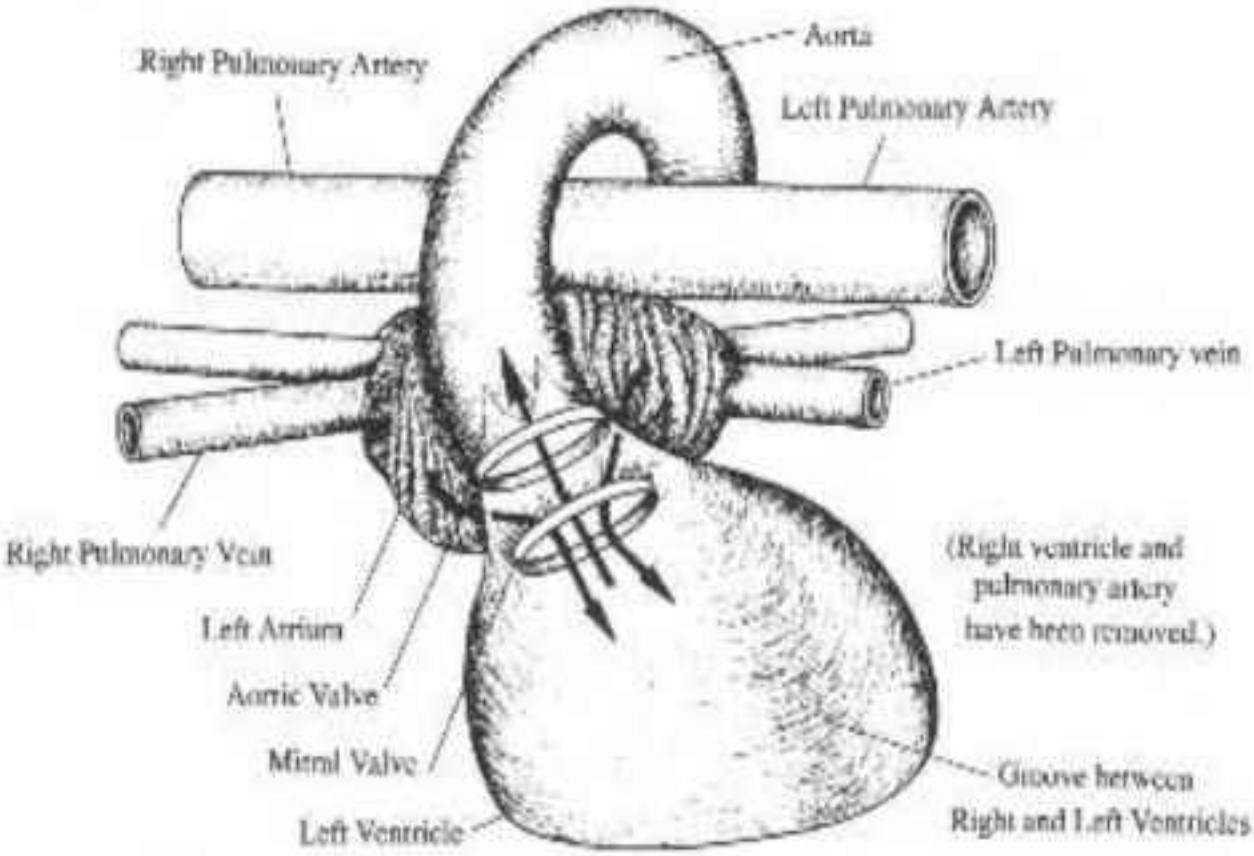
Atrium: A hall (Greek). The atria serve as reservoirs of blood to rapidly pack the ventricular pumping chambers during diastole.

Tricuspid: Though the aortic, pulmonic, and tricuspid valves all have three cusps, only the tricuspid got the name. Heart cusps work like a reed valve, maintaining forward flow by flopping together when blood tries to flow backwards, much like your lips do when you try to suck air into your mouth with your jaw shut.

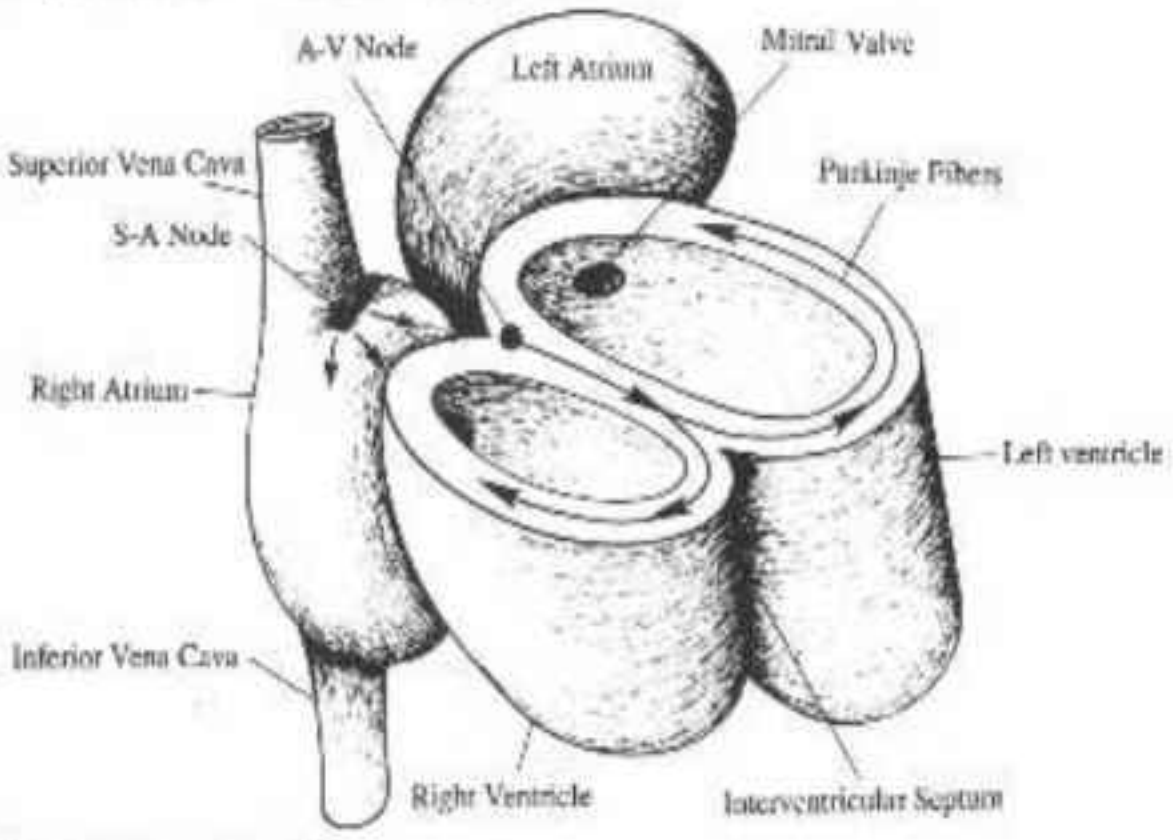
Mitral: A bicuspid valve named for its resemblance to a miter, the headdress worn by bishops.

Aortic Pressure: The left ventricle has a thicker wall than the right ventricle, because the left ventricle must pump against an aortic pressure of 120mm, while the right ventricle faces only 25mm of pressure in the pulmonary artery.

Stenotic: Narrowed (by scar tissue).



Contraction of the heart is initiated once a second by a jolt of electricity beginning in a special nubbin of right atrial tissue[9] called the sinoatrial (S-A) node. From here, an advancing front of electricity spreads out across both atria stimulating them to contract. This front converges on the atrioventricular (A-V) node situated on top of, and between, the two ventricles in the interventricular septum[10]. From the A-V node, electricity is rapidly shunted to both ventricles along a specialized bundle of electrically excitable fibers called Purkinje fibers.[11]



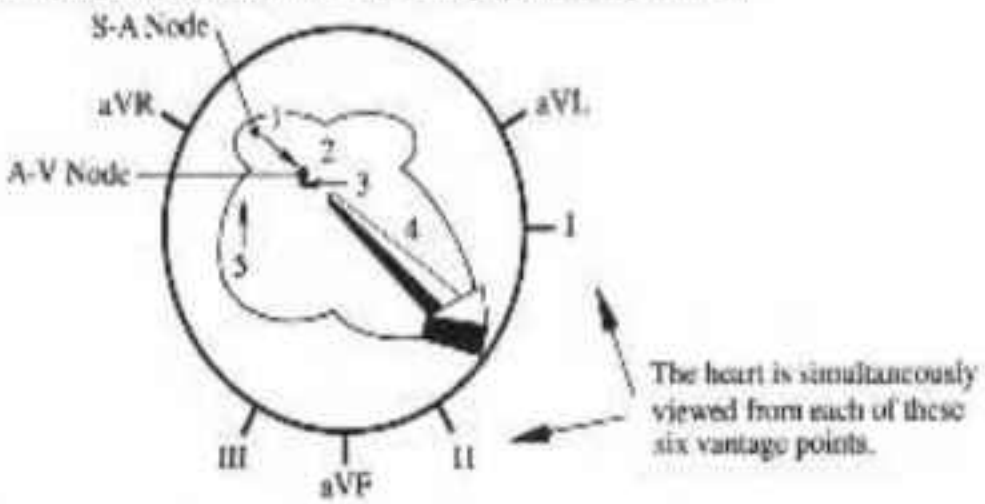
Tissue: A thin slice of any organ, thin like tissue paper.

Septum: A partition, like the nasal septum separating the two nostrils.

Disturbances of electrical conduction*—arrhythmias—occur for one of two reasons: either the conducting system is blocked, or it is usurped by a premature electrical impulse erupting from an area of (usually abnormal) heart muscle before the normal impulse arrives from the S-A or A-V node.

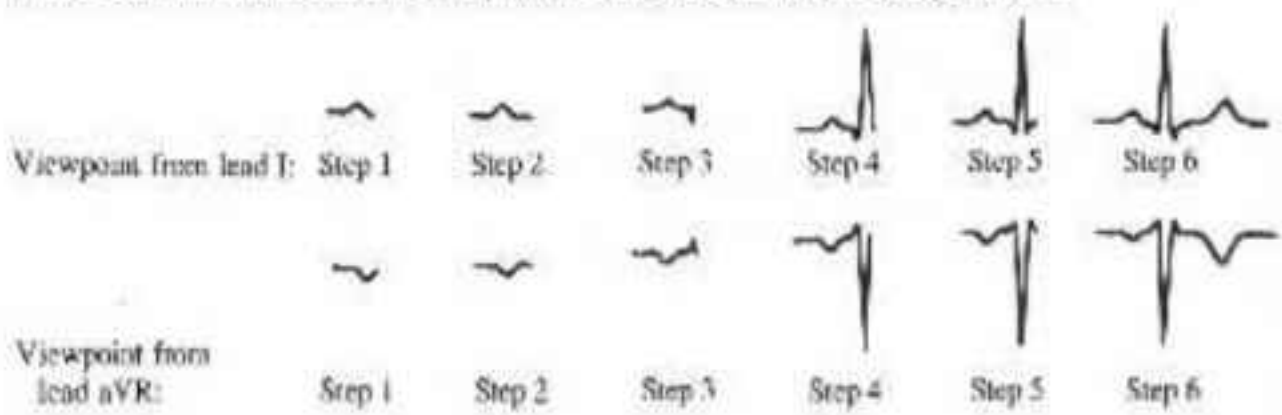
Disturbances of Electrical Conduction: An electrocardiogram (EKG) records the heart's electrical activity. Each heart beat requires six sequential electrical impulses. The direction of each electrical impulse is represented by a "vector" indicating the net direction and force of that electrical impulse (the longer the vector, the more electrical force). Electrodes are attached to the arms, legs, and chest wall to record these electrical vectors from varying vantage points. If the vector comes toward the sensing electrode, the recording pen on the EKG machine deflects upward. And conversely, when the vector is aimed away from the electrode, the pen deflects downward.

With just four electrodes—one on each limb—six vantage points are generated

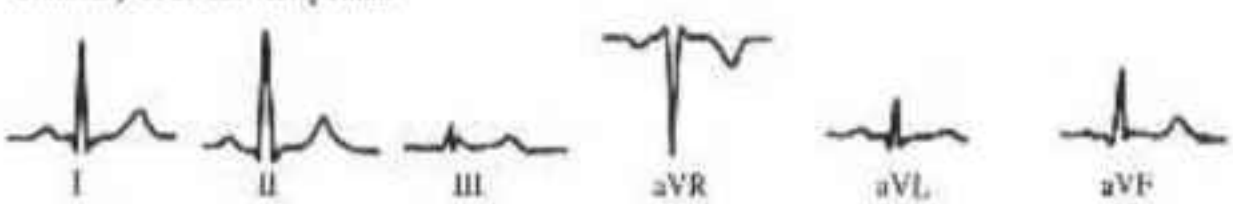


Step 1—S-A node discharges the atria (vector 1): P Wave
Step 2—A-V node discharges (no electrical movement, so no vector): P-R Interval
Step 3—Interventricular septum discharges (vector 3): Q Wave
Step 4—Purkinje system discharges (vector 4): R Wave
Step 5—Terminal twigs of the Purkinje system discharge (vector 5): S Wave
Step 6—Purkinje system repolarizes (recharges) along the same direction as vector 4: T Wave

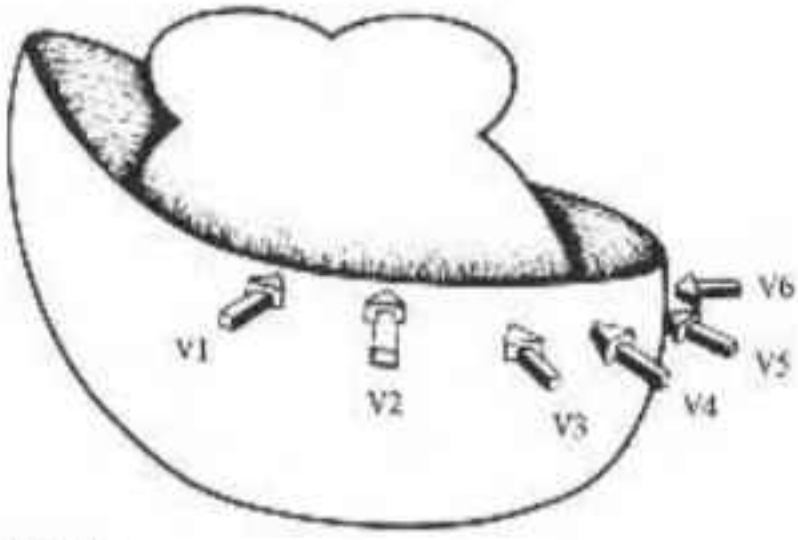
If the vector is aimed toward the viewpoint, the pen goes up; away, the pen goes down.



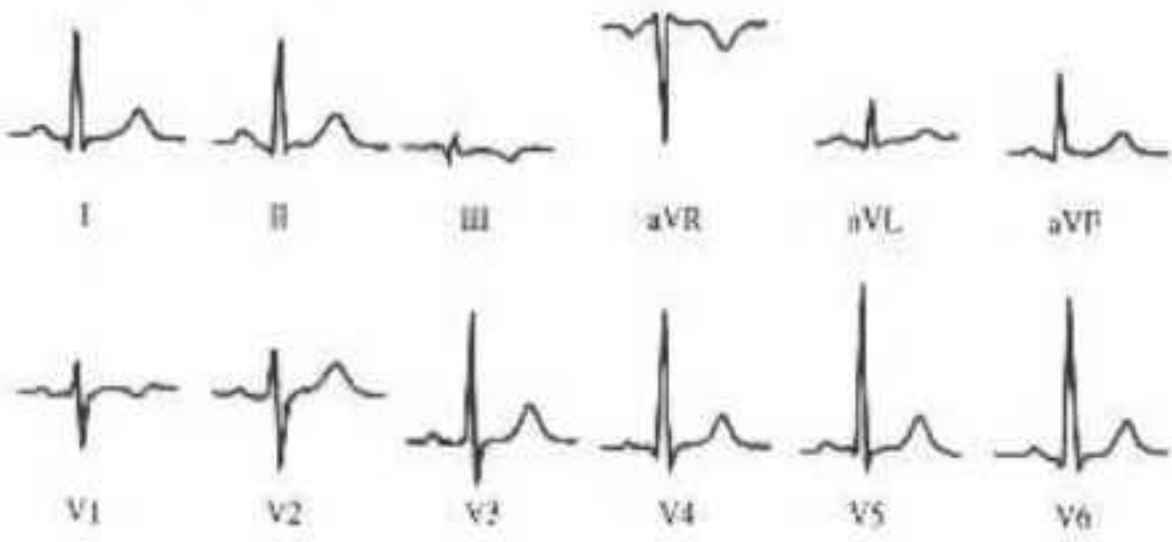
Summary of all six viewpoints:



Six additional vantage points are provided by six electrodes placed across the chest wall—the 'V' leads:

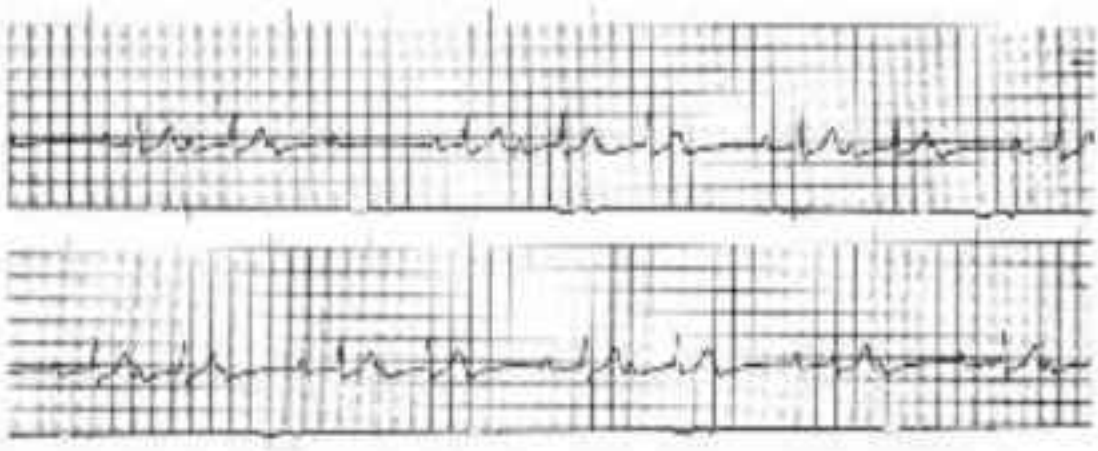


A normal EKG looks like this:



Example of an arrhythmia:

Wenckebach (Type II) Second Degree Heart Block:



Note that each PR interval lengthens until the P wave is blocked. The cycle, called Wenckebach, then repeats itself.

GASTROINTESTINAL (GI)

Food consists of carbohydrates, lipids (fats), and proteins. Supplies of carbohydrate—enough to last two or three days—are stored as glycogen in the liver and muscle, but for longer periods of starvation, the body must rely on fat* and protein (mainly from muscle). Proteins are huge molecules built from individual amino acids* linked together. There are about twenty amino acids, each with a different size and shape, and each carrying a positive, a negative, or no electrical charge. These electrical charges attract and repel each other enough to curl the protein up into a specific configuration*, the exact configuration dependent on the sequence of amino acids. Through trial and error over eons of time, Mother Nature has quietly honed each protein to the best possible shape for its specific job. If the protein triggers a cell to action, it's a hormone (insulin is a good example). If a protein hastens a chemical reaction, it's an enzyme*. If it latches onto a foreign protein, it's an antibody. The remainder are carrier* or structural proteins.

Carbohydrates are the first of the three foodstuffs to be attacked during digestion—by amylase*, an enzyme secreted into the mouth from the parotid* and other salivary glands.

Fat: Fat was a critically important evolutionary innovation because it compacted energy into a small volume, thereby allowing animals a mobile existence not enjoyed by plants which store their energy as cellulose, a bulky carbohydrate.

Amino Acids: Proteins can be converted into glucose or fat, but neither fat nor glucose can be converted into protein because man is incapable of synthesizing (from glucose, fat, or other amino acids) certain 'essential' amino acids, ones that must therefore be derived from dietary protein.[1] Plants can synthesize every amino acid, but in order to do so, they must consume nitrogen, the element that helps distinguish amino acids from carbohydrates and lipids. There is some nitrogen in the soil, but there's a lot more in the air (80% of air is nitrogen). Unfortunately, only a few 'legume' plants can fix (incorporate) nitrogen from the air; peas, beans, and lentils are examples. Most plants must be supplemented with nitrogenous fertilizers prepared by combining hydrogen with nitrogen in the air, known as the Haber process. It was this commercial breakthrough that allowed Germany to sustain World War I without outside sources of nitrogen for fertilizers or explosives. Current genetic splicing research may soon extend nitrogen fixing prowess to all vegetable plants.

Configuration: Unraveling a protein molecule—a process called denaturation—renders a protein useless. A good example is frying an egg, which transforms translucent egg white (a protein called albumin) into opaque, denatured protein. Whipping egg whites also denatures egg albumin. Copper stabilizes the denatured albumin, preventing the foam from running—which is why you should prepare meringue in copper bowls.[2]

Enzyme: An enzyme hastens a chemical reaction by embracing a molecule and then either tearing it apart or reassembling it into another molecule. To use an analogy, a mother must cradle her child in different positions for drinking, feeding, soothing, etc. If you had a thousand mothers whose arms were permanently fixed in rigid positions so that they could only perform one task, you'd have a thousand equivalents of enzymes, each with a fixed configuration for a single function. To handle the body's thousand or more chemical reactions, there are about as many enzymes.

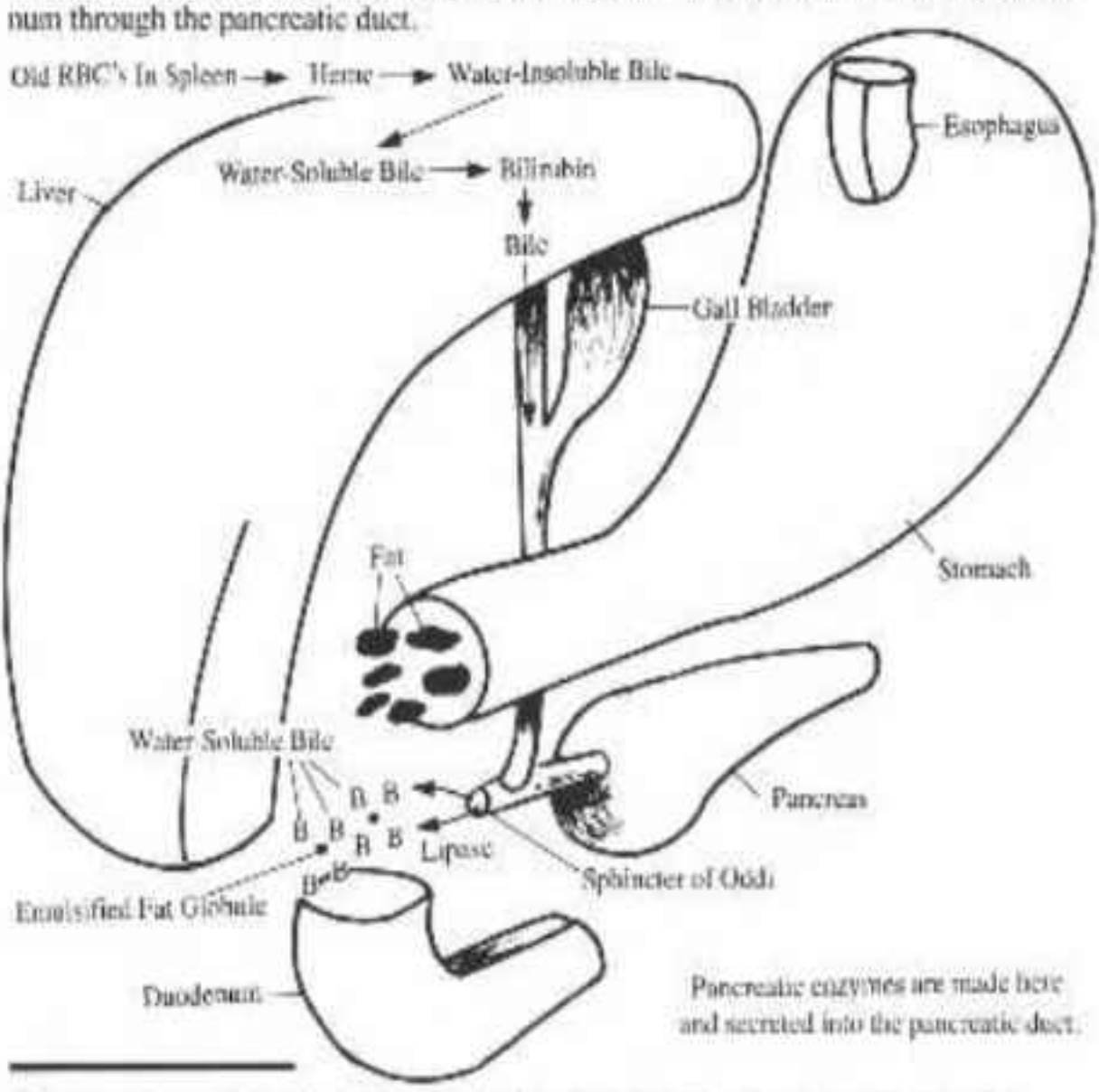
Carrier: All sorts of things are carried by proteins in the blood: hormones, water-insoluble lipids, oxygen, drugs. Inside cells, too, proteins shuttle molecules about.

Amylase: It's puzzling that man never evolved the enzyme for digesting nature's most abundant carbohydrate: cellulose (in plants). The enzyme is found in lowly bacteria living symbiotically within the intestines of termites and cows.

Parotid: Para (next to) otid (ear). The salivary gland located just above the angle of the jaw.

Skirting by the closed epiglottis (which prevents anything but air from entering the trachea), food is propelled by peristalsis* through the esophagus into the stomach where acid* and enzymes secreted by the stomach begin protein digestion. Another crucial protein secreted by the stomach is intrinsic factor which attaches to vitamin B12, permitting B12 absorption later through the ileum*.

After gastric (stomach) digestion*, food is squirted through the pyloric sphincter* into the duodenum*, the first part of the small intestine. Proteins, carbohydrates, and fats are furiously attacked here by potent pancreatic enzymes which enter the duodenum through the pancreatic duct.



Peristalsis: Coordinated waves of muscular contraction which propel food along the intestines.

Acid: Parietal cells in the stomach wall secrete hydrochloric acid, while chief cells secrete pepsin, the main gastric enzyme. Pepsin needs an acid environment to function properly. When food is squirted into the alkaline duodenum, pepsin is inactivated, and alkaline-activated pancreatic enzymes take over. The stomach also secretes a thick mucous coating to protect itself from ulceration by its own hydrochloric acid and pepsin.

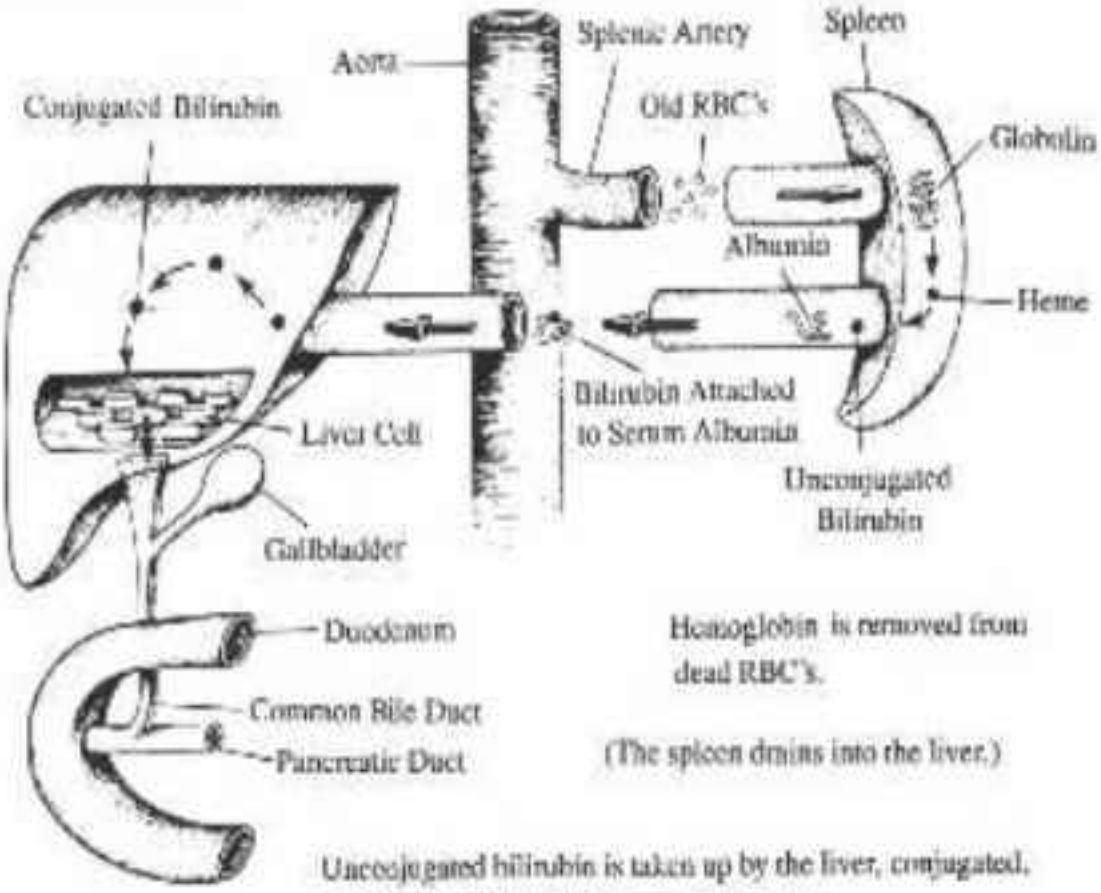
Ileum: Originally, ileum meant twisted intestine, a common cause of intestinal obstruction. Over the years ileum was used to refer to the intestine itself.[1]

Digestion: Proteins are digested into fragments called peptides, named after the enzyme, pepsin. A polypeptide, then, is simply any protein molecule.

Pyloric Sphincter: Pyel (gate) ouros (guard). A sphincter is a muscle that opens and closes an opening, like the anal sphincter.

Duodenum: Means twelve, twelve finger-breadths long.

In order to be digested, fats, being water insoluble, must first be emulsified* into tiny droplets by bile, a greenish goop concocted from deceased red blood cells. When old red blood cells die, the heme part of hemoglobin is metabolized* in the bloodstream to bilirubin, a water-insoluble bile which the liver takes up, converts to a water-soluble form, and secretes into the gall bladder for storage. Fats entering the duodenum stimulate the gall bladder to discharge bile down the bile duct which connects up to the pancreatic duct* just before entering the duodenum. Emulsified fats are then split apart in the jejunem* and ileum by the pancreatic enzyme, lipase, for absorption into the body.



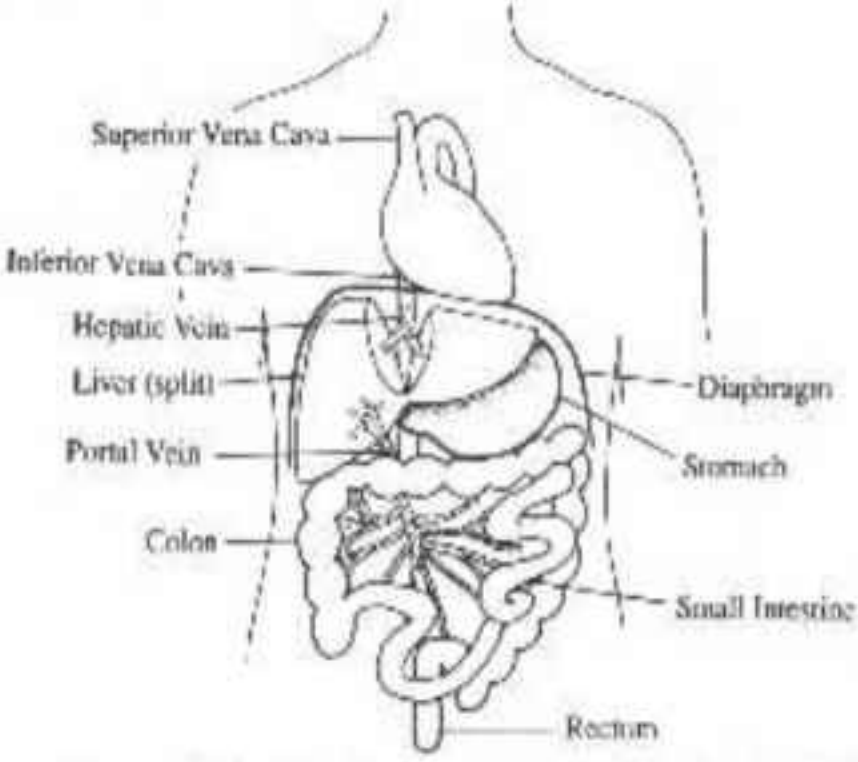
Emulsified: Being both water *and* lipid soluble, emulsifiers can surround individual lipid-soluble molecules and suspend them in water. Soap is a typical emulsifier; it emulsifies water-insoluble grease.

Metabolized: The body metabolizes a 'precursor' molecule by breaking it apart, deleting a section, or adding another small molecule to it; the new compound is called a 'metabolite.' The hundreds of metabolic pathways for proteins, carbohydrates, fats, hormones, and neurotransmitters are simply a chemical blueprint of the body's operating and maintenance systems. To 'catabolize' a molecule is to break it apart specifically for energy use during periods of starvation. Conversely, to 'anabolize' is to construct molecules during periods of abundance. Athletes sometimes use anabolic hormones to build up their muscles.

Pancreatic duct: In sharing the same duct with the biliary system, the pancreas is vulnerable to damage should a gall stone lodge at the sphincter of Oddi. After recognizing that such gall stones primarily damage the exocrine pancreas and not the islets of Langerhans, Banting was able for the first time (1920) to isolate insulin by tying off the pancreatic ducts of dogs. Ironically, Charles Best, the medical student in Dr. MacLeod's lab who aided Banting in Dr. MacLeod's absence (and skepticism), did not share the Nobel prize with Banting; Dr. MacLeod did.

Jejunum: Empty, because it was always empty at autopsy. Together, the duodenum, jejunum, and ileum comprise the small intestine.

Digested food is absorbed through the intestinal wall into intestinal veins and then immediately drained via the portal venous system* into the liver to detoxify poisons, take up amino acids for protein synthesis, restructure lipids into cholesterol and triglycerides*, and store glucose in the form of glycogen. Later, if the blood sugar falls below normal (60–100 mg%*), the liver can break down its glycogen into glucose again for release into the bloodstream.



Most of the proteins synthesized by the liver are destined for life in the bloodstream to perform the following important jobs: prevent water from leaking out of the bloodstream (by oncotically† 'soaking up' the water), clot the blood, and carry hormones, metabolites, and lipids. Lipoproteins* carry triglycerides throughout the body for immediate energy production, or else to fat cells for storage. Cholesterol is also delivered throughout the body; not only is cholesterol an integral part of every cell wall, but it also serves as the precursor for the synthesis of adrenal and gonadal hormones.

Mg%: 1 cubic centimeter (1 cc) is the same as 1 milliliter (1 ml). If a cubic centimeter were filled with water, it would weigh 1 gram (1 gm). 1/1000 of this is 1 milligram (1 mg). Mg % means milligrams per 100cc.

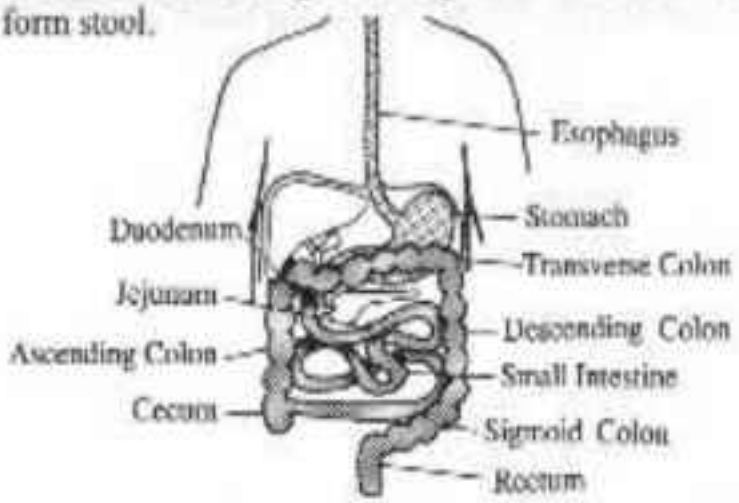
Portal Venous System: Drains all the blood from the intestines, spleen, pancreas, and gallbladder to the liver. Once through the liver, portal blood joins the inferior vena cava en route to the heart.

Cholesterol and Triglycerides: Both are lipids. Cholesterol is a four ring structure, triglyceride a long chain fatty acid.

Oncotically: Since proteins cannot escape the vascular tree, they act like miniature sponges, analogous to reconstituting a dried bean by soaking it in water.

Lipoproteins: Lipid-carrying proteins (lipoproteins) are another way, besides emulsification, to suspend lipids in aqueous solution. Cholesterol-carrying 'low density' lipoproteins—ones which sink slowly during high speed centrifugation—are a risk factor for atherosclerosis, while high density lipoproteins appear to protect against atherosclerosis. (Atherosclerosis, 'hardening of the arteries', is a disease in which arteries silt up with chips of cholesterol, calcium, and blood clots.)

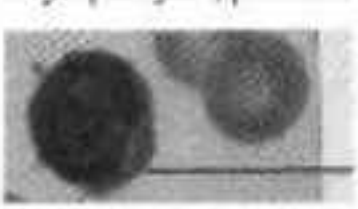
From the terminal ileum, where the vitamin B12/intrinsic- factor complex is absorbed, food passes through an ileocecal valve into the cecum*, the initial part of the large intestine (colon*). As this undigestible, bile-stained slurry travels the ascending, transverse, descending, and sigmoid* limbs of the colon, water is extracted* to form stool.



RETICULOENDOTHELIAL (or RE)

The reticuloendothelial system is the body's surveillance system, guarding against hostile organisms that might find the body a comfortable place to multiply. Which means that the reticuloendothelial system must be able to recognize as foreign such diverse threats as viruses, bacteria, fungi, protozoa, even tumor cells and slivers of wood, while accepting as friendly every cell normally found in that person. The reticuloendothelial system is so sensitive that it can even distinguish very subtle differences between its own organs and transplanted ones. How the body for over ninety years distinguishes between self and not-self is a mystery, yielding to immunologic research, but still a mystery.[1]

The body defends itself with two major weapons: antibodies and white cells. The body uses two different types of white cells in its defense: polymorphonuclear leukocytes* ("PMN's" or "polys" for short) and mononuclear cells ("monos"). There are, in turn, two different types of monos depending on their site of origin: those derived from the thymus gland*—T lymphocytes—and those derived from the bone marrow—B lymphocytes, plasma cells, and macrophages.





Cecum: Blind (i.e., dead end).

Colon: The colon is the lower GI system; the stomach and small intestine (duodenum, jejunum, and ileum) are the upper GI system.

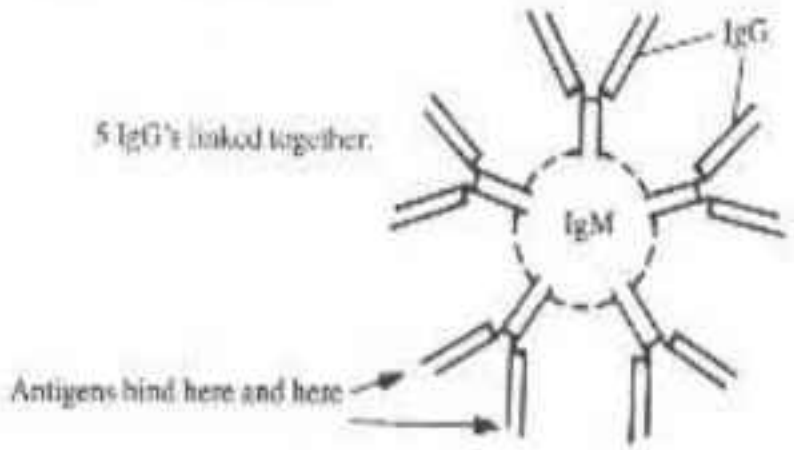
Sigmoid: Sigma is the Greek letter S, the shape of the sigmoid colon.

Water is Extracted: Many laxatives, like bran, Metamucil, and milk of magnesia work by keeping water in the colon, lending bulk and softness to the stool.

Polymorphonuclear Leukocyte (Neutrophil): Poly(many) morpho(shaped) nuclear leuko(white) cyte (cell).

Thymus Gland: The thymus sits behind the sternum (breastbone) and mysteriously involutes (shrinks) at about the time of puberty.

Antibodies, or immunoglobulins (abbreviated Ig), are large proteins that latch onto foreign antigens*, a tricky job considering all the thousands and thousands of molecules which don't belong in a human body. Structural design for the immunoglobulins was dictated by two specific requirements. First, there had to be enough different shapes to bind to a wide variety of antigens, and second, each immunoglobulin had to be able to bind the foreign antigen with an incapacitating hammerlock. Mother Nature's successful solution was a lobster-shaped protein. Each arm of the immunoglobulin is independently capable of binding a separate (but identical) antigen, an arrangement which allows immunoglobulins to return with their bounty as bulky lumbering targets for easy phagocytosis* by reticuloendothelial cells (mainly macrophages).



The versatility of immunoglobulins is found in their antigen binding sites which may have any one of a thousand or more configurations. No one knows for sure how many different shaped immunoglobulins there are, but it *is* known that the shape of each immunoglobulin is genetically determined, and that each immunoglobulin is synthesized by only one B lymphocyte, and *only* by a B lymphocyte (after the B lymphocyte is transformed into a plasma cell—see below).[15]

The standard immunoglobulin is called IgG. A couple of modifications lend other immunoglobulins special talents. For example, a small protein attachment allows IgA to be secreted onto outside mucosal surfaces—into the tears and breast milk and along the bronchi, gut, and urethra—to meet the enemy before it has a chance to penetrate those soft mucosal surfaces. A different protein attachment allows five separate IgM immunoglobulins to bind their tails together. When this circulating complex binds ten separate antigens, the resulting cluster becomes an especially easy mark for phagocytic macrophages. During acute* infections, IgM antibodies are generally manufactured before IgG. Both IgG and IgM may circulate unattached in the bloodstream or else travel like antennae on the outside of B lymphocytes circulating in the blood.

Antigen: Good examples of antigens are the A and B antigens on red blood cells. A person may have the A antigen alone, B alone, both A and B, or neither one on the surface of his red blood cells. The patient with A type blood automatically has anti-B antibodies which will destroy any type B or AB blood transfused into him. So an AB patient, with neither anti-A nor anti-B antibodies, is a universal recipient; conversely, universal donor blood, type O, can be given to anyone in an emergency. But since O blood contains anti-A and anti-B antibodies, it would be better, when transfusing whole blood, to transfuse a mixture of O red cells and AB serum (containing neither anti-A nor anti-B antibodies).

Phagocytosis: Phago(to eat) cyte(cell): a cell that eats.

Acute: Hours to days. Subacute is days to weeks to a few months. Chronic is many months to years.

Another immunoglobulin, IgE, projects from basophils* circulating in the blood and from mast cells* in peripheral tissues. When certain provocative antigens—typically pollen, poison ivy, and bee stings—come in contact with IgE, the underlying basophil or mast cell immediately releases potent chemicals (histamine, serotonin, bradykinin, and slow reacting substance) that then precipitate an allergic asthma or hay fever attack, or perhaps a swollen, itchy rash. Anaphylaxis*, a severe allergic reaction characterized by sudden shortness of breath and hypotension, occurs when these chemicals cause capillaries* throughout the body to suddenly leak massive amounts of fluid into alveoli and peripheral tissues.[16]

Circulating antibodies and mononuclear cells make surveillance rounds through all peripheral tissues (except the brain*) by slipping between capillary endothelial cells*. To get back to the bloodstream, antibodies and monos reenter other delicate channels called lymphatics. The whole body (except the brain) is riddled with these tiny lymphatic channels which converge into a major lymphatic duct, called the thoracic duct. The thoracic duct slips upward through the chest and eventually dumps circulating antibodies and mononuclears back into the superior vena cava.

At key points—in the groin, along the neck, in the armpits, plus many internal sites—lymphatics are interrupted by lymph glands (nodes) where thousands of reticuloendothelial cells monitor the friendliness of lymph percolating by. Large collections of reticuloendothelial cells are found, quite naturally, at entry sites into the body: in the nasopharynx (adenoids), back of the throat (tonsils), along the gut* (Peyer's patches and appendix), throughout the liver (to monitor what's absorbed from the gut), and throughout the lung (to monitor what's inhaled). Internally, protected up under the left rib cage is the spleen which, jammed with millions of nesting reticuloendothelial cells, acts like a giant lymph node for the bloodstream.

Basophil: Baso refers to the basic pH of the stain used to stain the cell for microscopy; phil (short for philic) is the opposite of phobic.

Mast Cell: Virtually the same as a circulating basophil, except that mast cells are found in peripheral tissues, particularly in the lungs.

Anaphylaxis: Ana = against phylaxis = protection, in contrast to prophylaxis.

Capillaries: Tiny (invisible to the naked eye), thin-walled vessels connecting arteries to veins.

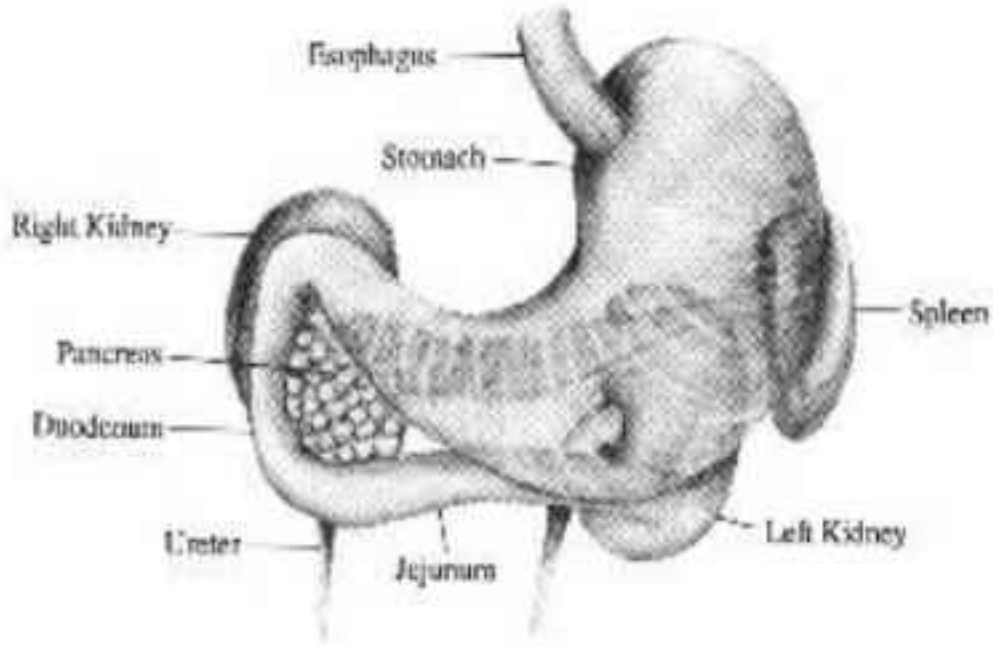
Except the Brain: A small 'microglial' cell is probably the brain's own reticuloendothelial cell, but there is still debate about whether blood-borne lymphocytes routinely roam through the brain.

Endothelial Cells: Cells forming the interior lining of arteries, veins, capillaries, and lymph channels.

Along the Gut: Immunologic surveillance by Peyer's patches and the appendix is one reason we can eat almost any bacterium without fear of infection. Salmonella, however, is the one exception. Salmonella may escape destruction in the gut by holing up in the gall bladder and continually contaminating that person's stool. The most famous reservoir of salmonella was Typhoid Mary, a New York cook who was eventually incarcerated as a public health hazard; to this day, kitchen personnel are regularly screened for salmonella in their stool. Unfortunately, pet turtles also harbor salmonella.

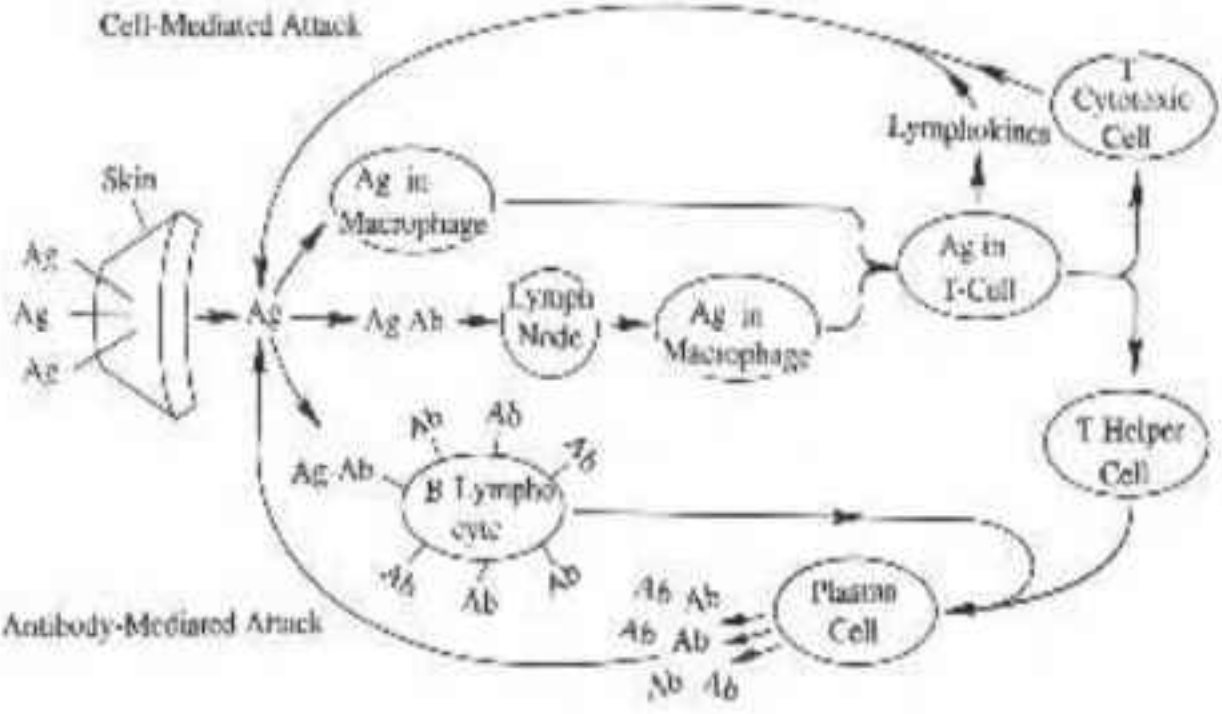
Active infection with salmonella—typhoid fever—produces high fevers, painful bloated abdomen, and intestinal hemorrhages.[17] Salmonella may also settle in the bones; a bone infection is called osteomyelitis.

Besides maintaining immunologic surveillance of all intestinal contents, lymphatics within the intestinal wall absorb almost all lipids from the intestine. By absorbing lipids before they have a chance to enter the portal venous system, intestinal lymphatics detour dietary lipids around the liver before dumping them into the systemic circulation at the superior vena cava.



Say an antigen penetrates the skin. One of three things may immediately befall the antigen: it may be latched onto by a free antibody, or by an antibody projecting from a B lymphocyte; or the antigen may be phagocytized by a wandering macrophage. If a free antibody latches onto the antigen, the resulting antigen-antibody complex drains into the nearest lymph node where a macrophage phagocytizes them. Once a macrophage has the antigen, either in peripheral tissues or in a lymph node, the antigen is processed in some way and then transferred to another cell, the T lymphocyte.[18]

After analyzing this processed antigen, the T cell does several things. First, it clones itself into (at least) two different kinds of cells: *T helper* cells and *cytotoxic T* cells. The T helper cell triggers antibody production within those B lymphocytes that also encountered the antigen at the site of skin penetration. Without that T helper cell the B lymphocyte would not produce antibodies, but with its help, the B lymphocyte converts into a mighty plasma cell, blasting out thousands of antibodies specifically directed against the foreign antigen. Meanwhile, a posse of cytotoxic T cells is headed out to kill and devour the intruder, a job made easier by those newly synthesized antibodies which (after binding to the antigen) flag the antigen as foreign.[19]



Besides convincing a T lymphocyte to clone itself into T helper and cytotoxic T cells, a macrophage-processed antigen also prods the T lymphocyte into synthesizing lymphokines, molecules (? proteins) which attract polys, macrophages, and cytotoxic T cells to the antigen.[20] Polys (neutrophils) are rapidly mobile, but dispensible knaves thrown into the front lines of battle, well before the cytotoxic T cells and macrophages which follow hours to days later to help destroy, catalog, and remember the invader for future battles. To macrophages is left the chore of mopping up the remains of the inflammatory battle (pus*).

Sometimes an antigen-antibody complex may accidentally escape phagocytosis and float free in the bloodstream. Later, the complex can deposit in arterial walls or in kidney glomeruli (see below) where the immune complex elicits a damaging inflammatory attack by polys and monos, called, respectively, arteritis and glomerulonephritis*. What mediates the inflammatory attack is not the usual sequence of macrophage, T lymphocyte, T helper, cytotoxic T, and lymphokines, but rather a completely separate set of circulating proteins called complement proteins. Normally, complement comes into play when certain (complement fixing) antibodies, on attaching themselves to a bacterium, automatically bind the first component of complement. A rapid chain of chemical binding ensues involving eight additional components of complement. When the dust settles, the bacterium has a torpedo-size hole in it, and polys and mononuclear cells are headed into battle*.[21] Unfortunately, the resulting cellular overkill can, when it attacks an antigen-antibody complex within arterial walls or kidney glomeruli, inadvertently damage those innocent structures. These two 'immune complex' diseases are closely related to 'autoimmune' diseases, like systemic lupus erythematosus, in which the patient directs an immunologic attack against his own body; in autoimmune diseases the patient himself is the primary target, not an innocent bystander.[22]

Pus: Pus is a gooey, yellowish collection of white blood cells, bacteria, and microscopic remnants of destroyed tissue. For thousands of years pus was thought to be healthy until the 1500's, when Ambrose Pare discovered that cleansing the wound of pus improved soldiers' chances of survival.

All pus should be cleaned or drained from a wound, because pus makes the eradication of an infection difficult if not impossible. Without a rich blood supply, pus can harbor bacteria beyond the reaches of either antibiotic drugs or white blood cells. To facilitate the drainage of pus to the outside skin surface, any infection close to the skin surface should be soaked to soften the overlying skin. To hasten the drainage, surgeons 'lance' the collection of pus (abscess or boil), and then leave a rubber 'drain' in the wound to continue the drainage. Surgeons routinely leave drains in a wound after an operation to prevent blood and lymph from accumulating and subsequently getting infected.

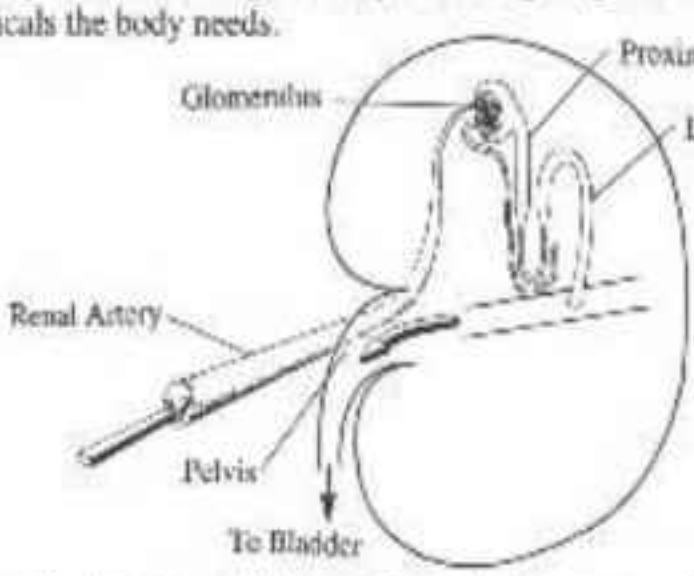
Glomerulonephritis: 'Itis' at the end of a word means inflammation. Similarly, 'oma' means tumor, 'ase' means enzyme, 'ose' means carbohydrate, and 'one' means hormone.

Inflammation is not synonymous with infection. The inflammation may be directed against a lump of cancer, a piece of dirt, an immune complex, or hemorrhaged blood.

Headed Into Battle: The complement system was probably originally designed to kill bacteria without the help of phagocytosis.

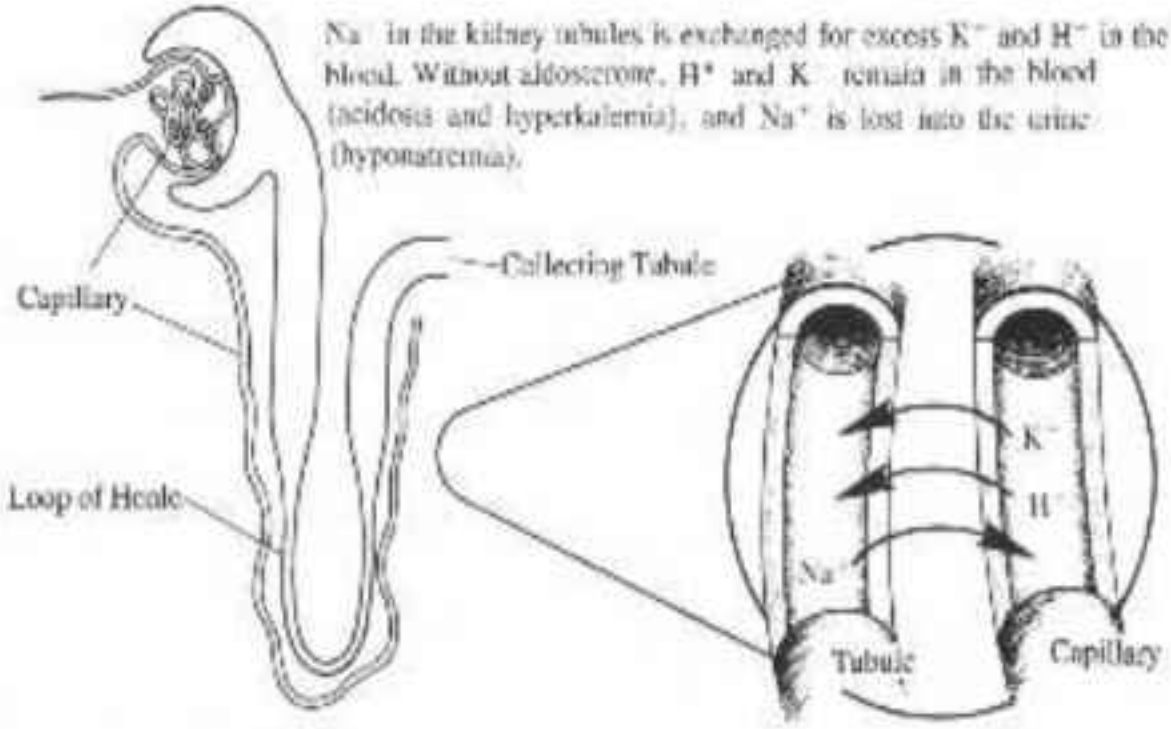
UROLOGIC

Two kidneys clear the blood of toxic chemicals normally made by the body in its day-to-day operations. Blood is first strained through the kidney glomerulus*, removing all cells and protein. The resulting transudate*, now topologically outside the body*, slowly courses through kidney tubules giving the kidney time to reabsorb those chemicals the body needs.



Transudate, filtered into the proximal tubule, may contain small proteins, but no lipids, red cells, white cells, or larger proteins like albumin.

Together with the lungs, kidney tubules help regulate the acidity of blood by absorbing or discharging bicarbonate, or by exchanging H^+ ions in the blood for sodium ions (Na^+) inside the distal tubule.

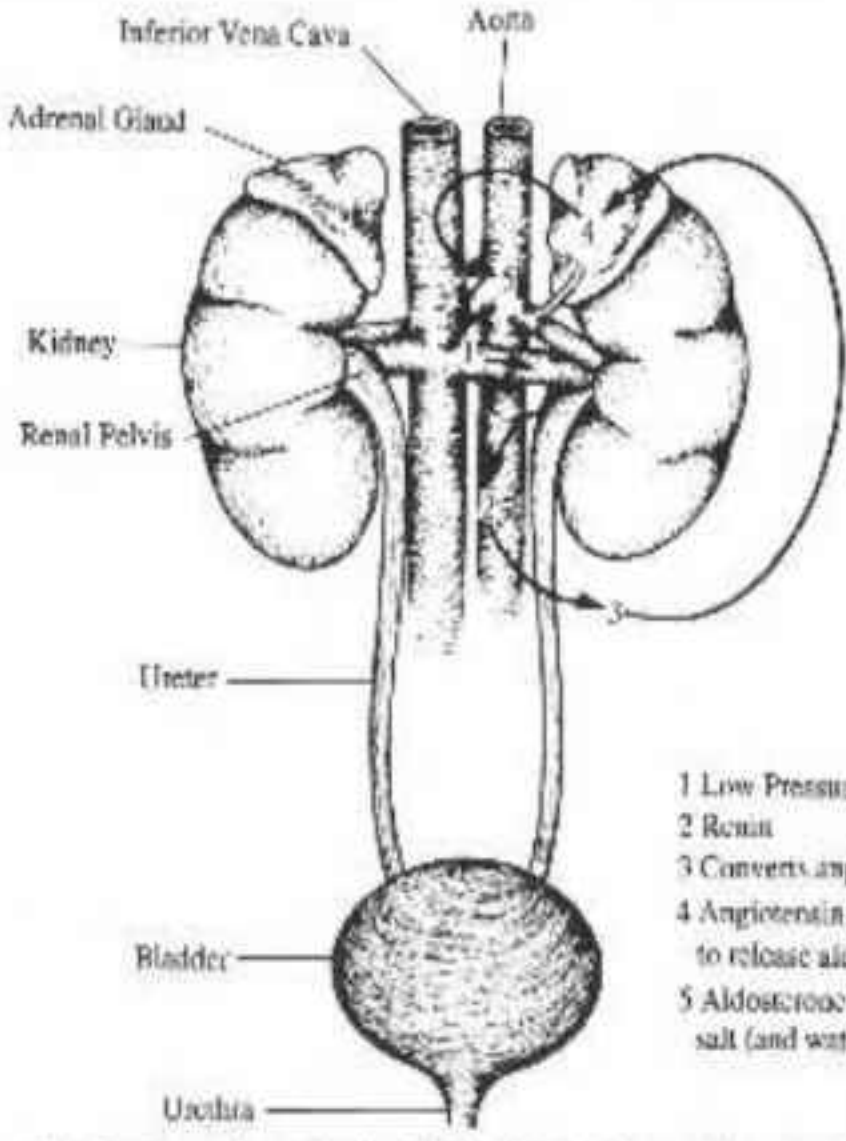


Glomerulus: Glomus is a ball; glomerulus is a small ball. (Latin)

Transudate: A protein-free solution filtered across a cellular membrane. An exudate is a thick, protein-containing fluid which oozes out *between* cells. Exudates commonly occur during inflammation as white cells and plasma pour through the capillary walls to reach the site of inflammation. A scab is the dry, crusted remains of an exudate.

Topologically Outside the Body: It does seem like a lot of unnecessary work to filter everything out of the bloodstream and then to select back what's needed—two steps—instead of simply excreting the toxins in one step. But in that one simple step, glomerular filtration isolates all the blood's filterable toxins into a small, protein-free solution for cleansing by the kidney tubules.

The body also uses this distal tubular exchange system to rid itself of excess potassium* (K^+) by exchanging intravascular potassium for urinary Na^+. Activity of the potassium/hydrogen ion exchange enzyme is regulated by the hormone aldosterone, which is itself regulated, surprisingly, not by the level of potassium or hydrogen ion in the blood, but by the vigor of blood flow through the kidney. A drop in kidney perfusion pressure* stimulates the kidney to release an enzyme called renin, which splits apart another circulating protein, angiotensinogen, unleashing angiotensin I. Circulating angiotensin I is then converted by the lungs to angiotensin II, which instructs the adrenal cortex to release aldosterone into the bloodstream. On reaching the kidney distal tubule, aldosterone activates the exchange of intravascular K^+ or H^+ for Na^+ coursing down the distal tubule. The extra sodium on the blood can now attract water into the bloodstream to augment the intravascular volume.



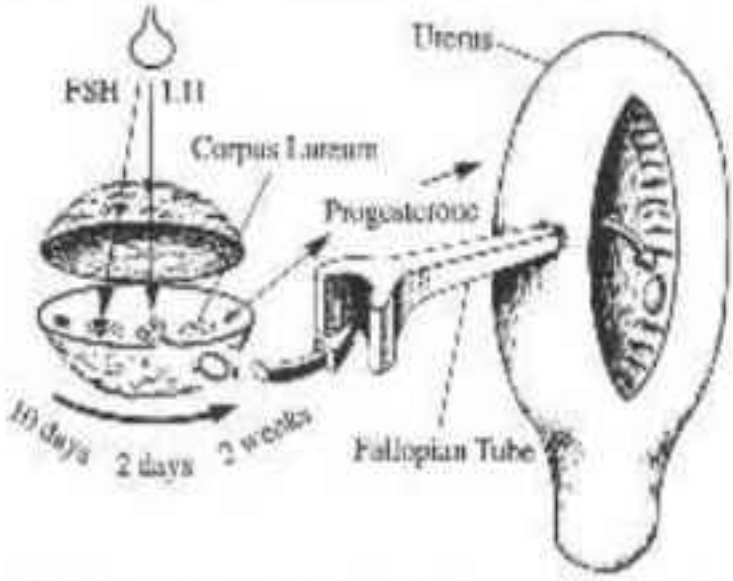
The final product of all this filtering, reabsorption, and exchange is urine, which dribbles from the terminus of thousands of kidney tubules into a long-necked funnel called the ureter. From here, it's simply down the ureter, into the bladder, and out the urethra to the outside world.

Potassium: Potash (same root as potassium), the garden fertilizer, is simply potassium combined with either chloride, sulfate, or nitrate.

Perfusion Pressure: The blood pressure forcing blood through an organ's arteries, capillaries, and veins.

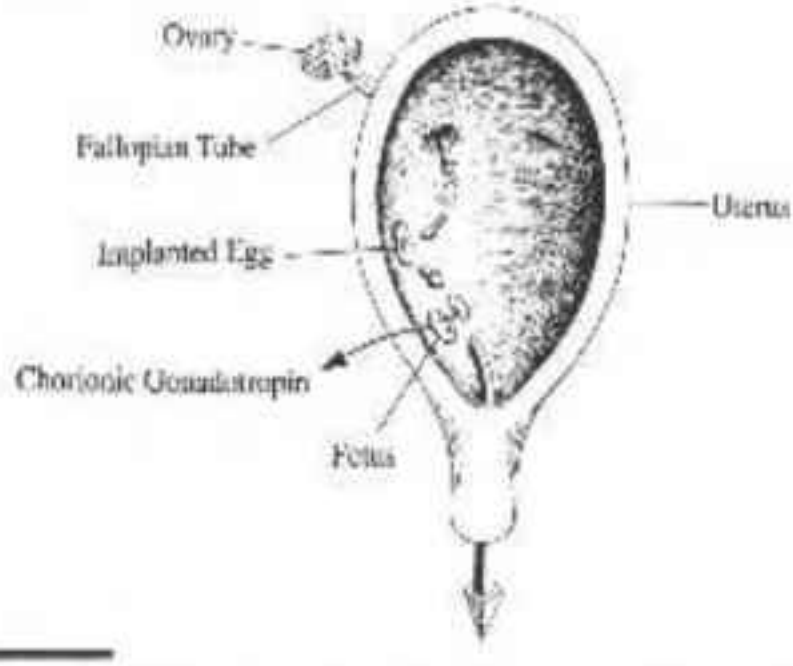
GENITAL

Midway between menstrual periods, under the combined influence of FSH and LH, one of the two ovaries releases an egg into an adjacent Fallopian tube where fertilization takes place within one or two days.



Progesterone stimulates proliferation of blood vessels in the uterine wall and also makes uterine lining 'sticky.' If no egg implants, the corpus luteum dies, progesterone levels fall off, and the endometrium is shed as menstruation.

While the fertilized ovum is slowly tumbling down the Fallopian tube, the corpus luteum in the ovary is busy secreting progesterone to prepare the uterus for implantation. To *keep* the corpus luteum producing progesterone, the fertilized ovum immediately begins synthesizing a new hormone, chorionic gonadotropin*. Eventually, the placenta itself will manufacture enough progesterone to be independent of the corpus luteum. Nine months of gestation later, under the influence of oxytocin, the uterus shoves the fetus past the cervix through the vagina.

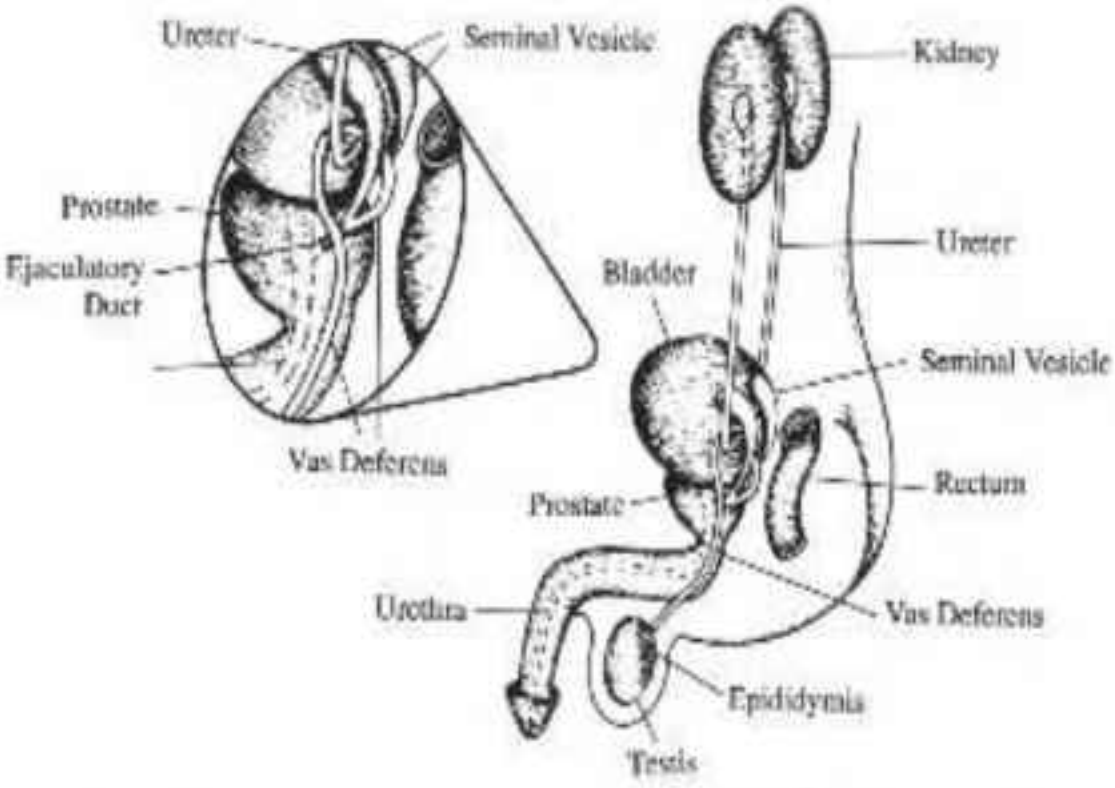


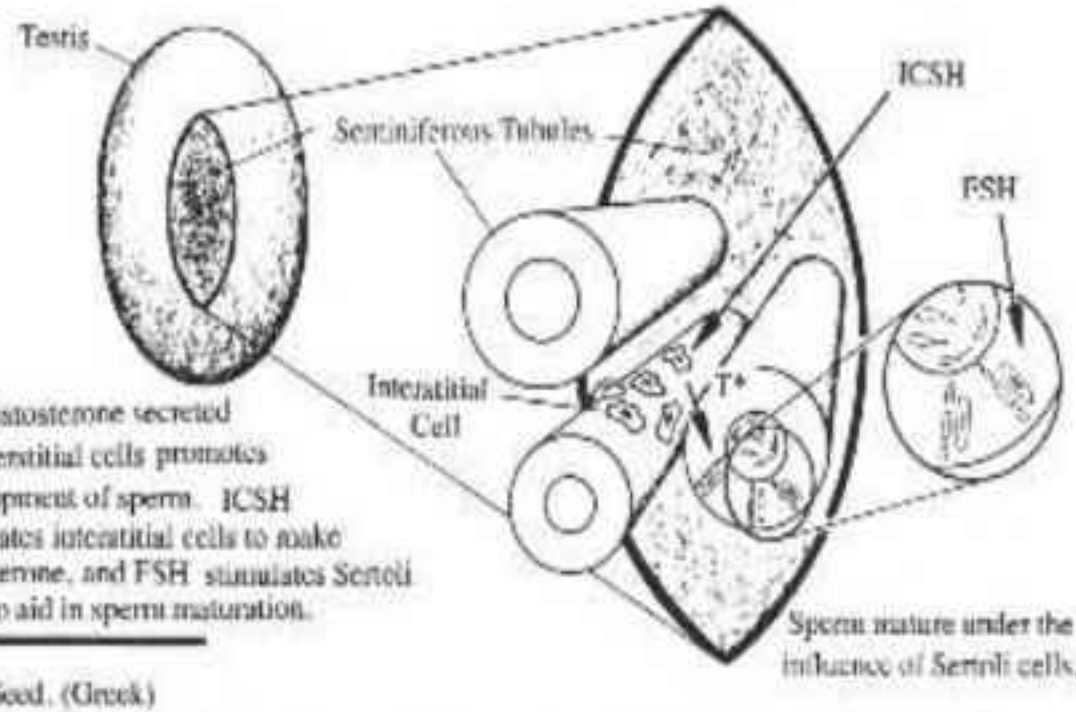
Chorionic Gonadotropin: Chorion (membrane—in this case, amniotic membrane around the fetus); gonad(sex gland) trop(in(to nourish).

Pregnancy detection kits are made up of two suspensions: #1 containing antibodies against chorionic gonadotropin, and #2 containing antibodies against the antibodies in suspension #1. A sample of urine is mixed with suspension #1. If the woman is pregnant, antibodies in suspension #1 bind to chorionic gonadotropin. Then, when suspension #2 is added, there are no free antibodies left for suspension #2 to bind to and clump (visible with the naked eye). Clumping by suspension #2, then, means the woman is not pregnant.

Sperm*, manufactured and stored in the testes*, are ejaculated up the vas deferens* into the ejaculatory duct, which links up with the urethra passing through the prostate gland* nestled beneath the bladder. To sustain sperm during their trek up the uterus and Fallopian tubes, nutritious semen is pumped into the ejaculatory duct by the seminal vesicles, and into the urethra by the prostate gland encasing the urethra*.

The breasts are also included in this organ system.





T*: Testosterone secreted by interstitial cells promotes development of sperm. ICSH stimulates interstitial cells to make testosterone, and FSH stimulates Sertoli cells to aid in sperm maturation.

Sperm: Seed. (Greek)

Testes: A small earthenware pot used by alchemists for chemical experiments, hence the term 'test' tube (referring to the pot, not the experimental test). Testes may also share the same origin as the word testify, a legal privilege probably denied women in ancient Rome.

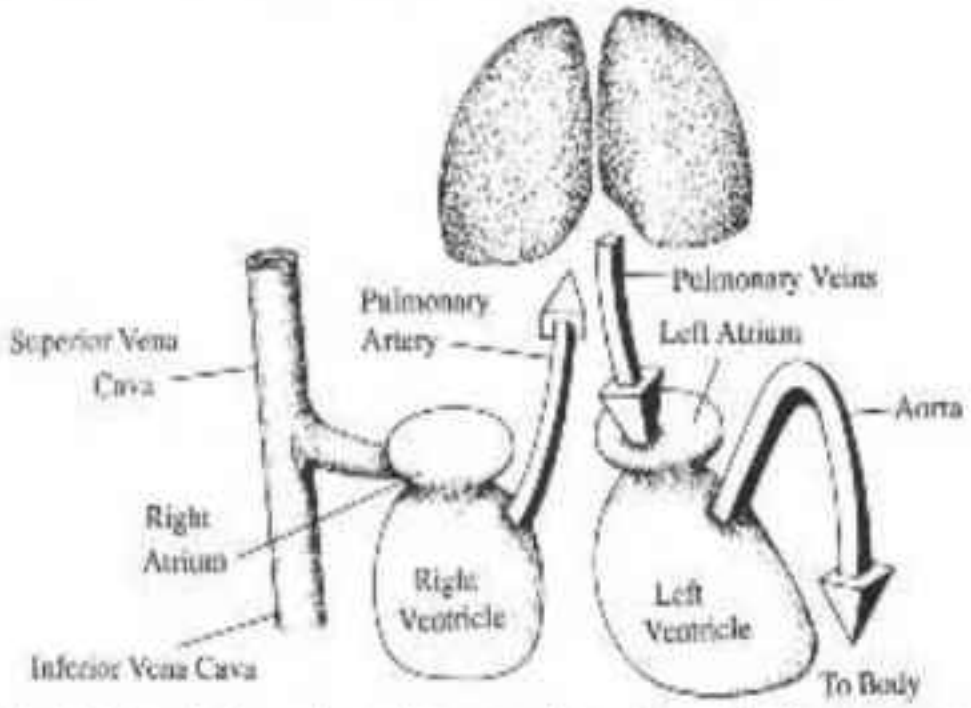
Prostate Gland: Pro(before) state(standing) – standing before the bladder.

Vas Deferens: Vas (vessel) deferens (carrying away).

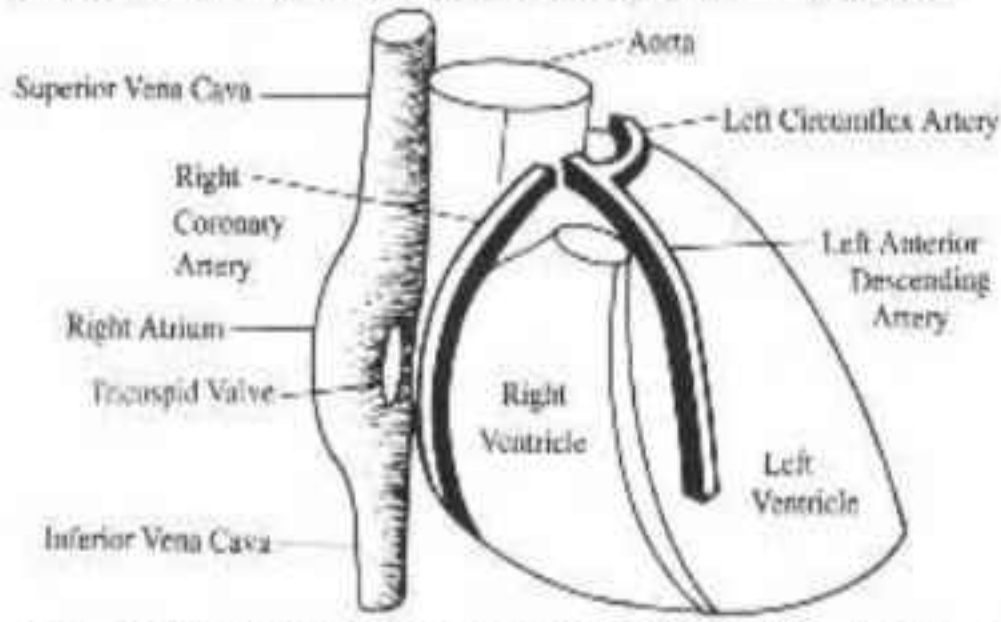
Encasing the Urethra: This curious anatomic arrangement allows prostatic enlargement – a common occurrence in old men – to pinch off the urinary stream.

VASCULAR

Arteries* carry blood away from the heart; veins carry it back. The color of blood (red = oxygenated, blue = deoxygenated) is irrelevant to the definition of an artery or vein, only the direction of flow. For example, pulmonary arterial blood from the right ventricle is blue; pulmonary venous blood, after passage through the lungs, is red.

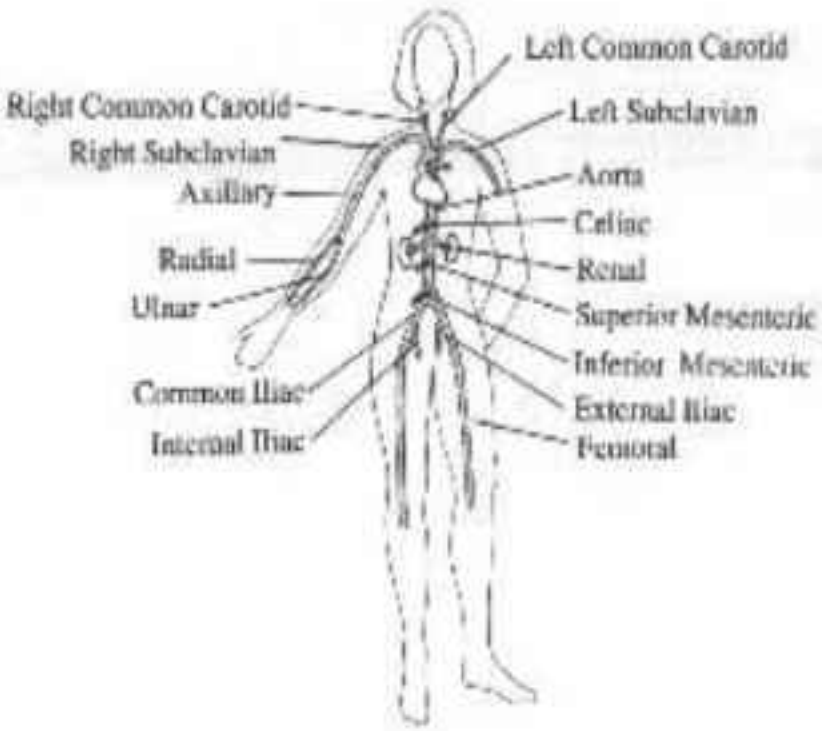


Blood exits the heart into the aorta where, immediately, two coronary arteries branch off. The right coronary feeds the right ventricle and A-V node, while the left coronary feeds the left ventricle, and occasionally the A-V node, too.



After passing through large arteries and small arterioles, blood enters tiny thin-walled capillaries out of which oxygen, glucose, amino acids, and other nutrients diffuse to feed the body's tissues. Blood returns to the heart through small venules, large veins, and eventually the superior or inferior vena cava.

Arteries: 'Windpipes.' The ancient Greeks thought that arteries carried a creative, airborne spirit inhaled by the lungs (pneuma = wind). Prior to the knowledge of oxygen, what explanation would you have given for breathing?



HEMATOLOGIC

This system includes the five important components of blood: red blood cells (RBC's or erythrocytes*), white blood cells (WBC's or leukocytes), platelets, proteins, and lipids. RBC's, WBC's, and platelets are made in the bone marrow. Plasma proteins (other than immunoglobulins made by B lymphocytes) and lipids are synthesized by the liver.

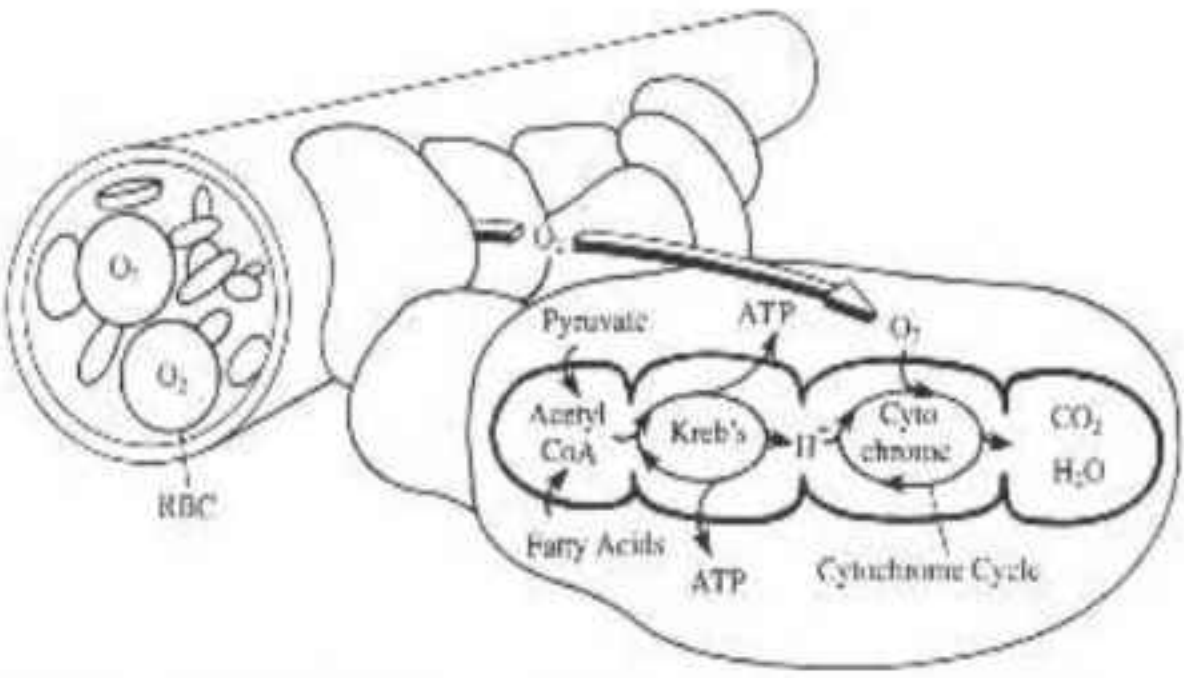
Red cells contain hemoglobin, a protein that scoops up oxygen in the lungs and releases it* in peripheral tissues. Oxygen is used by cells to make ATP (adenosine triphosphate), a kind of chemical battery for every cell's enzymatic reactions. Synthesis of ATP takes place in tiny cellular chambers, called mitochondria*, which convert oxygen and acetylcoenzyme A (acetyl CoA)—supplied mainly by glucose and fat, some from protein—into ATP, releasing carbon dioxide as a byproduct. The name of this vital chemical pathway is the Krebs cycle.

Erythrocyte: Erythro is red, in Greek.

Releases It: The startling feature of hemoglobin is not simply its ability to bind oxygen, but its adaptive binding power: in areas of high oxygen (the lungs), hemoglobin binds oxygen firmly; in areas of low oxygen (peripheral tissues), hemoglobin lets it go.[23] This happens because each hemoglobin molecule is capable of binding four separate oxygen molecules, and each time an oxygen molecule in the lungs binds to hemoglobin, the next oxygen binds easier than the previous one. Conversely, in the periphery when one of the four oxygen molecules leaves hemoglobin for an oxygen starved cell, the other three oxygen molecules suddenly find themselves loosely bound, and hemoglobin's marriage to oxygen falls apart.

How oxygen facilitates its own binding puzzled early biochemists.[24] The only explanation—a striking concept when first proposed—is that with each additional oxygen, hemoglobin changes shape, and each new shape must make it easier for the next oxygen molecule to bind. Numerous examples of changes in protein configuration have subsequently been uncovered throughout the body.

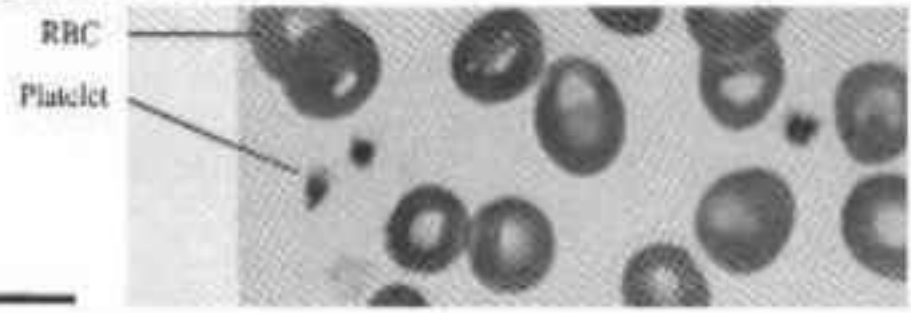
Mitochondria: Mito=thread, chondrion=granule.



Without mitochondria—or without oxygen or acetyl CoA to run them—cells can still manufacture small amounts of ATP, but only at the expense of accumulating lactic acid, the chemical which makes your muscles hurt when you exercise too long.

The life span of a red cell is about one hundred days, so one percent of the blood is replaced every day by new red cells, called reticulocytes*. An elevated 'retic count' means the bone marrow is working overtime to restore blood which is either being destroyed, or lost through the gut, kidneys, or vagina. Defunct red cells* are taken up by the spleen where they are disassembled for recycling. The reusable iron is carried to the bone marrow by a circulating protein called haptoglobin. Heme, you recall, is metabolized in the bloodstream to bilirubin and transported by albumin to the liver where, after conjugation* into a water-soluble form, bile is secreted into the duodenum to emulsify fats.

For obvious survival reasons, Mother Nature built in several mechanisms to staunch any hemorrhage from the vascular tree. First off, severed arteries and arterioles immediately squeeze shut with intense vasoconstriction. In small vessels, especially venules (which are incapable of vasospasm), vascular holes are plugged by platelets, tiny pellets floating in the bloodstream.



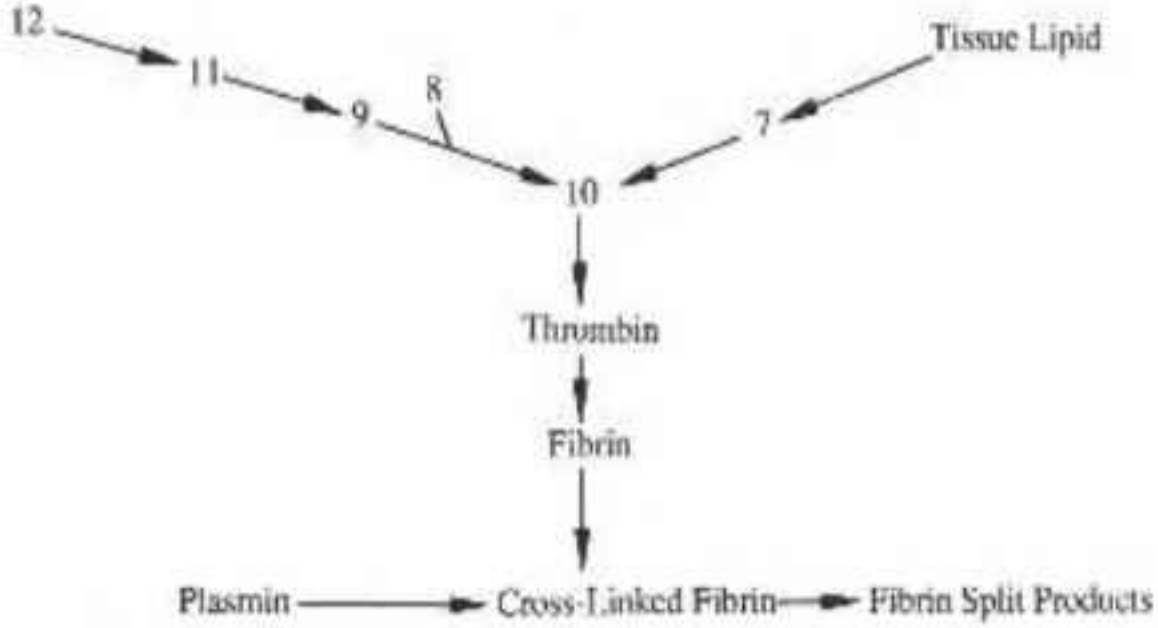
Reticulocyte: A reticulum is a fine network of fibers resembling a cobweb. Immature red cells (reticulocytes) stain with a blue reticular pattern called basophilic stippling.

Defunct Red Blood Cells: Some hematologists feel that red cells never die—they just vent (to) their spleen.

Conjugation: To join together, as in conjugal visits. In this case bilirubin is conjugated to another molecule to make bilirubin water-soluble.

Simultaneously, special clotting proteins, also circulating, join the platelet plug in a rather delicately choreographed cascade of 'intrinsic' clotting factors to form a fibrin blood clot, called a thrombus. If that weren't enough, there's a separate, fail-safe backup system which can also trip the clotting cascade at the site of a vascular tear. This 'extrinsic' system is precipitated by a lipid in the surrounding tissue leaking through the vascular hole into the blood vessel.[25]

To prevent too much clotting, Mother Nature devised a demolition crew of fibrinolytic* enzymes to dissolve the clot. Then she made an inhibitor of the demolition crew to prevent excessive fibrinolysis. A finely tuned system indeed; any slip-up may cause a serious bleeding diathesis (tendency), or rarely, life-threatening hypercoagulation.



Centrifuging fresh blood eliminates the red cells, white cells, and platelets, leaving the plasma proteins in the supernatant. If, before centrifugation, you allow the blood to clot*, centrifugation would also sediment all the clotting proteins; this protein-containing supernatant—now minus the clotting proteins—is called serum*.

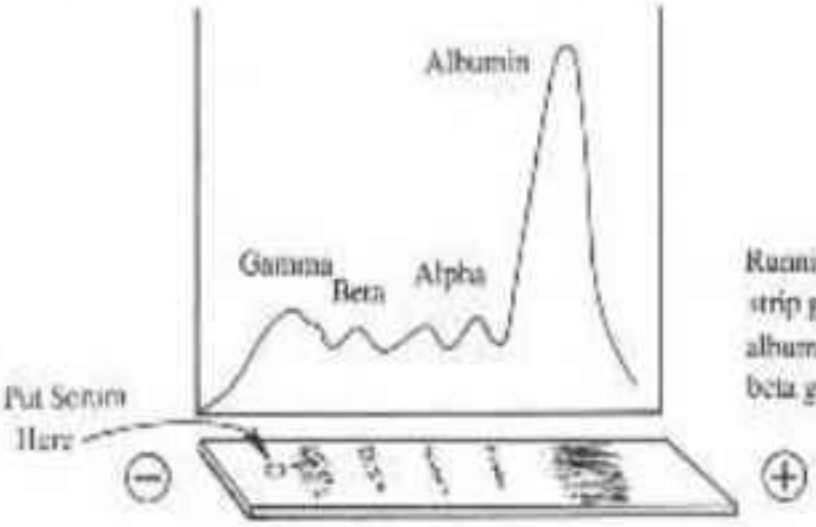
When you apply an electrical charge to serum, individual proteins migrate toward or away from the electrical poles depending on their electrical charge* (determined by the particular composition of amino acids). Serum proteins thus separated fall into four groups: albumin, alpha and beta globulins, and gamma globulin. Albumin and alpha/beta globulins are the carrier and water retaining proteins; gamma globulins (immunoglobulins) are the antibodies synthesized by B lymphocytes.

Fibrinolytic: Lysis means to dissolve or loosen. So glycolysis means to break down glycogen; hemolysis, to break open red blood cells; osteolysis, to dissolve bone.

Clot: Preventing blood from clotting after collecting it in a glass bottle was a serious problem around the turn of the century when blood transfusions were finally recognized as the correct treatment of shock. (Prior to that time shock was thought to be a neurologic problem requiring stimulants like strychnine.) Calcium binding agents, like citrate, were soon discovered to prevent blood from clotting. For this reason, when administering pints and pints of calcium free blood, you also have to give calcium to prevent a drastic lowering of the patient's serum calcium.

Serum: Serus is Latin for late, referring to the last part of blood to remain after clotting.

Electrical Charge: This simple idea, called electrophoresis, won Arne Tiselius the Nobel prize in 1948.



Running a densitometer across this strip gives the electrophoretic peaks: albumin, alpha globulins, beta globulins, and gamma globulins.

BONE AND JOINT

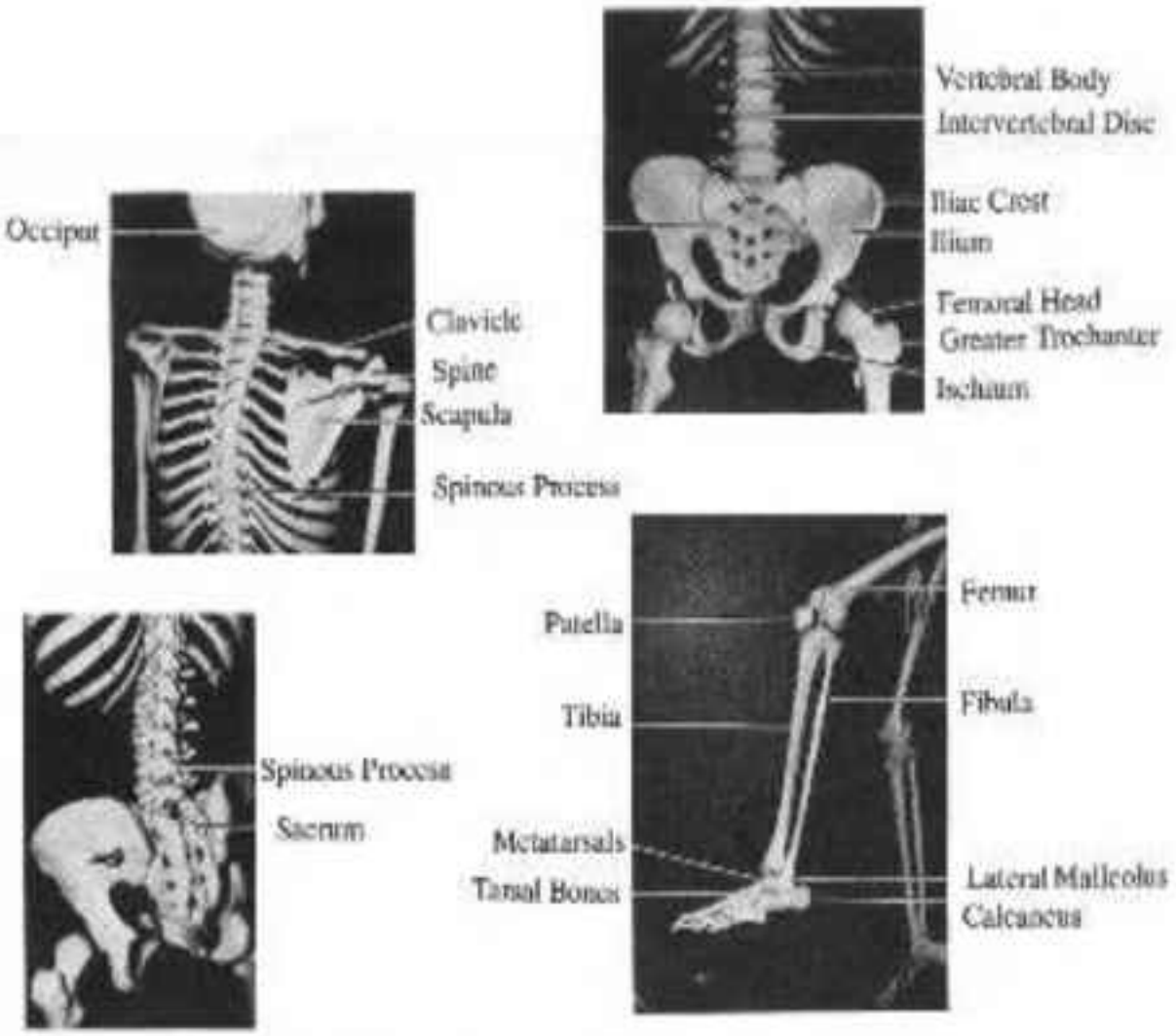
Bones are held together at joints by tough bands of tissue called ligaments. Muscles move bones by tapering into tough cords, called tendons, which firmly anchor the muscles to bones.











COVERINGS AND CONNECTIVE TISSUE

'Coverings' refers to those structures which 1) cover bones, tendons, and muscles (structures like cartilage*, synovial membranes*, bursae*, tendon sheaths, periosteum*, and fascia*), or 2) line the body spaces (like the meninges*, dura*, visceral* and parietal* pleura*, pericardium, and peritoneum).

Cartilage: Gristle. Your ear and nasal septum are good examples of flexible, compressible cartilage.

Synovial Membranes: Syn(along with) ova(egg)—fluid resembling egg white. Synovial membranes line the outskirts of joint spaces.

Bursa: A wine skin.

Periosteum: Peri(around) osteum(bone)

Fascia: Band (Latin). A fasces is a bundle of sticks wrapped by a band with an axe protruding; a symbol adopted by the Fascists.

Meninges: Membrane in Greek.

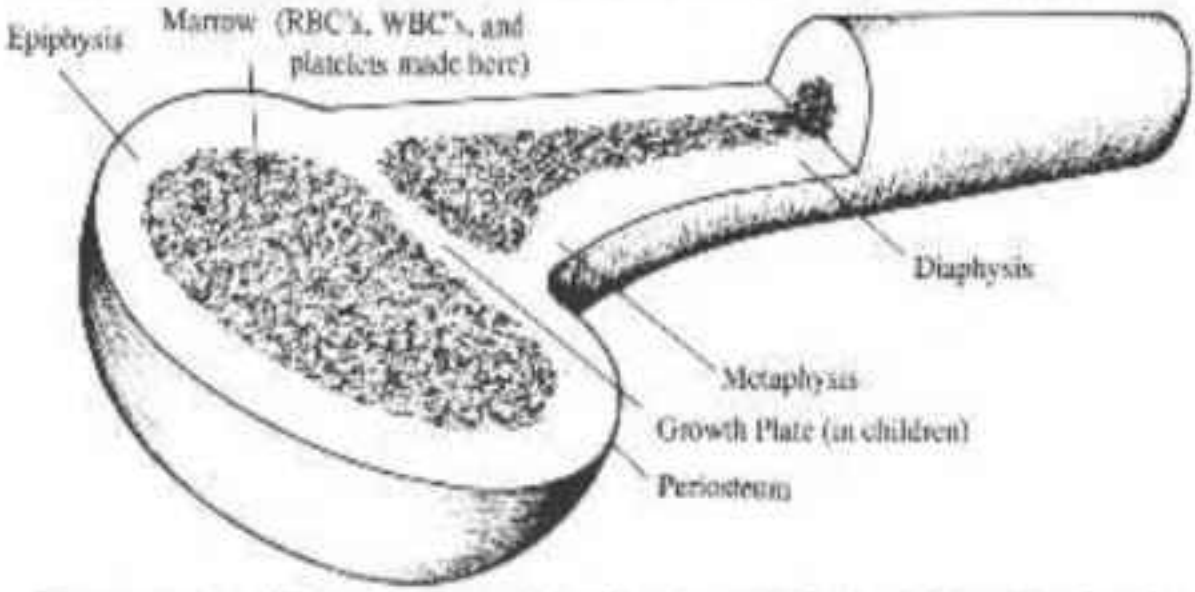
Dura: Tough, durable. (Latin)

Visceral: The viscera are the internal organs: lungs, heart, intestines, liver, pancreas, spleen, kidneys, and bladder. From Latin viscus, meaning sticky.

Parietal: A wall. (Latin)

Pleura: Side.

To reduce friction, each mobile surface in a joint is plated with a layer of *cartilage*. Half-inch thick slabs of cartilage, the vertebral discs, cushion each vertebral body and, by being compressible, add flexibility to the spine. To further reduce joint friction, a thin fluid, called synovial fluid, oozes into each joint from *synovial membranes* encasing the joint. Adjacent to many joints are soft fluid-filled sacs, called *bursae*, which cushion neighboring bones from one another and, like the *tendon sheaths*, allow tendons to glide smoothly over bony ridges and bumps. Every bone is covered with a *periosteum*, a thin membrane from which new bone is formed* and in which travel blood vessels supplying the bone. Likewise, blood vessels supplying muscles travel over the surface of the muscle in a thin membrane called *fascia*.



The *meninges* are thin membranes lying directly on the brain surface. The *dura* is a thick covering overlying the meninges and plastered up against the skull. The thoracic* *visceral pleura* is a membrane covering the lung; the *parietal pleura* lines the inside of the chest wall (page 17). The lung has a natural tendency to collapse, but a thin layer of fluid in the pleural space between the parietal and visceral pleurae keeps the lung expanded against the chest wall, like two panes of glass held together by a bit of water between them. So during inspiration the expanding chest wall can, with surface tension between the parietal and visceral pleurae, help the diaphragm* expand the lung. The *pericardium* is a thick sack loosely encasing the heart, and the *peritoneum* is a thin membrane lining the inside of the abdominal wall (analogous to thoracic parietal pleura).

"Connective tissue" refers to the widely scattered background substance that provides the pliable framework for such tissues as the skin, subcutaneous tissue, and gut. The primary ingredient of connective tissue is a rugged protein called collagen—scar tissue is a good example—secreted by a small, ubiquitous cell called a fibroblast.

New Bone Is Formed: Bones begin in infancy as cartilage, and over the years, with the help of vitamin D, calcify into hardened bones. Flexible cartilage helps prevent young children from breaking their bones from trauma. Bone lengthening takes place along the growth plate, the junctional area between a bone's epiphysis and diaphysis. Bone thickening is done by the periosteum which lays down newer and newer coats of bone along the surface.

Thoracic: The thorax is the chest.

Diaphragm: The diaphragm descends with each breath and expands the interior of the thoracic cage. This lowers the intrathoracic pressure, sucking air into the lungs.

THE PRESENTING ORGAN SYSTEM

IN GENERAL, diseases present in one organ system at a time. When that organ system is injured, it can complain with only a limited, but fortunately distinctive, repertoire. Moreover, each organ system's characteristic complaints are independent of the nature of the insult; they simply signify that the organ system is not working properly. These complaints fall into two broad categories: symptoms and signs. A symptom is something the patient complains about, and a sign is something detectable on physical examination. A symptom is a subjective finding, and a sign is an objective one.

The symptoms and signs which bring a patient to the doctor represent malfunction of the 'presenting' organ system, the organ system which surfaces first. The first step in making an anatomic diagnosis is to establish the presenting organ system. To do this you need a characteristic list of symptoms for each organ system—a 'review of systems.'

REVIEW OF SYSTEMS

Organ System	Symptom
Systemic:	fever, chills*, weight loss, fatigue*, anorexia*, night sweats*.
Skin:	rash, ulcer, alopecia*, urticaria*.
Neuromuscular:	headache, syncope*, seizures*, confusion, forgetfulness, delusion*, hallucination*, paranoia*, depression, mania*, dysphasia*, blindness, red washout*, diplopia*, facial numbness, chewing weakness, facial weakness, tinnitus*, dizziness, vertigo*, hearing loss, dysarthria*, hoarseness, dysphagia*, drop attacks*, gait disturbance, weakness, incoordination, numbness/tingling, uncertainty if bladder is full, hesitancy*, diminished force of stream, double voiding*, incontinence*, impotence*, difficulty with sweating.
Eyes:	difficulty seeing, blurring, halos*, night blindness.
Ears:	deafness, tinnitus, dizziness, vertigo.
Endocrine:	polyuria*, polydipsia*, heat or cold intolerance, amenorrhea*, galactorrhea*, weight change, hirsutism*, hoarseness, constipation, diarrhea, increased sweating, tachycardia, nervousness, loss of libido, head, hand, or foot enlargement*.

Respiratory:	epistaxis*, hoarseness, dyspnea* on exertion, hemoptysis*, wheezing*, cough, sputum* production.
Cardiac:	angina*, dyspnea on exertion, paroxysmal nocturnal dyspnea*, orthopnea*, irregular or rapid heart beat, pedal edema*.
GI:	burning tongue*, dysphagia, hematemesis*, nausea, vomiting, jaundice, tea-colored urine, light colored stools*, loss of taste for cigarettes*, diarrhea, constipation, melena*, hematochezia*, change in bowel habits*, mucus in stool, fatty stools*, tenesmus*.
RE:	enlarged glands.
Urologic:	urgency*, frequency*, nocturia*, hesitancy, diminished force of stream, dysuria*, double voiding, polyuria, hematuria*, incontinence.
Genital:	breast mass, breast discharge*, vaginal (or penile) discharge, menorrhagia*, diminished periods.
Vascular:	claudication*, Raynaud's phenomenon*.
Hematologic:	bleeding diathesis*, burning skin*.
Bone:	arthralgia*, joint swelling or tenderness, morning stiffness.
Coverings & Connective Tissue:	joint swelling or tenderness.

SYSTEMIC:

Chills: Significant chills—teeth-chattering ones—usually mean bacteria in the normally sterile bloodstream. (Sterile means no living infectious agent is present—no bacteria, virus, fungus, or parasite.) Everything inside the body not directly in contact with the air is sterile—blood, lymph, urine, spinal fluid, and all the internal organs. The mucosal surfaces of the nose, mouth, upper trachea, and intestines are colonized by friendly bacteria, viruses, and fungi.

Bacteria in the bloodstream is a highly dangerous situation called sepsis. In capturing the bacteria, white blood cells release potent chemicals that make a patient hypotensive and delirious.

Fatigue: Fatigue is not the same as weakness. Fatigue means you start out with normal strength, but tucker out prematurely. Weakness means you start out weak.

Anorexia: Loss of appetite. (An = without, orexia = desire.)

Night Sweats: Significant night sweats are pajama-changing ones.

SKIN:

Alopecia: Hair loss. (Alopex is Greek for fox, a frequent sufferer of mange.)

Urticaria: A bumpy, pruritic (itchy) rash—hives. (From the nettle plant of the genus urtica.)

NEUROMUSCULAR:

Syncope: Fainting. (Kopto, to cut off, in Greek.)

Seizure: An electrical thunderstorm beginning in one area of the brain and either confining itself there or spreading throughout the entire brain. Seizures manifest as recurrent, stereotyped spells ranging from jerking of a thumb, to spells of bizarre behavior, to frank convulsions (patient falls and shakes all over). Synonyms: epilepsy, fit, spell.

Delusion: A thought which the patient believes is true, but he's the only one in the world who does. The thought is held despite facts that would normally lead one to a rational, logical alternative. If only two people believe something illogical, the delusional situation is called "folie a deux." A logically impossible idea shared by a *group* of people—that Moses separated the Red Sea or that Jesus rose from the grave—is called a belief.

Hallucination: A visual or auditory delusion: a vision or voice which no one but the patient believes he experienced. A dream, for example, is not a hallucination because everyone agrees you experienced it, regardless of how bizarre it was. An illusion, in contrast, is a disturbance of a *real* sensation, like mistaking a distant tree trunk for a human torso.

Paranoia: A state of suspicion, jealousy, secretiveness, and imagined persecution.

Mania: Unproductive, hyperactive, euphoric skipping from task to task, or idea to idea. A manic patient is a maniac. (Mene is Greek for moon, as luna (lunatic) is in Latin.)

Dysphasia: Speech which contains spelling or grammatical mistakes (over and above the patient's usual speech). (Dys = defective, phasis = speech.)

Red Washout: The color red does not appear as brilliant and rich.

Diplopia: Double vision. In Greek, diplous is double (actually doubled over, folded, like a diploma) and opsis is vision.

Tinnitus: Ringing in one or both ears.

Vertigo: A spinning sensation or a feeling of movement (as if you were on board a ship).

Dysarthria: Slurred speech. Dysphonia is a disturbance of the voice: hoarse, soft, nasal, etc.

Dysphagia: Difficulty swallowing.

Drop Attacks: A sudden collapse to the ground, lasting seconds, without loss of consciousness.

Hesitancy: Having to wait for the urinary stream to start.

Double Voiding: After emptying the bladder, having to return within minutes to urinate again.

Incontinence: Urinating or defecating on oneself.

Impotence: Difficulty getting an erection, or difficulty ejaculating.

EYES:

Halos: Usually seen around bright objects. Van Gogh may have suffered from this.

ENDOCRINE:

Polyuria: Urinating large amounts of urine. The opposite of polyuria is oliguria (oligo = few or little)

Polydipsia: Excessive drinking.

Amenorrhea: No periods.

Galactorrhea: Milk dribbling from the breasts.

Hirsutism: Excessive hair growth.

Head, Hand, and Foot Enlargement: Frequent symptoms of acromegaly (acro=extremity megaly=enlargement), a condition caused by a growth-hormone-secreting pituitary tumor. Enormous heights may be obtained if the tumor occurs before the child has stopped growing.

RESPIRATORY:

Epistaxis: Nosebleeds.

Dyspnea: Difficulty breathing, shortness of breath. Pneo (to breathe) is also the root for pneumonia.

Hemoptysis: Coughing up blood.

Wheezing: Spasm (narrowing) of bronchial tubes causes high pitched wheezing by obstructing air flow, like letting air escape through a balloon's tightly stretched neck.

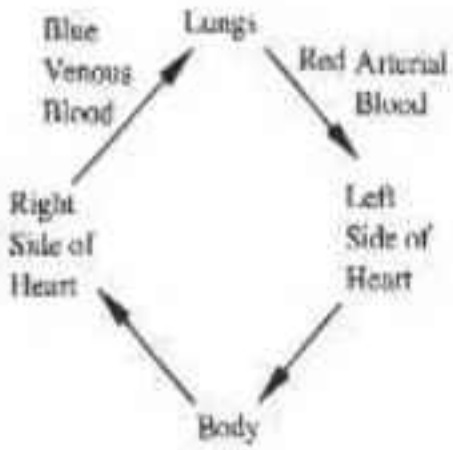
Sputum: Infected sputum is yellow or green (pus).

CARDIAC:

Angina: Chest pain due to inadequate coronary artery blood supply to the heart during periods of either exertion, sudden exposure to cold, or emotional excitement. The pain usually overlies part of the sternum and frequently radiates down one or both arms, or into the neck and jaw.

Paroxysmal Nocturnal Dyspnea (PND): Sudden shortness of breath during sleep due to daytime-accumulated pedal edema reentering the vascular system, overloading a weak heart, and backing up as pulmonary edema in the lungs.

Orthopnea: Shortness of breath while lying down, almost always due to heart failure:



The heart has a right and left side separated (functionally) by the lungs which oxygenate right-sided venous blood before returning it to the left ventricle. Heart failure dams up venous blood behind the left ventricle into the lungs, and behind the right ventricle into the body. High venous pressure in the pulmonary veins forces plasma to exude from delicate pulmonary capillaries into dry alveoli (resulting in pulmonary edema), while high venous pressure in veins throughout the body forces edema into the body's tissues. On account of gravity, edema in the body collects in the legs and feet as pedal edema. In the lungs, pulmonary edema accumulates at the lung bases during the day when the patient is upright, but redistributes throughout the lungs when the patient lies down. Wet lungs cannot breathe, hence the orthopnea. The solution patients usually stumble upon is to prop themselves up with an extra pillow or two.

Pedal Edema: Besides heart failure, any condition which causes excess fluid accumulation in the body, or which obstructs venous return to the right atrium (e.g. pericardial effusion) will also result in pedal edema. (An effusion is a puddle of fluid in one of body's spaces, typically resulting from a slowly leaking covering like the pleura, pericardium, or peritoneum.)

GASTROINTESTINAL:

Burning Tongue: A painful burning tongue, usually bright red and shiny smooth, is called glossitis, often a symptom of a vitamin deficiency.

Hematemesis: Vomiting blood. (Heme = blood, emesis = vomiting.)

Jaundice, Dark Urine, Light Colored Stool: Bile duct obstruction and certain liver diseases prevent bile excretion into the duodenum, so no pigment darkens the stool. Instead, bile builds up in the bloodstream, staining the eyes and skin yellow (jaundice) and spilling over into the urine (brownish, jaundiced urine). If the skin and eyes are jaundiced, but not the urine, then the obstruction must be somewhere before the liver conjugates intravascular bilirubin into water-soluble bile.

Loss of Taste for Cigarettes: A frequent, but unexplained, occurrence in liver disease.

Melena: Blood in the stool. If GI bleeding occurs in the stomach where gastric acids and enzymes can digest the blood, the released iron (from hemoglobin) turns the stool black, like tar, just as the stool turns black when you take iron pills.

Hematochezia: Bright red blood in the stool, indicative of bleeding in the small or large intestine beyond the reach of digestive enzymes.

Change in Bowel Habits: Cancer of the colon causes progressively worsening constipation, often associated with intermittent diarrhea as patients try to treat their constipation with laxatives. The diarrhea is often present on awakening and usually contains mucus and blood. Sometimes, patients note pencil-thin stools as the cancer strangulates a narrow stretch of colon.

Fatty Stool: Steatorrhea (steato = fat, rheo = to flow) results from intestinal malabsorption, allowing fat to escape into the colon. Because they float, the bulky greasy stools require several toilet flushes.

Tenesmus: Painful straining during urination or defecation.

UROLOGIC:

Urgency: Having to run to the toilet.

Frequency: Urinating many times a day.

Nocturia: Getting up at night to urinate.

Dysuria: Burning on urination.

Hematuria: Blood in the urine.

GENITAL:

Discharge: Fluid oozing from an orifice (hole).

Menorrhagia: Excessively heavy periods.

VASCULAR:

Claudication: Pain in an extremity on exercise. Muscles are crying in pain because of lactic acid accumulation from an inadequate blood supply. Analogous to angina.

Raynaud's Phenomenon: Recurrent bouts of arterial spasm which first produce blanching (no blood), then cyanosis (blood stagnating in tissues loses its oxygen and turns cyan, or blue), then rebound arterial dilation turning the skin red.

HEMATOLOGIC:

Diathesis: Susceptibility. Manifested as easy bruisability, bleeding from the gums, or excessive bleeding from a cut.

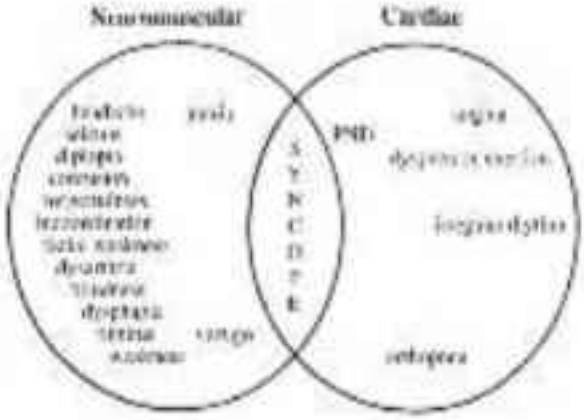
Burning Skin: Too many red cells and too much plasma protein sludge the blood. Sluggish blood flow through the skin makes the skin burn and tingle.

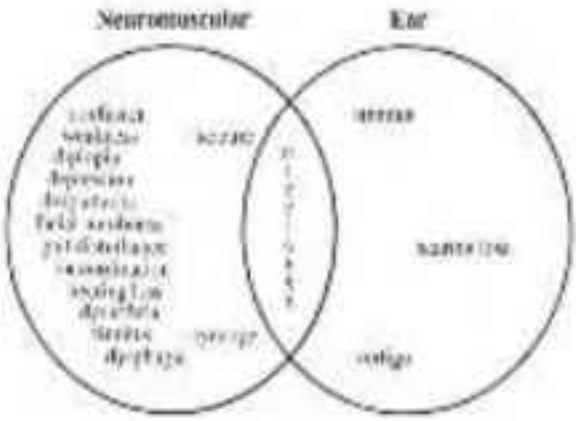
BONE:

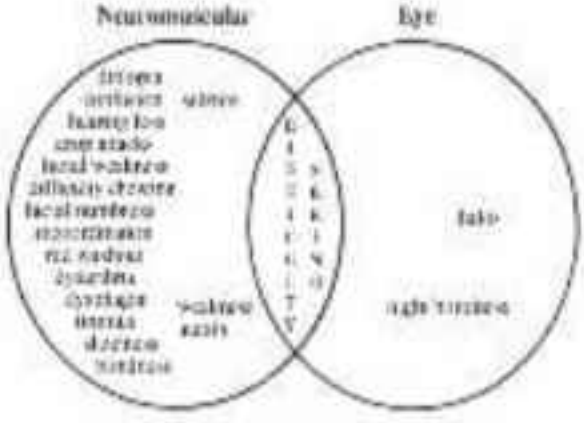
Arthralgia: Bone or joint pain.

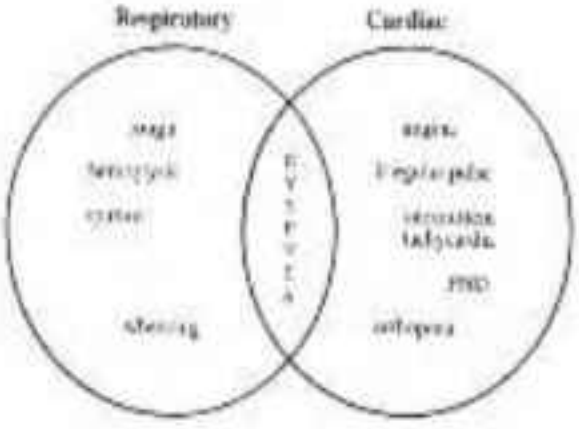
From the list of review of systems it should be apparent that allocating symptoms to a particular organ system is not always easy. Certain 'overlap' symptoms like dizziness, syncope, difficulty seeing, dysphagia, shortness of breath, and difficulty urinating do not fit neatly into one organ system. These overlap symptoms complicate the first step in physical diagnosis—establishing the presenting organ system.

To sort out which organ system an overlap symptom belongs to, *postulate* that it belongs to one of the overlapping organ systems. Then ask for the entire cluster of symptoms of your postulated organ system. If the patient denies those associated symptoms, try another postulated system. Schematically, the two overlapping organ systems are merely two overlapping Venn diagrams with the presenting symptom straddling the middle. As you seek the constellation of symptoms for each of the two overlapping organ systems, the patient's responses will soon reveal the symptomatic organ system through guilt by association.











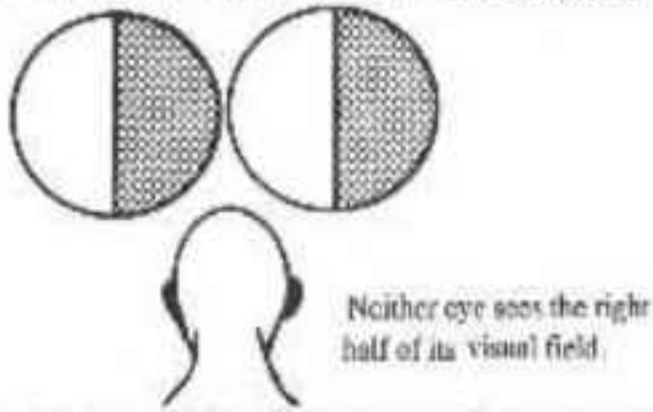


If the presenting organ system is still not obvious, ask any other questions which might help confirm the presenting organ system. For example, a history of *prior* insults to an organ system (like a past heart murmur) may provide strong circumstantial evidence. Even more helpful are questions reflecting knowledge of anatomy and physiology. A complaint of difficulty seeing, which by your questions crystallizes into a homonymous hemianopia*, immediately fingers the neurologic system as the presenting organ system.

Not uncommonly, however, it is impossible by the history alone to place the overlap symptom into either one of the overlapping organ systems, either because the patient denies all other symptoms besides the presenting one, or the patient's other symptoms are not specific enough to confidently implicate one of the overlapping organ systems. In this circumstance either consider both sites simultaneously in the anatomic differential diagnosis (chapter 3), or simply choose the more natural* overlapping organ

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Homonymous Hemianopia: Homonymous means 'the same' in both eyes. Hemi(half) an(no) opia(sight):



More Natural: By this I mean 'final common pathway.' For example, dysphagia more naturally belongs to the gastrointestinal system, because the final common pathway for all causes of dysphagia is the GI system. Analogously, syncope more naturally belongs to the neurological system, difficulty seeing to the eye, dyspnea to the respiratory system, and bladder symptoms to the urologic system.

system as the site of the presenting symptom. As you will see in chapter 4, the other organ system will then be considered in the etiologic differential diagnosis.

It should also have been apparent from the list of review of systems that pain is not pathognomonic of any one organ system. Pain can affect any organ system, and thus has no localizing value until you determine the characteristic constellation of associated symptoms directing you to the presenting organ system. The most helpful historical features for pain are:[2]

1. When was the first time in your life that you ever had a pain like this?
2. When did you first notice this particular pain?
3. Exactly what were you doing when the pain began—lying, sitting, stooping, standing, lifting, reaching, etc.?
4. Show me with one finger where it hurt you.
5. How long did the pain take to reach its maximum?
6. Did the pain go anywhere?
7. Did you have any other symptoms?
8. How long did the pain last?
9. Did the pain return? Was it the same pain?
10. How often do you have the pain?
11. What time of the day is it worst? Does it awaken you from sleep?
12. What kinds of things do you have to avoid because it will bring on the pain? (For example, pleuritic pain* suggests inflammation in the pulmonary pleura; exercise induced pain is commonly ischemic*.)
13. Can you make the pain go away? (With medication, or by resting or changing position, or by some other specific activity?)
14. What kind of pain is it? (Burning, electric pain is usually from peripheral nerves; pulsatile pain* is typically vascular; colicky pain* stems from a hollow organ such as gall bladder, stomach, intestine, ureter, or bladder.)

Analogous to pain, systemic symptoms of fever, chills, weight loss, fatigue, anorexia, and night sweats also have no localizing value unless associated with other more specific symptoms. Which means you must run through the list of review of systems until you find the upset organ system.

Pleuritic Pain: Sudden, sharp chest pain on inspiration, usually due to inflamed parietal and visceral pleurae rubbing against each other.

Ischemia: Ischemia is organ dysfunction resulting from an inadequate blood supply, almost always caused by arterial obstruction, venous obstruction, or low blood pressure. Claudication and angina are two good examples. From isc: to suppress, and hema: blood.

Actual death of an organ (or part of an organ) from an inadequate blood supply is called an infarct (or infarction). The dead tissue (tissue is any small area of an organ) undergoes necrosis (cell death).

Pulsatile Pain: Throbbing pain from excessive arterial pulsations.

Colicky Pain: Pain due to spasm of a hollow organ (intestine, gall bladder, ureter, bladder). The pain crescendos over approximately ten to twenty seconds and then gradually fades.

THE ANATOMIC DIFFERENTIAL DIAGNOSIS

THE CENTRAL TENET OF MEDICAL DIAGNOSIS is, first, make an anatomic diagnosis, then an etiologic diagnosis. Making an anatomic diagnosis means finding the upset organ system and then figuring out exactly where the lesion is within that organ system. Figuring out the exact anatomic diagnosis within an organ system is not always easy, because every one of the symptoms listed in chapter 2 may be caused by lesions in any number of anatomic sites within the presenting organ system. Shortness of breath, for example, may be due to a lesion almost anywhere from the nose to the alveoli. All these possible anatomic sites taken together are known as the anatomic differential diagnosis. Your first job in history-taking is to establish the anatomic differential diagnosis for the patient's chief complaint. You then use additional history to narrow the anatomic differential diagnosis.

Let's take it from the beginning again. A patient comes to you with a symptom. You determine the upset organ system and, based on your knowledge of anatomy and physiology, list the anatomic differential diagnosis within that organ system. For some symptoms, the anatomic differential diagnosis extends beyond a single organ system into two (rarely more) overlapping organ systems. If further history-taking does not favor one of these overlapping organ systems, then you have a choice. You can either include both in the anatomic differential diagnosis or choose the more natural one and allow the other will to be considered in the etiologic differential diagnosis (next chapter). The latter choice is preferable, because working simultaneously with two separate organ systems involves juggling too many anatomic sites in the anatomic differential diagnosis.

How you establish the anatomic differential diagnosis is up to you. Sometimes you will use your knowledge of anatomy, other times physiology, and most of the time anatomy and physiology together. For example, jaundice may result from excessive breakdown of red blood cells (hematologic system), inadequate uptake of bilirubin from the blood, impaired conjugation within the liver, or obstruction of bile flow from the liver or gall bladder.

The anatomic differential diagnosis does not only pertain to symptoms and signs. *Everything* in medicine—symptoms, signs, laboratory abnormalities, xray findings—has an anatomic differential diagnosis. Take anemia. What's its anatomic differential diagnosis? The presenting organ system is obviously the hematologic system, but

pathophysiologically* the patient is either not making blood, destroying it, or losing it. The anatomic differential diagnosis, then, is the bone marrow (where blood is made); spleen or bloodstream (where blood is destroyed); or intestines, kidneys, or uterus (where blood is lost).

Regardless of how you establish your anatomic differential diagnosis, anatomy always comes before etiologies. Physical diagnosis *begins* with an anatomic differential diagnosis. Whatever it takes—anatomy, physiology, biochemistry, pharmacology, bacteriology—*establish the anatomic differential diagnosis first*.

Trojan Horses

You began constructing the anatomic differential diagnosis by pinpointing the upset organ system and then listing possible sites for the lesion within that presenting organ system. But the anatomic differential diagnosis is more than a selection of sites within the presenting organ system. The presenting organ system may only be an innocent bystander to the real battle taking place between the etiologic insult and those arteries, veins, blood, lymph, connective tissue, or nerves *within* the presenting organ system. In other words, to disrupt the presenting organ system an etiologic agent need not directly attack the presenting organ system. It can accomplish the same damage by attacking any one of the Trojan Horses within the presenting organ system. Merely because of anatomic intimacy, every organ system is vulnerable to the bane of its "Trojan Horse" organ systems*.

In practice, it is nearly impossible to separate primary dysfunction (malfunction) of the presenting organ system from secondary dysfunction resulting from a primary attack on one of its Trojan Horses. For this reason, the anatomic diagnosis—which began with multiple sites within the presenting organ system—must always be expanded into an anatomic differential diagnosis that includes the Trojan Horse organ systems.

The anatomic differential diagnosis is a critical step in physical diagnosis. Only *after* you've established an anatomic differential diagnosis can you begin to consider etiologies. Physical diagnosis is nothing more than a search for the original etiology, the one that first shoved the patient off balance. To find that original etiology, you need to identify not the presenting organ system, the one that surfaced first, but rather the one that *failed* first—the "primary" organ system, the one that first suffered the primary insult. By including the Trojan Horses, the anatomic differential diagnosis merely widens the search for that primary organ system.

Armed with an anatomic differential diagnosis, we can turn our attention now to etiologies.

Pathophysiologically: Pathophysiology is the mechanism by which an etiologic insult causes an organ system to malfunction. The term is shortened from "pathologic physiology."

Trojan Horse Organ Systems: Just as they welcomed the Trojan horse within its walls, so does every organ system harbor one or more potentially harmful organ systems.

ETIOLOGIES

ESTABLISHING A WELL-THOUGHT-OUT ANATOMIC DIFFERENTIAL DIAGNOSIS greatly simplifies the search for the etiologic diagnosis. Instead of trying to memorize a separate list of etiologies for every conceivable symptom and sign, you can simply take each site in the anatomic differential diagnosis and consider etiologies for each site. This will focus your attention better and allow you to approach the patient's problem in a logical, consistent manner.

What we need now is a logical way to consider all the possible etiologies for any given site. How *likely* a particular etiologic insult is depends on your knowledge of diseases. Learning which of the thousands of etiologic insults can do what to which organ systems is called medical school.

Most doctors organize etiologies into half a dozen or so general categories. The ones I use are: **D**rugs, **I**nfection, **G**enetic/Degenerative, **I**mmunologic, **T**umor, **T**rauma, **O**rgan Dysfunction, and **M**echanical (**DIG IT TOM**).

Drugs refers to any exogenous agent like drugs, of course, but also to things like food, intravenous transfusions, vitamins, radiation, and excessive heat or cold. **Infection**[1], **Immunologic**[2], and **Tumor**[3] etiologies are self-explanatory. **Genetic/Degen-**

Infection: Infections are caused by bacteria, fungi, viruses, spirochetes, rickettsia, or parasites.

Bacterium: An organism made up of only one cell without a nucleus, i.e., the DNA floats freely in the cytoplasm. Bacteria are identified by their staining properties. If the Gram stain turns it blue, the bacterium is Gram positive; if it stains pink, the bacterium is Gram negative. Mycobacteria (tuberculosis), impermeable to the Gram stain, require a tightly binding Ziehl Neelsen stain which even acid can't leech out, making mycobacteria 'acid fast.'

Fungus: Molds and yeasts. A mold lengthens by budding newborn cells from its tips, forming long, delicate, branching filaments (fuzzy mold on stale bread is a good example). A yeast multiplies by releasing individual buds.

Virus: An infinitesimally small sac of DNA which ingeniously injects itself into a cell and pirates the cell's machinery to make new viruses.

Spirochetes: Spiral-shaped, single-celled organisms which move by spinning like a corkscrew.

Parasite: Any organism, ranging from unicellular amebae to complex tapeworms, which lives off the earnings of others. Rickettsia are intracellular parasites.

Immunologic: Mediated through the reticuloendothelial system.

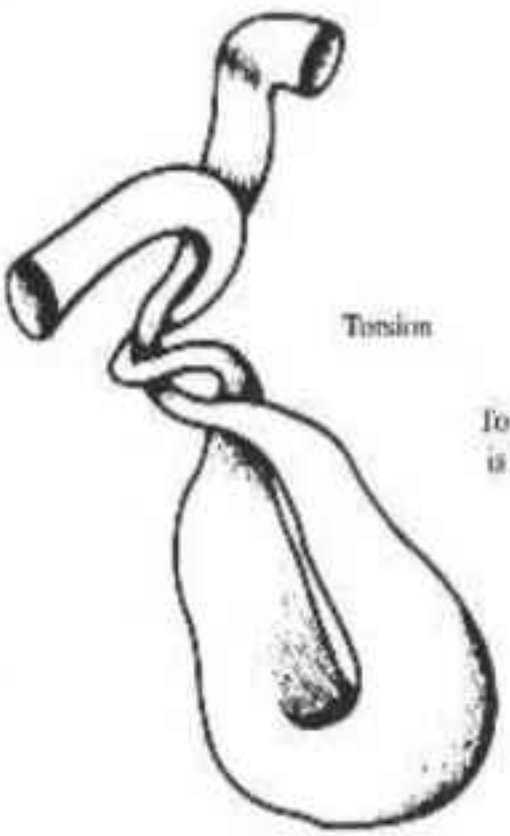
Tumor: A benign tumor grows as a lump, allowing easy total removal with no recurrence. Benign does not mean the tumor won't kill—it will if it's in the right location. Malignant tumors (cancer) cannot, in general, be completely removed for two reasons: either delicate strands of tumor cells have infiltrated widely into neighboring tissues (resembling the legs of a crab—crab in Latin is cancer, carcinoma in Greek), or else the cancer has already metastasized (spread to a distant site) beyond the reach of surgery. Subtotal (incomplete) removal of cancer is often followed up with radiation or chemotherapy (drugs active against cancer).

erative refers to genetic, congenital*, and degenerative illnesses*. **Mechanical** refers to pressure, obstruction, constriction, distension, compression, torsion*, intussusception*, herniation*, prolapse*, aneurysmal* dilation, or diverticulum* of an organ. **Traumatic** means that the insult—which may spring spontaneously from within the patient's body or may result from an external force—caused a tearing, perforating, rupturing, dislocating, dissecting*, or crushing injury.

Congenital: An illness which was already present at the time of birth, having been acquired 'in utero' (sometime during the nine month gestation).

Degenerative Illness: An idiopathic (no known cause) illness that causes an unrelenting downhill course. Degenerative is a term of ignorance. If we knew the presumed chemical or viral explanation for the degeneration, the etiology would be re-categorized.

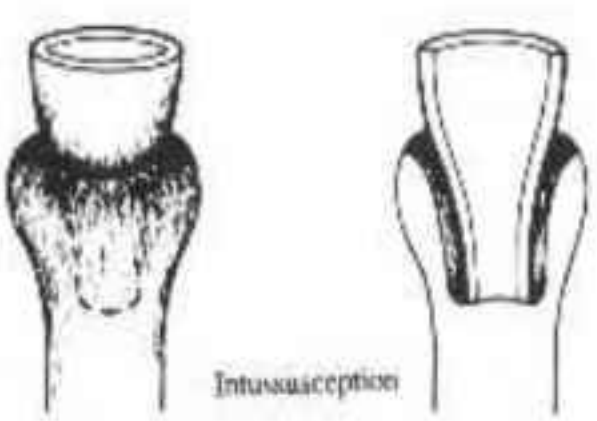
Torsion: Twisting. Causes obstruction.



Torsion

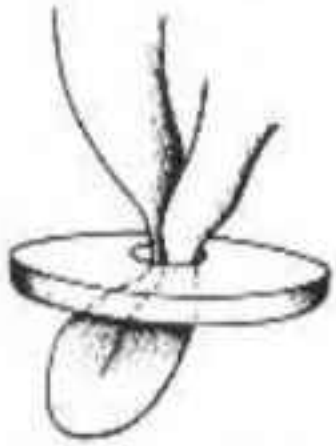
Torsion affecting the colon is called volvulus.

Intussusception: Telescoping, almost always a telescoping of the intestines. Gut intussusception causes obstruction.

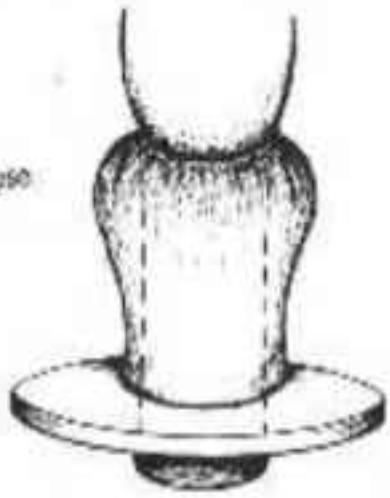


Intussusception

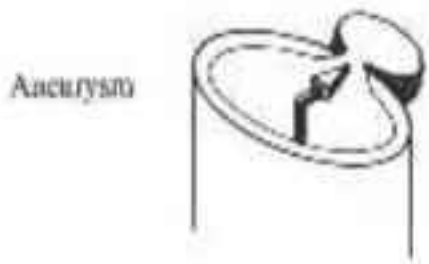
Herniation: Bulging of an internal organ through a hole in the cavity containing the organ. Usually refers to the intestines bulging through the abdominal wall or up through the diaphragm, but can refer to the brain herniating through gaps in the membranes and bones encasing the brain. A common analogy for herniation is an inner tube herniating through a hole in the tire tread.



Prolapse: Sagging of a internal organ, often through a normal opening, like the rectum through the anus, the uterus through the vagina, or the umbilical cord through the cervix.



Aneurysm: Bulging of the wall of an organ because of a structural defect in the wall. Aneurysms only occur in the heart's ventricular wall, or along arteries or veins.



Diverticulum: Like an aneurysm, a diverticulum is a bulging (actually a small outpouching) of the wall of an internal organ (almost always the gut) due to a defect in its wall. Diverticuli occur most commonly in the large intestine at spots where blood vessels enter and leave the colonic wall. Not uncommonly these diverticuli bleed, sometimes profusely.

Dissecting: To slip between tissue layers, separating the layers instead of destroying them. A common example is dissection between the layers of an arterial wall by blood leaking *into* the arterial wall. The danger of arterial dissection is acute obstruction of the artery itself or of a major branch off the artery.

Organ Dysfunction is the failure of a distant organ system, separate from the presenting one, to carry out certain important functions which other organ systems normally depend on. Once one of these distant organ systems fails, the effects may be felt—usually via the bloodstream—in far-off places like the presenting organ system. Almost every organ system may play a 'Distant Domino' function. Below is a list of these important Distant Domino functions:

Organ System	Relevant Function
Systemic:	Maintain normal temperature and blood pressure*.
Skin:	
Neurologic:	Prevent seizures, maintain the psyche*, prevent weakness.
Eyes:	
Ears:	Maintain normal labyrinth function.
Endocrine:	Maintain normal blood levels of calcium*, phosphate*, thyroid hormone*, cortisol*, glucose*, estrogen, and testosterone.
Respiratory:	Maintain normal blood PO_2*, pH, and pCO_2*.
Cardiac:	Maintain regular rhythm, normal valves* and heart wall*, and keep venous pressure low*.
GI:	Maintain normal esophageal and intestinal peristalsis*, normal gastric acid and intrinsic factor secretion, normal pyloric opening, normal hepatic and gall bladder function*, normal pancreatic juice secretion*, and normal small intestinal absorption*.
RE:	No excessive platelet or erythrocyte consumption by the spleen.
Urologic:	Creatinine* and BUN* excretion, electrolyte* and uric acid* regulation, free water* regulation.
Genital:	Maintain secondary sexual characteristics.
Vascular:	Prevent hemorrhage, obstruction*, vasospasm* or vasodilation*.
Hematologic:	Maintain normal hematocrit*, normal WBC count*, normal platelets*, normal lipids*, normal protein*, and clot the blood* normally.
Bone:	
Coverings & Connective Tissue:	Prevent constriction or stiffness of the underlying internal organ.

SYSTEMIC:

Blood Pressure: Hypotension becomes truly worrisome when the systolic falls below 90 mm, unless that's the patient's usual pressure. Symptoms often occur if the blood pressure *suddenly* drops, regardless of the level it falls to.

NEUROMUSCULAR:

Psyche: Emotional well-being. Persecuted by the goddess Venus, Psyche symbolizes humanity's struggles of the mind.

ENDOCRINE:

Calcium: Normal value: 8.5–10.5 mg%. Since calcium is carried by serum albumin, a low calcium level may reflect a low serum albumin instead of a true disturbance of calcium.

Phosphate: Normal value: 2.5–5.0 mg%. Phosphate levels see-saw with the calcium level (the higher the calcium, the lower the phosphate, and vice-versa).

Thyroid Hormone (Thyroxine): Normal value: 5–12 mcg% (a microgram is 1/1000th of a milligram). *Euthyroid* means the thyroid is functioning normally.

Cortisol: Normal value: 6–24 mg% (8 a.m.); 3–12 mg% (4 p.m.).

Glucose: A normal fasting glucose is between 65 mg% and 120 mg%. Like hypotension, a precipitous fall in glucose might produce symptoms that a gradual fall wouldn't.

RESIRATORY:

pO_2: A normal arterial pO_2 is 100mm. Less than this, called hypoxia (hypo-oxia), is determined by directly measuring the pO_2 in arterial blood, blood obtained by (usually painful) arterial puncture. An arterial pO_2 less than 90 mm is an eyebrow raiser; less than 80 mm should make you stir in your chair; less than 70 mm should make you get up and do something.

pCO_2: Anything above a normal pCO_2 of 40 mm should alert you to possible impending respiratory arrest unless you know the patient walks around (usually smoking) with a pCO_2 of 45 mm or more. The arterial pO_2, pCO_2, and pH are the "blood gases."

A sensitive test of the lungs' ability to move air is the "vital capacity," the number of cc's exhaled after a deep breath. Men should exhale over 4 liters, women 3–3.5 liters. Dangerous vital capacities are below 1 liter; less than half a liter (500 cc) usually requires intubation (insertion of an endotracheal tube through the mouth or nose into the trachea) and artificial ventilation.

CARDIAC:

Normal Valves: Valves which don't fully open are stenotic; those that don't close completely are insufficient or regurgitant (blood regurgitates back through them).

Normal Heart Wall: The heart wall, or myocardium (myo= muscle, cardium=heart) should be smooth, and free of blood clots or holes in the atrial and ventricular septae. Nor should the ventricular wall have an aneurysm (the scar tissue which forms in the heart wall after a heart attack may bulge outward during systole).

Venous Pressure Low: A normal heart pumps blood as fast as blood is delivered to it from the superior and inferior vena cavae, but a failing heart causes venous blood to back-up behind it. Venous pressure then rises above its usual 2-4 mm Hg (mercury), or its equivalent 2.5-5.0 cm water (1 mm Hg = 1.3 cm water). A right atrial or superior vena cava pressure (they're equivalent since there's no valve between them) above 13 cm water suggests right ventricular failure (or obstruction to blood flow through the right ventricle); a left atrial pressure above 18 cm water reflects a failing left ventricle.

These pressures can be measured with catheters (tubes) passed via a peripheral vein into the right atrium, or on through the pulmonic valve into the pulmonary artery. A Swan Ganz catheter wedged into a branch of the pulmonary artery can measure left atrial pressure transmitted backwards through the pulmonary veins.

GASTROINTESTINAL:

Peristalsis: Absent esophageal peristalsis is called achalasia; absent small or large intestinal peristalsis is called ileus.

Hepatic Function: Hepar is Greek for liver. The liver has four major jobs: to absorb bile from the bloodstream, to detoxify poisonous food and harmful metabolites, to synthesize serum proteins, and to store glucose (as glycogen) for later release into the bloodstream when the serum glucose falls.[1]

Old red blood cells (destroyed in the spleen) release hemoglobin into the bloodstream. The heme part of the hemoglobin molecule is metabolized intravascularly to water-insoluble bile, called indirect bilirubin. The liver picks up this bile from the blood, converts it into a water-soluble form, called 'direct' bilirubin, and secretes direct bilirubin via bile ducts into the gallbladder for storage. One manifestation of hepatic dysfunction is a rise in either the indirect or direct bilirubin, depending on whether the block is before or after conjugation of indirect to direct bilirubin. Normal serum bilirubin is less than 1 mg% (indirect bilirubin less than 0.70 mg%, direct bilirubin less than 0.30 mg%). The serum bilirubin may also rise because of overproduction of bilirubin, for example, when hemolyzing red blood cells release their heme (destined to become bilirubin) into the bloodstream.

Hepatic enzymes metabolize toxins which have either made their way into the body from the outside or have else formed as byproducts of the body's normal chemistry, called intermediary metabolism. Liver damage releases those hepatic enzymes into the bloodstream where they are detected by a simple blood test. SGPT (serum glutamic pyruvic transaminase) is a relatively specific hepatic enzyme; SGOT (serum glutamic oxaloacetic transaminase) and LDH (lactic dehydrogenase), though strongly suggestive of liver damage, may also come from damaged muscle. Another hepatic enzyme, alkaline phosphatase, is normally secreted in the bile, so an elevated serum alkaline phosphatase suggests a block in bile secretion in the liver itself or else somewhere along the bile duct. Alkaline phosphatase is also used to resorb bone whenever the body wants to raise the serum calcium or remold a bone. An elevated serum alkaline phosphatase, therefore, must be 'fractionated' to determine the percentage from liver and bone.

Finding low levels of circulating coagulation factors (synthesized in the liver) is another useful way to detect liver dysfunction. The simplest test for this is the prothrombin time, a blood test which measures the speed of blood coagulation. Prolongation of the 'protime' beyond the normal twelve seconds raises the risk of spontaneous bleeding into the brain, gut, kidney, and retroperitoneal space (between the peritoneum and back muscles).

Pancreatic Juice Secretion: The pancreas' job is to secrete an adequate amount of enzymes and to confine those enzymes within its pancreatic ducts. Should pancreatic digestive enzymes leak into normal pancreatic tissue, the pancreas will begin digesting itself, a painful and dangerous inflammatory condition called pancreatitis. During pancreatitis, intracellular pancreatic enzymes escape from the inflamed pancreas into the bloodstream, detectable as an elevated serum amylase. Pancreatic dysfunction, especially chronic dysfunction, may also be detected by finding undigested meat fibers or excessive fat in the stool.

Small Intestinal Absorption: One simple screening test is the serum carotene, a fat-soluble vitamin normally absorbed by the small intestine. Slightly more complicated is the D-xylose excretion test: intestinal malabsorption prevents oral xylose from being absorbed, detectable by finding low levels of xylose in the urine after a standard 25 gram oral dose.

Vitamin B12 absorption also requires normal small intestinal function, but a low serum B12 level still needs a Schilling test to distinguish insufficient intrinsic factor secretion by the stomach wall from impaired absorption of the B12/intrinsic factor complex through the terminal ileum.[2] In the Schilling test, like the D-xylose test, urine levels of radioactive B12 are measured after a standard oral dose of radioactive B12. But unlike xylose, B12 is used by the body; there are innumerable receptors throughout the body for B12 to attach to instead of entering the urine. To prevent attachment of radioactive B12 to normal receptors, a large dose of non-radioactive B12 is first injected intramuscularly (bypassing small intestinal absorption) to saturate those B12 binding sites. Then, when radioactive oral B12 is absorbed, it has no place to go but into the urine. If a low urine B12 level is found, the B12 was not absorbed by the gut. The test is then repeated with intrinsic factor. If the urine B12 level now rises, then the reason the patient didn't absorb B12 is that his stomach didn't secrete intrinsic factor. If the urine B12 level remains low, then small intestinal absorption is abnormal. (A few other possibilities exist, like tapeworms or excessive intestinal bacteria consuming the B12/intrinsic factor complex inside the small intestine.)

UROLOGIC:

Creatinine: Normal muscle metabolism releases creatine into the bloodstream where creatine is converted to creatinine and excreted by the kidney. The serum creatinine should be less than 1.5 mg%. A level of 2–2.5 mg% often means the kidneys are working at only about half capacity. A creatinine of 10 mg% usually means the kidneys need help (i.e., dialysis) to clean the blood. Kidney failure is called uremia: ur(urine) emia(in the blood). Azotemia (azote is nitrogen) is synonymous with uremia.

A more accurate assessment of kidney function is the creatinine clearance, a measurement of the volume of blood cleansed by the kidneys per minute. Men should cleanse over 100 cc/minute, women over 85 cc/min. Fortunately, dialysis isn't needed until the creatinine clearance falls to less than 10 cc/minute.

BUN (Blood Urea Nitrogen): In the normal turnover of proteins, the body rids itself of toxic nitrogen by hooking two nitrogens together into a urea molecule. The serum BUN should be below 20 mg%, roughly paralleling the serum creatinine by a factor of 10.

Since urea, but not creatinine, is capable of diffusing back into the body across the kidney tubules, the ureter, and the bladder, a BUN: creatinine ratio greater than 10 usually means slow urine flow anywhere through the kidney tubules, ureter, or bladder (giving urea time to diffuse back into the body).

Electrolytes:

	Normal Value	Too High/Too Low
Sodium (Na^+)	135–145 MEq/L	Hyper/Hyponatremia
Potassium (K^+)	3.5–5.0 MEq/L	Hyper/Hypokalemia
Chloride (Cl^-)	98–106 MEq/L	Hyper/Hypochloremia
Bicarbonate (HCO_3^-)	21–30 MEq/L	High/Low Bicarb

MEq/L = Milliequivalents per liter of blood

Uric Acid: A metabolic breakdown product of DNA. A uric acid level above 7 mg% may precipitate as crystals within joints, causing a painful gout attack.

Free Water: The 'free' refers to water that's not bound to another molecule—i.e., floating free.

VASCULAR:

Obstruction: Partial arterial obstruction deprives organs of oxygen, glucose, and other necessary nutrients, a condition called ischemia (organ dysfunction from an inadequate blood supply). Unless there are other, 'collateral,' arteries also supplying the same area, complete arterial obstruction causes infarction or necrosis (death) of the area normally supplied by that artery.

Venous obstruction is usually less serious than arterial obstruction, because venous collaterals are far more numerous than arterial collaterals.

The body responds to any area of infarction with an inflammatory assault. Blood vessels dilate to bring in new white blood cells, especially macrophages, to consume the dead tissue. Later, ubiquitous fibroblasts, cells which normally maintain and replenish the body's connective tissue, move into the infarcted area to lay down collagenous scar tissue.

Collagen deposition also results from infectious and immunologic inflammation. Though collagen provides firm support, it doesn't do anything. Excessive scarring may eventually leave the organ with little if any normal tissue.

Vasospasm: Too much vasospasm prevents blood from getting through.

Vasodilation: Too much vasodilation prevents blood from flowing by reducing the blood pressure.

HEMATOLOGIC:

Hematocrit: The percentage of whole blood (plasma and red cells) made up of red blood cells. The hematocrit is determined by centrifuging whole blood (which compacts the red blood cells), and then measuring the fraction of blood made up of red blood cells. In males, a hematocrit of 40–50% is normal, in females 37–47%. Above 55% (called polycythemia) is too high, the danger being blood sludging. A low hematocrit, called anemia, limits oxygen delivery to the body's organs.

WBC Count: The normal white blood cell count is less than 10,000 WBC's per cubic millimeter. Higher levels usually mean that the white blood cells are out looking for an inflammatory battle.

Since neutrophils (polymorphonuclear leukocytes) form the first wave of an inflammatory attack, an elevated blood neutrophil count signifies ongoing inflammation. Polys normally constitute about 50–75% of the total white blood cells. During inflammation this percentage may rise to 80–95%. Moreover, in its rush to manufacture more and more polys, the bone marrow spews out immature ones, called bands. A higher percentage of bands is known as a 'left shift,' almost as indicative of inflammation as a rise in the total WBC count or rise in percentage of neutrophils making up the total WBC count.

Platelets: Normally number between 150,000 and 400,000 per cubic millimeter.

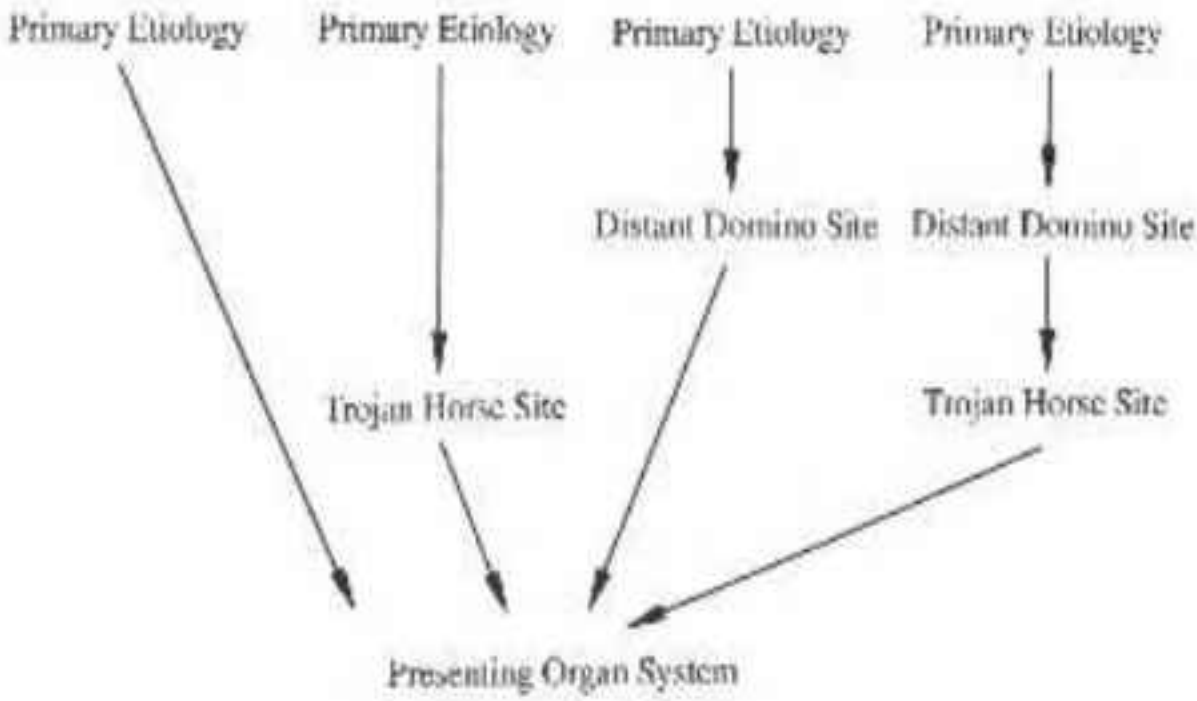
Lipids: The two major lipids are cholesterol and triglycerides. Cholesterol should ideally be less than 200 mg%, but 250 mg% is acceptable. Triglycerides should be less than 150 mg%.

Protein: Total serum protein should range between 6.5 and 8.0 grams %.

Clot the Blood: The prothrombin time (PT) measures the extrinsic limb of coagulation; the partial thromboplastin time (PTT) measures the intrinsic limb. More sophisticated tests can pick out which specific factor is missing when the PT or PTT is prolonged.

Pathways of Disease

The concept of Trojan Horses and Distant Dominoes is important in understanding how diseases can begin with an attack on the primary anatomic site but surface in a different location—in the presenting organ system. Primary etiologies may reach the presenting organ system in one of four ways. They may attack the presenting organ system directly, or else one of the Trojan Horses. Third, they may attack a Distant Domino which then attacks the presenting organ system, or finally, they may attack a Distant Domino which then attacks a Trojan Horse. In flow chart form:



What this diagram means is that every Distant Domino and Trojan Horse organ system plays a dual role. Beginning as mere anatomic sites, when victimized by an etiologic insult, Distant Dominoes and Trojan Horses are immediately converted into an etiologic accomplice against the presenting organ system!

Medical diagnosis requires that you reverse this order: once you believe that a Distant Domino is disrupting the presenting organ system, you must convert that 'criminal' distant organ system back into a 'victim' in its own right, and then seek the primary etiologic insult to *it*. This is done by treating the Distant Domino as any other other site in the anatomic differential diagnosis, namely, by running the Distant Domino through its own column of DIG IT TOM etiologic categories. In other words, if one of the possible etiologic insults happens to be another organ system, then consider all the possible etiologic insults to *that* organ system until you reach the original, primary insult. (This is automatically done for the Trojan Horses because the Trojan Horses are already included in the anatomic differential diagnosis.)

Let's take a typical case of someone complaining of dyspnea, which indicts the respiratory system. The presenting organ system is the respiratory system, but you must now decide if the *primary* pathology is in the lungs, or in one of the Trojan Horses in contact with the lungs—the blood vessels, blood, lymph channels, or pleura; or in a Distant Domino organ system completely separate from the lungs.

Examples of **primary** pulmonary disease include pneumonia, lung cancer[4], bron-

chiectasis*, and emphysema*. Alternatively, the primary pathology may just as easily lie in a **Trojan Horse** within or around the lungs like pulmonary arteritis*, pulmonary emboli*, lymphatic infiltration* by cancer cells, or a pleural effusion. Illnesses which fall into the **Distant Domino** pattern of disease might include weakness of the respiratory muscles* or pneumonitis from uremic* toxins. Heart failure, causing blood to back up into the lungs (water-logging them), is another example of a physically separate organ system presenting (via the bloodstream) in the respiratory system.

Should you decide that one of the Distant Dominoes is the etiologic agent against either the presenting organ system or one of the Trojan Horses, you must then decide why that Distant Domino malfunctioned. You need to convert that criminal Distant Domino into a victim itself and consider etiologic insults against *it*. In the example above, suppose you decide that heart failure caused your patient's dyspnea. Fine, but now you need to know why his heart failed. Is the heart suffering from viral myocarditis, a coronary arteritis, hyperthyroidism*, atherosclerosis, etc., etc.?

Simply tracking down the primary, instigating organ system—whether it be the presenting organ system, one of its Trojan Horses, or the first Domino—is not enough. You must then determine what insult caused the failure of that initial organ system. This is one of the reasons internal medicine can be so difficult. You have to understand the anatomy and physiology of each organ system well enough to appreciate the love-hate relationship of every organ system to its Trojan Horses and Distant Dominoes—how every organ system can be simultaneously dependent upon and vulnerable to its Trojan Horse and Distant Domino organ systems.

Bronchiectasis: Due to dilated bronchial tubes which cannot cough up phlegm: the phlegm subsequently puddles and becomes chronically infected.

Emphysema: Widespread alveolar wall destruction, which reduces the surface area of the lung and thus its oxygen absorbing capacity. In addition, the lungs' small bronchioles lose their surrounding support. So when the patient exhales, his bronchioles collapse, trapping deoxygenated air in the alveoli. Patients counter by pursing their lips when exhaling. The back pressure distends the bronchioles, allowing deoxygenated air to escape. Emphysema is almost always due to smoking.

Arteritis: Inflammation within the wall of an artery frequently obstructs blood flow through the artery, or on occasion destroys the wall, causing an arterial hemorrhage.

Embolus: A blood clot, bit of cholesterol, or clump of platelets, originally attached to the wall of an artery or vein, but which breaks away from the wall, floats downstream, and wedges itself into a smaller vessel, thereby obstructing blood flow through that downstream vessel.

Emboli from veins in the pelvis or legs float through the right ventricle and lodge in the lungs' arterioles where, hopefully, sufficient collateral blood flow will prevent lung infarction. In this way the lungs filter the body's venous circulation and prevent emboli from reaching the arterial circulation and causing dangerous infarctions of the internal organs.

Lymphatic Infiltration: Lymphatic obstruction dams up proteins into an organ or an entire extremity. The protein, in turn, soaks up fluid, causing edema (fluid accumulation), in this case pulmonary edema.

Respiratory Muscles: Besides the diaphragm, respiratory muscles include the intercostal muscles (inter = between, costal = rib), and, during labored breathing, some neck muscles.

Uremia: Renal (kidney) failure allows toxic metabolites normally cleared by the kidneys to accumulate and affect every organ system, including the lungs which may suffer initially from a non-infectious inflammatory attack directed at toxins depositing in the lungs.

Hyperthyroidism: Excessive thyroid hormone can whip the heart to the point of heart failure.

ETIOLOGIC DIFFERENTIAL DIAGNOSIS

THE ETIOLOGIC DIFFERENTIAL DIAGNOSIS is simply a list of all the diseases that could conceivably cause your patient's illness. You reach the etiologic differential diagnosis by first establishing an anatomic differential diagnosis, and then constructing an etiologic differential diagnosis for *each individual site* in the anatomic differential diagnosis. As you can imagine, a comprehensive differential diagnosis can be quite long, almost overwhelming. The purpose of history-taking is first to narrow the anatomic differential diagnosis and then to narrow the etiologic differential diagnosis.

Initially, the anatomic differential diagnosis consisted of the presenting organ system, but with the right questions, questions based on your understanding of anatomy and physiology, you quickly narrow the anatomic differential diagnosis to specific sites within the presenting organ system. By imagining the gross* and microscopic anatomy of those sites, you then list the Trojan Horse organ systems to complete the anatomic differential diagnosis. Now what? You have an anatomic differential diagnosis. How do you construct an etiologic differential diagnosis?

Naturally, any disease capable of injuring a site within the presenting organ system belongs in the etiologic differential diagnosis. So should any disease that's capable of injuring one of the Trojan Horse organ systems. To pare down all these etiologic possibilities, postulate each illness, and then elicit additional symptoms and other historical facts to confirm or refute each illness. Which means you have to start carrying around thumbnail sketches of every medical illness you encounter so that when you postulate an illness, you can compare your thumbnail sketch against the patient's signs and symptoms.

Let's, for example, take a typical symptom like dysphagia. As you recall, dysphagia is an overlap symptom which requires eliciting other complaints to decide if your patient's dysphagia is the tip of an iceberg for the gastrointestinal or neuromuscular system. Ideally, further questions would point you to one or the other organ system, and from there you would further narrow the anatomic differential diagnosis to a selection of possible sites within that presenting organ system.

Suppose, to make it tough on ourselves, that further questioning cannot distinguish which constellation of symptoms dysphagia belongs to. The patient denies other gastrointestinal symptoms of hematemesis, more difficulty with solids than liquids (esophageal narrowing), chest or abdominal pain, melena, or diarrhea. Likewise he denies neurologic symptoms of facial numbness, diplopia, dysarthria, nasal regurgitation, neck weakness, or weakness lifting his arms over his head. Because swallowing

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Gross: Gross anatomy is anatomy discernible to the naked eye.

is more intimately connected to the GI system, we'll make the GI system the presenting organ system. The Trojan Horses within the GI system include nerves, muscles, lymphatics, blood vessels, blood, and coverings & connective tissue.

By including the Trojan Horse organ systems, you have defined all the potential sites of primary (not just presenting) organ dysfunction—the anatomic differential diagnosis. To construct the etiologic differential diagnosis, list the anatomic differential diagnosis across the top of a page, and the etiologic categories down the left side.

Beginning with the first etiologic category, Drugs, think of all the possible exogenous agents that can affect the GI system or any one of its Trojan Horses to produce dysphagia. Then think of Infectious Diseases which might affect the GI system or one of the Trojan Horses. Continue with Genetic/Degenerative, Immunologic, Tumor, Traumatic, and Mechanical etiologies for each of the above organ systems. When you reach the last category, Organ Dysfunction, simply recall the normal Distant Domino functions listed in chapter 4. Try to think of any pathophysiologic mechanism by which a malfunctioning distant organ system can affect either the gastrointestinal system or any of the Trojan Horses within it. Below is a list of diagnoses which you should have considered:[1] (The last two categories, Mechanical and Organ Dysfunction, are reversed for convenience.)

	GASTROINTESTINAL	NERVES AND MUSCLES IN THE PHARYNX AND ESOPHAGUS	BT	VASCULAR	HEMATOLOGIC	COVERINGS & CONNECTIVE TISSUE
Drug	iron deficiency*					
Infection	retropharyngeal abscess*; candida* esophagitis herpetic esophagitis*; acute epiglottitis*	botulism*				
Genetic/ Degenerative		amyotrophic lateral sclerosis*; oculopharyngeal muscular dystrophy*; myotonic dystrophy* Arnold Chiari malformation*				
Immunologic	Crohn's disease*	myasthenia gravis* dermatomyositis* Guillain Barre* multiple sclerosis*				scleroderma*
Tumor	laryngeal carcinoma, nasopharyngeal carcinoma*, esophageal carcinoma*	nasopharyngeal carcinoma				
Trauma						
Mechanical	achalasia* esophageal spasm* malignant tumor Plummer Vinson syndrome*					

	GASTROINTESTINAL	NERVES/ MUSCLES	RETICULAR	IMMATURE	LININGS & CONNECTIVE TISSUE
	esophageal diverticulum*				
	cervical esophagus*				
	hiatus hernia*				
	cervical osteophytes*				
	goiter*				
	aortic aneurysm*				
Organ Dysfunction:					
systemic					
skin					
bone	globus	central nervous			
	hysteria*	system lesions*			
eyes					
ears					
endo		hyperthyroidism*			
respiratory					
cardiac					
GI					
RE					
neoplastic					
genital					
vascular					
hematologic					
bone					
coverings & connective tissue					

DRUGS:

Iron Deficiency: Besides causing anemia, iron deficiency somehow causes the esophagus to become raw and inflamed resulting in dysphagia.

INFECTION:

Retropharyngeal Abscess: The retropharynx is a surprisingly large bulk of tissue behind the back of the throat. If the tonsils become infected, the infection can spread into the retropharynx as a painful pocket of pus (abscess) which hurts when the patient swallows.[2]

Candida: A common yeast. In the mouth candida grows as white plaques along the mucosa, called thrush. When thrush extends down the esophagus, swallowing becomes painful. Vaginal yeast infections are usually caused by candida, too.

Herpetic Esophagitis: Herpes simplex, the virus responsible for cold sores on your lip, can also form painful cold sores along the esophagus.

Acute Epiglottitis: Besides generating pain on swallowing, an acutely infected (usually by Hemophilus influenza bacterium) epiglottis can swell enough to dangerously obstruct the trachea.[3]

Botulism: One of the few bacteria actually *inhibited* by oxygen, botulinum makes a toxin so poisonous that a cup or less could kill the entire population of the world. (No, it's not commercially available.) If canned food becomes contaminated with botulinum, anerobic conditions inside the can will allow botulinum to grow, which is why you shouldn't eat spoiled food inside a swollen can. Fortunately, you can still avert danger by heating the food hot enough (about 160°F for 30 minutes) to denature the toxin. In mountainous regions, where water boils at a relatively low temperature, denaturing botulinum toxin may not be so easy.

The toxin paralyzes muscles, especially muscles above the shoulders, impairing chewing, swallowing (dysphagia), speaking (dysarthria), seeing (diplopia and unreactive pupils), and holding the neck erect. The patient also becomes decidedly weak below the shoulders.

GENETIC/DEGENERATIVE:

Amyotrophic Lateral Sclerosis (ALS): View this disease as a form of slow, progressive (steadily worsening) polio (polio paralyzes overnight). ALS affects only motor neurons and can present almost anywhere in the body including the pharynx. ALS fatally weakens the patient over a period of years. Ever since the famous Lou Gehrig succumbed to this disease, it's also been been called Lou Gehrig Disease.

Oculopharyngeal Muscular Dystrophy: Muscular dystrophy is any progressive degenerative illness of muscle. The name of the muscular dystrophy often depends on the muscles affected. For example, Oculopharyngeal Muscular Dystrophy predominantly affects eye muscles and pharynx; Facioscapulohumeral Muscular Dystrophy affects facial muscles and muscles attached to the scapula and humerus (i.e., sparing the deltoid muscle).

Myotonic Dystrophy: Because of a fundamental but still mysterious defect in cellular membranes, practically every cell in the body is affected. Organ systems which bear the brunt of the illness include the skin (frontal baldness); neuromuscular (personality and intellectual problems, weakness of chewing muscles, dysphagia, sternocleidomastoid atrophy, myotonia, hand/foot weakness, eyes (cataracts), endocrine (poor response to insulin); cardiac (arrhythmias); RE (low immunoglobulins); and genital (testicular atrophy).

Arnold Chiari Malformation: A malformation of the brain, including the brainstem which controls swallowing. The brain is shaped like an ice cream cone. The cone part—the brainstem—controls functions shared by all animals: consciousness, eye movements, chewing, facial movements, swallowing, breathing, blood pressure, and heart rate.

Though usually manifest at birth, Arnold Chiari may present in midde life with cerebellar and lower cranial nerve disturbances (chapters 18 and 20).

IMMUNOLOGIC:

Crohn's Disease: An idiopathic inflammatory illness affecting the ileum and colon, and occasionally the esophagus.

Myasthenia Gravis: My—muscle asthenia—weakness gravis—grave. An immunologic disease of muscles which afflicted Aristotle Onassis. Like botulism, myasthenia gravis predominantly affects the muscles above the shoulders—eyes, face, pharynx, and neck—but also muscles below the shoulders.

Dermatomyositis: Dermatomyositis differs from Myasthenia Gravis by mainly affecting muscles below the neck, especially the shoulder and pelvic muscles, but occasionally the pharynx, too. "Dermato" refers to an associated rash over the upper chest, eyes, knuckles, and knees.

Guillain-Barre: Myelin is a living structure formed by the Schwann cell wrapping itself round and round an axon like a roll of tape. Gaps in the myelin between consecutive Schwann cells allow electricity to 'saltatere' (jump) down the axon. Guillain-Barre is a widespread immunologic attack on myelin, initially involving nerves in the legs but quickly followed by the arms and face. The patient becomes diffusely weak, or if the attack is severe enough, paralyzed. Eventually, over weeks to months, the myelin repairs itself and the patient recovers. A descending form of Guillain-Barre may begin in the face and throat (with dysphagia), involving the arms and legs later.

Multiple Sclerosis: Multiple sclerosis consists of recurrent, random bouts of central nervous system (brain and spinal cord) demyelination in which myelin is stripped off its axons and then imperfectly repaired over weeks to months.[6] The central nervous system brand of myelin-forming cell is the oligodendrocyte which, like the peripheral nervous system's Schwann cell, wraps itself around axons. Demyelination in the brainstem (which controls swallowing) may cause dysphagia.

Scleroderma: An immunologic disease in which collagen is slowly deposited throughout the body: in the skin, lungs, heart, GI tract, and kidneys. Scleroderma also commonly causes Raynaud's syndrome—episodes of severe vascular spasm in the hands and feet.[5]

TUMOR:

Nasopharyngeal Carcinoma: Cancer of the nasopharynx injures not only the muscles of the pharynx and esophagus, but also the nerves to those muscles (resulting in the same weakness as direct muscle damage).

Esophageal Carcinoma: Cancer of the esophagus strangles the esophagus, so patients choke on bulky solid food but handle liquids somewhat better.

TRAUMA:

Tracheo-Esophageal Fistula: A fistula is an abnormal passageway between two structures. Patients with tracheo-esophageal fistulas choke and cough when they eat and drink as food is routed into the trachea.

MECHANICAL:

Achalasia: Food is propelled down the esophagus by peristalsis. No waves (achalasia), no propulsion.

Spasm: Instead of no waves, if the esophagus contracts too much and too frequently, the coordinated sequence of propulsive waves is lost.

Mediastinum: The space between the two lungs; the heart is in the mediastinum.

Plummer Vinson Syndrome: An illness characterized by obstructive webs across the esophageal lumen, abnormalities of the pharyngeal and esophageal mucosal lining, and (?caused by, resulting in?) iron deficiency anemia.

Esophageal Diverticulum: A small outpouching in which food gets caught.

Esophageal Stricture: Strangulation of the esophageal lumen by a band of scar tissue within the esophageal wall. Analogous to coarctation.

Hiatus Hernia: Upward herniation of the stomach through the hole in the diaphragm normally used by the esophagus to get to the stomach. Hiatus hernia allows gastric acid to reflux (regurgitate) back into the lower esophagus, causing painful inflammation. Simple heartburn is nothing more than minor amounts of esophageal reflux.

Cervical Osteophyte: Cervical means neck. An osteophyte is a wear-and-tear induced spur of bone extending from a vertebral body. Osteo—bone, phyte—plant (phyton), i.e., bony overgrowth. Large osteophytes in front of a vertebral body may compress the esophagus.[6]

The more general term for wear-and-tear degeneration of the vertebrae is *spondylosis*. *Spondylolysis* is a congenital defect of part of a vertebral lamina. *Spondylolisthesis* indicates a slippage (usually forward slippage) of one vertebral body.

Goiter: Enlarged thyroid. A large goiter can compress the esophagus.

Aortic Coarctation: A narrow, constrictive band, usually along the descending aorta. Aortic dilation above the coarctation can compress the adjacent esophagus.

ORGAN DYSFUNCTION:

Globus Hystericus: An emotional sensation of food sticking in the throat or esophagus.

Central Nervous System Lesions: Brain lesions cause dysphagia by weakening the pharynx or by disrupting the proper sequence of pharyngeal movements. For example, the epiglottis may fail to close, so with each swallow, food and drink are aspirated into the trachea.

Hyperthyroidism: Excessive thyroid hormone can selectively weaken the pharyngeal muscles.[7]

As you can see, for each site in the anatomic differential diagnosis, there's an etiologic differential diagnosis. As each etiologic diagnosis is considered during the history-taking, you say to yourself: "If she had such and such a disease, then she should have such and such symptoms," and you ask her about each symptom. For example, if she had hyperthyroidism, she should have weight loss, excessive sweating, tremor, nervousness, heat intolerance, rapid heart rate, and diarrhea; so ask her about these symptoms. Not only are you beginning to sound like a doctor, but you've also just stumbled across the guts of medical school—learning the symptoms and signs of diseases so that, after postulating an illness, you can return to the patient to seek the characteristic symptoms of that suspected illness*.

Step 1: Presenting Symptom
↓ Elicit Further Symptoms
Step 2: Presenting Organ System
↓ Knowledge of Anatomy and Physiology
Step 3: Specific Sites Within the Presenting Organ System
↓ Knowledge of Anatomy and Physiology
Step 4: Trojan Horses
↓ DIG IT TOM and Knowledge of Diseases
Step 5: Postulated Etiologies Specific Questions to Rule In or Out Specific Etiologies

Once you know the symptoms of each disease, your questions begin to have some logical direction. Instead of mindlessly asking a list of questions, or worse, letting the patient aimlessly tell his story, you skip immediately to particularly pointed questions whose purpose is to determine not only the presenting organ system and possible sites of primary pathology, but also the etiologic insult. This means, of course, that you must know, stone-cold, the symptoms of each organ system, the DIG IT TOM etiologic categories, *and* the organ systems that each disease attacks.

In the category Organ Dysfunction, if your questions point strongly to a particular Distant Domino, that etiologic agent is converted back into a victimized anatomic site by moving the Distant Domino to the head of its own column of DIG IT TOM etiologic categories. In the example of dysphagia, symptoms of hyperthyroidism would graduate the Endocrine system (or more specifically the thyroid gland) to the top of its own DIG IT TOM column.

Initially, it may be necessary to prepare your own chart as we did for dysphagia. Eventually, though, notes will become unnecessary as practice and natural logic enable you to chart the etiologies in your head.

Suspected Illness: It's far easier to memorize the symptoms and signs of diseases if you break down every disease into its effect on each of the sixteen organ systems. Label a 3 by 5 card with a disease and on the flip side list the effects of that disease on each organ system.

PERSONAL LOGIC

Looking back over the differential diagnosis for dysphagia, you may reasonably argue that goiter, a compressive lesion, belongs under 'Organ Dysfunction' against the GI system. That's fine. The DIG IT TOM categories are not strict. They reflect shortcuts doctors take when analyzing clinical problems. Depending on how a doctor thinks—which shortcuts he takes—a particular insult may reasonably fall under more than one etiologic category. *You*, for example, may consider a subdural hematoma* a mechanical (compressive) insult, while another doctor may consider it a traumatic insult:

Veins Over the Surface of the Brain —*Trauma*→ Subdural Hematoma —*Mechanical* (Compression)→ Cerebral Malfunction

The subdural was originally caused by Trauma, but the subdural then turned around and caused cerebral malfunction by Mechanical compression. What's the correct etiologic category, Trauma or Mechanical? Well, it depends on your mental connections and your point of view. As long as the DIG IT TOM list jogs your memory to *think* of subdural hematoma, which etiologic category you choose is irrelevant.

Take another example, a stroke caused by sickle cell disease*.[5] The pathophysiologic steps are:

Blood —Because of a *Genetic* Insult→ Abnormal Hemoglobin —Because of *Organ Dysfunction* (hypoxia)→ Sludging of Sickle Cells

Abnormal Hemoglobin —Because of *Mechanical* Obstruction of an arterial lumen→ Thrombosis —Because of *Organ Dysfunction* (vascular)→ Stroke

Subdural hematoma: 'Oma' almost always signifies tumor—carcinoma, meningioma, fibroma, sarcoma, etc.—but the term hematoma acknowledges the original meaning of the term—growth or mass.

A subdural hematoma is a collection of blood over the surface of the brain between the meninges lying directly on the surface of the brain, and the dura plastered up against the skull bone. Subdurals are caused by trauma which, in older people, may be relatively trivial. If large enough, the hematoma may compress the brain, requiring surgical removal of the hematoma. (See chapter 37.)

Sickle Cell Disease: Many Africans (and Black Americans) carry a hemoglobin that, because of a slightly different amino acid sequence, protects against malaria. Unfortunately, when exposed to modest hypoxia, these red cells curl up into a sickle shape which causes the blood to sludge into a vicious cycle of hypoxia—sickling—sludging—hypoxia.

You see the patient at the end of this chain of events when he presents with a stroke. Is the correct etiologic category Organ Dysfunction, Mechanical, or Genetic? In part, it depends on whether you see the brain (the presenting organ system), the vascular system, or the blood as the one bearing the brunt of the disease:

	Brain	Vascular	Hematologic
Drugs			
Infection			
Genetic			Sickle Cell
Immunologic			
Tumor			
Trauma			
Mechanical		Sickle Cell	
Organ Dysfunction			
vascular	Sickle Cell		

Regardless of what leaps of logic you use to recall specific diseases, as long as you first establish an anatomic differential diagnosis, the breadth of etiologic categories in DIG IT TOM will generate a thorough and consistent etiologic differential diagnosis.

Given the enormous number of etiologic diseases, it should be clear that you cannot simply approach every clinical problem with a memorized list of etiologies. You need a systematic way of approaching clinical problems that maximizes your ability to remember all the etiologic diagnoses. The purpose of anatomic/etiologic cross-indexing is to string enough memory trip wires and then to walk you through a systematic line of reasoning that maximizes your chances of tripping one of these wires.

Separating anatomy from etiology also prevents you from looking in too many directions at once. Take a patient with dyspnea. One of the etiologies is pulmonary emboli. Should you order a venogram* of the legs to see if he has blood clots there? No, the first step is anatomy. First establish what structure in the lung is causing his shortness of breath? Only when you've fingered the vascular system is it legitimate to look for etiologies against the vascular system. The reason it's so important to adhere to a strict 'anatomy *then* etiology' approach is that people walk around with abnormal tests all the time, abnormalities which have nothing to do with the current illness. They have what's known as 'true, true, and unrelated:' yes, they have a symptom, yes, they have an abnormal laboratory test, but the two have nothing to do with each other.

What if you *had* found blood clots in your dyspneic patient's legs? Without first proving that his dyspnea was due to pulmonary emboli, you cannot automatically attribute his dyspnea to the blood clots in his legs. It's too easy to believe what you want to believe, and before you know it, you're off treating a disease that never existed.

Venogram: A plain xray cannot distinguish the individual internal organs and soft tissues because their densities are too alike. To make an internal organ stand out, a dye must be injected into its lumen, in this case by injecting dye into a vein and rapidly xraying the veins before the dye leaves.

ELICITING THE HISTORY

THE HISTORY ALONE can often ferret out a patient's entire anatomic and etiologic illness. Occasionally, the physical exam or laboratory data may detect an abnormality in an unsuspected site, but clearly, the history unravels the lion's share of the anatomic and etiologic differential diagnosis. In fact, with a good history, the physical exam should simply confirm dysfunction of the organ system you have already decided is abnormal. Because of its pivotal role and the ease with which it leads to a sound differential diagnosis, history-taking is one of the most productive and satisfying aspects of medicine. In addition, correct history-taking makes your subsequent oral or written presentation of the patient's illness easier to remember, and easier for the listener or reader to follow and understand.

Hospital history-taking begins by knocking on the patient's door before walking in: it lets the patient know that you respect his or her privacy. After the initial introductions, ask the patient to sit up before you elicit the history. A reclining patient is too relaxed, too slow, too likely to wander. Besides, you get a better look at him sitting, and can often do part of the physical while taking the history (skin color, respiratory effort, neurologic signs, pedal edema, etc.).

Now devote your full attention to the patient. Try to give the impression that you're in no hurry, that nothing is more important than what the patient is about to say. It's easier to feel this way if you sit down directly facing the patient, either in a chair or on the side of the bed with no more than a few feet, not even a desk, separating you from the patient. Look the patient in the eye, and crank up your attitude to 'upbeat.' You're going to enjoy this patient because he's different from any patient you've interviewed before. His problem is different, his life is different, even you—your outlook, your approach—are different from last year, or even last month. Besides, you're grateful, grateful because you know how lucky you are not to have to grind it out at some monotonous job all day, every day.

If at all possible, take the patient's history out of earshot of other patients. Both you and the patient will have less difficulty concentrating on the symptoms and signs if you don't have the feeling someone is eavesdropping on your conversation. If the family is in the room, ask the patient if he'd like them to remain in the room. If he wants them to remain, politely tell the family to fill in the gaps *after* you are done talking with the patient. This will reassure them that you are interested in their thoughts, while allowing you to concentrate on the patient's rendition of his complaints. Now ask the patient what you can do for him, what is bothering him *most*. This will not only help you (and the listener to whom you present the case later) orient your thoughts to the presenting organ system, but will also keep you focused on whatever problem the patient is most concerned with, thereby insuring another satisfied customer.

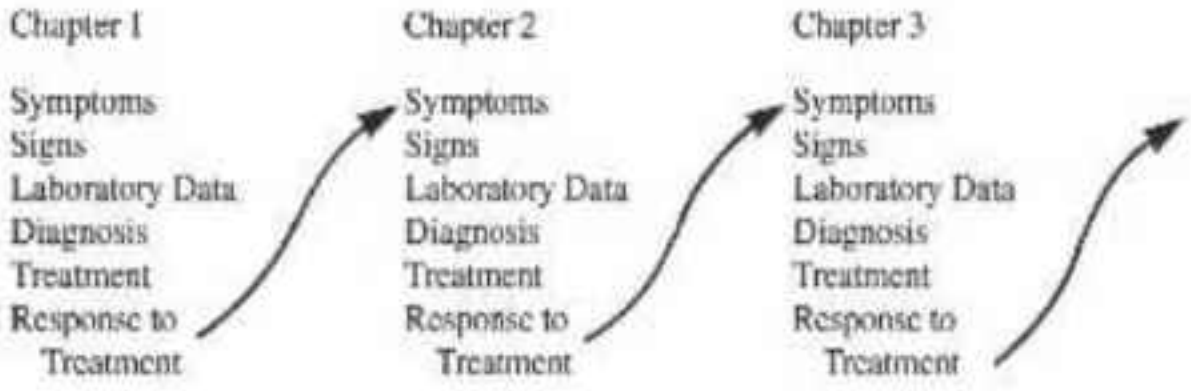
To get a feel for what you're in for, ask the patient whether fixing his most pressing problem would make him feel perfectly well. If he states a second problem, what if you fixed that, too? And so on. This gives you a list of problems to work with, which you can lump together or attack separately.

Also early on, find out who the patient lives with, how the patient is going to cope with such taken-for-granted activities as getting out of bed, on and off a toilet, in and out of a bathtub, shopping for food, taking medicines, and feeding himself. Not only will this information immediately get the ball rolling for possible nursing home placement, but will also help you tailor your treatment to that patient's specific needs.

Next, ask the patient what medicines he takes regularly. Establish this early because it may guide you toward an etiology (such as drug toxicity), or perhaps direct your attention toward a potential Distant Domino organ system. After this, take the patient back to the first moment the symptom was noticed or, if the symptom is one of many for a particular organ system, take the patient back to the first moment he noticed any symptom of that organ system. As you did with the symptom of pain, find out exactly what the patient was doing when the symptom began, how long it took to reach its maximum, how long it lasted, associated symptoms, subsequent pattern of the symptom, aggravating factors, and ameliorating factors (especially the effect of drug treatments).

From here on, the overall structure of a patient's history is like chapters in a book, each chapter centering around a hospitalization or a major change in therapy. Each chapter is divided into the following logical sequence: *Symptoms, Signs, Laboratory Data, Diagnostic Impression, Treatment, and Symptomatic Response to Treatment*. Follow this sequence when taking the history and again when reciting it later.

Chapter one begins with the chief complaint and associated **Symptoms** up until the first doctor visit. Ask him if the doctor found anything abnormal on that first physical examination (**Signs**). Then what tests were performed, and what were the results (**Laboratory Data**)? Next, what was the doctor's **Diagnosis**? What **Treatment** did he give you? How did you do after that (**Response to Therapy**)? This logical sequence—Symptoms, Signs, Laboratory Data, Diagnosis, Treatment, and Response to Treatment constitutes the first chapter of the patient's history. The last part, Response to Treatment, is actually the beginning of the next chapter, and thus provides continuity in your presentation.



Don't be afraid to press the patient for details of previously abnormal signs, laboratory results, dosages of medicines, and dosages of radiation; patients and their families will surprise you in their recall of these specific details.

Taking a history is not a passive job of listening to everything the patient feels is important. From the chief complaint and concomitant symptoms you determine the presenting organ system. From your knowledge of anatomy, the presenting organ system immediately establishes the anatomic differential diagnosis consisting of key sites in the presenting organ system and the Trojan Horses. You then gently but firmly lead the patient through the framework of Symptoms, Signs, Laboratory Data, Diagnosis, Treatment, and Symptomatic Response to Treatment.

As each chapter of the patient's history evolves, you *simultaneously* filter through the etiologic categories for each site in the anatomic differential diagnosis, giving consideration to specific illnesses. These etiologic considerations will, of course, be refocused by each chapter as new symptoms, signs, laboratory data, therapy, and response to therapy are revealed. As you consider each specific illness, ask the necessary questions to rule that disease in or out.

Don't forget to inquire into the family history and pertinent past medical history (past surgeries, past diseases) where you may stumble upon significant circumstantial evidence. For example, pulmonary emboli may be suggested by a past history of congestive heart failure; a past splenectomy* for splenic rupture following an auto accident may now explain his current bone infection* (osteomyelitis); or what was thought to be a simple mole removed five years ago may now explain his current liver mass*.

Your breadth of knowledge of diseases—their characteristic symptoms, signs, abnormal laboratory results, typical responses to therapy, genetics, demographics*, and association with other illnesses—will naturally determine not only the range of your etiologic considerations, but also the accuracy of the questions asked to rule each diagnosis in or out. This is the hard part of doctoring—knowing the diseases well enough to ask the appropriate questions to rule out each disease.

The amount of note-taking during an interview is unimportant as long as you don't look like a stenographer. That is, if you're obviously *thinking* about possible anatomic and etiologic diagnoses—interjecting here and there with amplification and clarification questions—and keeping the patient on the track of symptoms, signs, lab, diagnosis, treatment, and response to treatment—as long as you're in control of the interview, the amount of notes you take is irrelevant to the doctor-patient relationship.

With this overview of the history, let's take a 55 year-old woman and slowly walk through her history. Watch for the following in this contrived dialogue: (1) Will she need nursing home placement or nursing visits to the home to help with medical treatments? or medicines? (2) What is her major complaint? (3) Is her chief complaint an isolated problem or one of many? (4) What is the presenting organ system? (5) Symptoms, Signs, Lab, Impression, Treatment, and Response to Treatment.

Splenectomy: Surgical removal of a spleen. 'Ectomy' means removal from the body. 'Otomy' is a procedure that makes a hole, like laparotomy (an incision into the abdomen). 'Ostomy' is a procedure in which a hole is cut into an organ and then brought to the skin surface, like a colostomy.

Bone Infection: Splenectomy predisposes to infections by pneumococcus and salmonella.[1]

Liver Mass: That simple 'mole' may have been a malignant melanoma.[2]

Demographics: The study of populations—their geographic patterns, migrations, size, and density.

Doctor: Hello Mrs. Adams. I'm Dr. Margulies. (Sits down) Where are you from?
Patient: Baltimore.
Doctor: Do you live in a house here in Baltimore?
Patient: No, I live in an apartment.
Doctor: Who do you live with?
Patient: My husband.
Doctor: Anyone else?
Patient: No, just my husband.
Doctor: Does he make you clean the house and do all the grocery shopping?
Patient: I did until this morning, but I'm not sure I can do it now.
Doctor: Are you working?
Patient: I'm a bookkeeper for the Social Security Administration.
Doctor: Well, let's see if we can figure out your problem. What is the main thing bothering you right now?
Patient: My left side is weak.
Doctor: Since when?
Patient: It began when I was making coffee this morning but it happened once before and I'm hoping it'll go away again.
Doctor: If it weren't for your weak left side, would you feel perfectly well?
Patient: I think so.
Doctor: What medicines do you take?
Patient: Digoxin, a water pill, and aspirin.
Doctor: Let's go back to the beginning. When was the first time in your life you had any trouble with weakness or blindness or trouble walking or talking?
Patient: Well, I was doing fine until three months ago when I woke up with numbness down my left side.
Doctor: How long did that last?
Patient: About three hours. My doctor said I had a stroke*.
Doctor: By numb do you mean the skin felt funny? (Numbness may mean hypesthesia*, weakness, or incoordination to different patients.)
Patient: Yes, like the dentist when he gives you a shot.
Doctor: Were you also weak or clumsy on the left side?
Patient: I sure was.
Doctor: Was your face also weak and numb?
Patient: Yes, it was.
Doctor: Did both the numbness and weakness go away in three hours?
Patient: Yes.
Doctor: When did you see your doctor?
Patient: That afternoon.
Doctor: Did your doctor find anything abnormal on physical exam?
Patient: I don't know.
Doctor: Were any of the tests abnormal?
Patient: No, I don't think so.
Doctor: What did he think happened to you?

Stroke: A sudden neurologic deficit due to sudden interruption of the blood supply to a focal area of the brain or spinal cord.

Hypesthesia: Hypo(less than normal) esthesia(touch)

Patient: He said I had a stroke.
Doctor: Did he give you any medicine?
Patient: A water pill and aspirin.
Doctor: What's the name of the water pill?
Patient: Hydro something.
Doctor: Did he also give you potassium, a foul tasting liquid?
Patient: No.
Doctor: How did you do?
Patient: Okay, I guess, until this morning when it happened again.
Doctor: How long did it take for your weakness to reach its maximum?
Patient: It seemed like just a minute.
Doctor: Is your weakness worse, the same, or better than this morning?
Patient: A little better; I can move my hand now but I couldn't before.

After also reading the referring letter (or past clinic notes), your presentation might go like this:

"This is the first hospital admission for a 55 year-old right-handed Black female bookkeeper with a chief complaint of left-sided weakness of six hours duration. The patient was well until three months prior to admission when she awoke with numbness and weakness of her left side, including her face, all lasting several hours.

"She consulted her family physician who found a blood pressure of 190/105, no carotid bruits*, normal superficial temporal arteries*, and no abnormality on neurologic examination. A CBC*, platelet count*, and sedimentation rate* were normal, and the diagnostic impression was transient ischemic attack* associated with hyper-

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Carotid Bruit: Normally blood flows in a smooth "laminar" pattern like a deep, wide river. When the blood becomes turbulent, it also becomes audible, like river rapids. Each heart beat of turbulent blood is audible with a stethoscope as a pulsatile bruit. A carotid bruit is frequently due to partial obstruction (stenosis) within the carotid artery, a situation often requiring surgical correction. (Carotid, by the way, means to stupefy, or lose consciousness, which happens when the carotids are compressed.)

Sometimes blood flowing *very* rapidly may also tumble and become audible as a pulsatile bruit. This situation may occur in the carotid arteries when one carotid becomes completely occluded, forcing the opposite carotid to carry the blood for both carotids. The bruit is then heard over the *normal* carotid.

Superficial Temporal Arteries: Swollen, tender, non-pulsatile temporal arteries imply temporal arteritis (giant cell arteritis), an old people's disease of unknown etiology. Though the inflammation may theoretically affect any medium sized artery in the body, arteries of the head, especially the superficial temporals, are almost always involved. A readily treatable condition (with steroids), if left untreated, temporal arteritis may cause blindness or stroke from inflammatory obstruction of medium-sized cerebral arteries.[5]

CBC: Complete Blood Count – hematocrit and white blood cell count.

Platelet Count: Too many platelets (more than around 800,000/mm^3) make the blood sticky and likely to clot.

Sedimentation Rate: The rate at which red blood cells sediment when spun in a centrifuge. A high sedimentation rate, often associated with inflammation, may suggest temporal arteritis.

Transient Ischemic Attack: Any transient neurologic deficit due to ischemia. A TIA is usually due to a tiny embolus dislodging from a thrombus in the neck where the common carotid artery bifurcates (branches) into the internal and external carotid arteries. (A thrombus is a blood clot consisting of accumulated red cells, platelets, fibrin, and calcium.)

tension*. The patient was begun on two aspirin* tablets per day and hydrochlorothiazide* 50 mg per day.

"She remained asymptomatic* until six hours prior to admission when, while making coffee, she developed a profound left hemiparesis* including the face. Over the six hours prior to admission, her hemiparesis improved to approximately 50% of its initial deficit.

"On examination here her blood pressure was 150/90, pulse was irregular at 76 beats per minute and respirations 12 per minute. Neurologic exam revealed a modest left hemiparesis with a subtle left homonymous hemianopia.

"Her current medications also include digoxin*. She has no family history of strokes or other neurologic disease."

This presentation gives you the skeleton of a fluid presentation: symptoms, signs, lab, diagnosis, treatment, response to treatment, and current admission signs. It's clear that the nervous system is the presenting organ system. But missing from this bland presentation is the examiner's opinion of either the primary organ dysfunction (and how it secondarily affected the presenting system, in this case, the nervous system) or the etiology of the primary organ dysfunction. This presentation is nothing more than high-class reporting, a mere compilation of historical facts—no thought, no committment, no synthesis of the bare-bone facts into an explanation for this woman's two neurologic events.

Let's return to the patient, but only after properly arming ourselves with a comprehensive anatomic and etiologic differential diagnosis. After establishing the presenting organ system, list the possible Trojan Horses. In this case, the presenting organ system is the brain. The Trojan Horse organ systems in the brain are the vascular and hematologic systems. This now gives us three systems to consider for primary sites of pathology—the brain itself, the vascular system, and the hematologic system. Move on now to possible etiologic diagnoses for the presenting organ system and each of the Trojan Horses. Diagnostic possibilities are listed below: (The diagnoses in parentheses are possible ones, but extremely unlikely in this case.)

Hypertension: Hastens atherosclerosis—widespread narrowing and hardening of arteries over the years as cholesterol, platelets, blood clots, and calcium silt up along arterial linings.

Aspirin: Keeps platelets from sticking together, thereby helping to prevent formation of blood clots that might obstruct arteries or serve as sources of emboli.

Hydrochlorothiazide: A commonly used diuretic (water pill) which rids the body of excess salt, a contributor to high blood pressure. Unfortunately, diuretics also cause the patient to urinate away potassium. Unless the potassium is replaced with fruits or potassium supplements, the subsequent hypokalemia may cause generalized weakness or cardiac arrhythmias (especially if the patient is also taking a digitalis preparation). Hydrochlorothiazide also lowers the blood pressure by acting directly on blood vessels and/or the brain.

Asymptomatic: Without symptoms.

Hemiparesis: Weakness (paresis) of an arm and leg on the same side of the body.

Digoxin: Digoxin is a purified form of the original digitalis leaf, first described as a treatment for congestive heart failure in the late 1700's. When too much is given, arrhythmias develop.

	Neuromuscular	Vascular	Hematologic
Drugs	(Brain Abscess*)	(IV* Amphetamine*)	(Oral Contraceptives^)
Infection	(Bacterial Meningitis*) (Viral Encephalitis^) (Fungal Meningitis)	Syphilis*	
Genetic/ Degenerative			Sickle Cell Anemia
		Unruptured AVM*	Hyperlipidemia*
Immunologic	(Multiple Sclerosis)	(SLE*) Temporal Arteritis (Rheumatoid Arthritis^)	
Tumor	Glioma* Meningioma^ Metastatic*		Leukemia* Lymphoma* Polycythemia Vera* Multiple Myeloma^ Waldenstrom's Macroglobulinemia^ Thrombocytosis*
Trauma		Aortic Dissection* Carotid Dissection* Ruptured AVM Ruptured Aneurysm* Hypertensive Hemorrhage*	
Mechanical	Subdural Hematoma*	Middle Cerebral Thrombosis* Internal Carotid Occlusion* Embolus from:[12] Carotid Bifurcation Thrombus Arrhythmia* Mitral Valve Disease* Mitral Valve Prolapse^ Mural Thrombus^ SBE* (Marantic Endocarditis*) Atrial Myxoma* (Paradoxical Embolus*) Spasm/ Migraine*	
Organ Dysfunction			
Systemic			
Hypotension^			
Skin			
Neuro	Seizure with Todd's Paralysis*		
Eyes			
Ears			
Endo	Hypoglycemia*		
Respiratory			
Cardiac			
GI			
RE			
Urologic			
Genital	(Eclampsia*)		
Vascular			
Hematologic			
Bone			
Coverings & Connective Tissue			

DRUGS:

IV: Intravenous.

Amphetamine: Speed, uppers, psychic energizers. IV amphetamines may produce a cerebral infarction or hemorrhage.[4]

Oral Contraceptives: The pill (especially a high estrogen one) raises the risk of stroke primarily in women over the age of 35, a risk compounded by smoking and hypertension.[5] The few autopsies of women on the pill who've died of strokes reveal arterial narrowing.[6]

INFECTION:

Abscess: A collection of pus surrounded (corralled) by a wall of inflammatory white blood cells and scar tissue.

Meningitis: Inflammation of the meninges covering the brain. There are many different kinds of meningitis depending on the agent: bacterial, tuberculous, fungal, viral, carcinomatous, and chemical (blood, xray dye, etc).

Encephalitis: Inflammation within the substance (parenchyma) of the brain.

Syphilis: Causes an arteritis. This disease was apparently named after the shepherd, Syphilis, immortalized in a poem published in 1530 describing his illness.

GENETIC/DEGENERATIVE:

AVM (Arteriovenous Malformation): A congenital tangle of abnormal arteries and veins without capillaries separating them. The absence of capillaries allows high-pressure arterial blood to shunt directly into low-pressure veins resulting in slow enlargement of the AVM over many years. Pressure on, or theft of blood from, neighboring brain tissue produces seizures and focal brain dysfunction. Since AVM's may also rupture into the brain (intracerebral hemorrhage), AVM's should be surgically removed before they have a chance to do so.

Hyperlipidemia: Excessively high serum lipids hasten atherosclerosis.

IMMUNOLOGIC:

SLE (Systemic Lupus Erythematosus): An immunologic disease of young people in which the reticuloendothelial system attacks immune complexes being deposited within blood vessel walls, resulting in an arteritis.

Rheumatoid Arthritis: Rheumatoid arthritis, an inflammatory disease of synovial tissues and joints, is accompanied in some patients by an arteritis which may involve cerebral arteries.

TUMOR:

Glioma: A malignant tumor of the brain's glial tissue (astrocytes, oligodendrocytes); the neurons themselves rarely become malignant. Astrocytes surrounding neurons probably absorb potassium extruded from neurons during normal neuronal firing.[7] Oligodendrocytes form the myelin around central nervous system axons.

Meningioma: A benign tumor of connective tissue cells situated within the dura covering the brain and spinal cord.

Metastatic: A tumor which began at one site, but spread to another, distant site.

Leukemia: A cancerous overproduction of white blood cells by the bone marrow. Hordes of WBC's crowd out the platelet forming cells (megakaryocytes) resulting in abnormally low numbers of platelets (thrombocytopenia). Result: bleeding diathesis, especially in the brain. Sometimes there are so many WBC's in the bloodstream that blood flow becomes sluggish, predisposing to strokes.

Lymphoma: Cancer of lymph glands (including the spleen). May occasionally cause cerebral ischemia when malignant lymphocytes infiltrate around cerebral arteries.

Polycythemia Vera: A mildly malignant overproduction of red blood cells. Eventually degenerates into a more malignant state involving WBC's (leukemia).

Multiple Myeloma: Malignant overproduction of a single immunoglobulin (IgG) by an uncontrolled, rapidly reproducing clone of plasma cells which invade and destroy bones. Excess immunoglobulin makes the blood sluggish, causing ischemia.

Waldenstrom's Macroglobulinemia: A cousin of multiple myeloma in which a clone of plasma cells produces a very large immunoglobin, IgM, that sludges the blood even more than the smaller IgG produced in multiple myeloma. Waldenstrom's macroglobulinemia doesn't invade the bones like multiple myeloma, but it is still malignant: it killed President Boumedienne of Algeria.

Thrombocytosis: Overproduction of platelets. Tends to occur with malignancies, but also in certain chronic infections. A platelet count above about 800,000/mm^3 makes the blood more likely to clot.

TRAUMA:

Aortic Dissection: Sudden (usually painful) hemorrhage into the aortic wall frequently occludes arteries branching off the aorta, including the carotid arteries.

Carotid Dissection: Hemorrhage into the wall of the carotid artery may occlude the lumen.

Ruptured Aneurysm: Congenital absence of the middle, muscular layer of a cerebral artery allows a small patch of the arterial wall to slowly bulge outward over many years, eventually hemorrhaging around mid-life. If the patient is lucky, bleeding occurs only over the surface of the brain. If he's not, the hemorrhage is directed into the parenchyma of the brain. Considering that perhaps 1-2% of the population has modest to moderately sized aneurysms,[8] it's surprising that more of them do not hemorrhage. Congenital, or 'berry,' aneurysms cluster around the base of the brain where cerebral arteries take the brunt of the blood pressure.

Treatment consists of stapling the neck of the aneurysm as it blisters from the arterial wall. If this can't be done (because the neck of the aneurysm is too broad), the dome of the aneurysm is wrapped in a gluey gauze for added support.

The first man to clip an aneurysm was the famous neurosurgeon, Walter Dandy, in 1938.[9]

Hypertensive Hemorrhage: Chronic hypertension weakens small intracerebral arteries which may later rupture.

MECHANICAL:

Subdural Hematoma: A blood clot over the surface of the brain; usually caused by trauma. Subdurals may present as transient ischemic attacks or strokes.[10]

Middle Cerebral Thrombosis: A thrombus in the middle cerebral artery may, by obstructing the lumen, infarct the area supplied by the middle cerebral. Most strokes affect the middle cerebral artery which also, unfortunately, happens to supply a large segment of the brain.

Occlusion: About 75% of the blood supply to the brain is carried through the two common carotid arteries lying on either side of the trachea (where you can feel their pulsations). About half way up the neck, each common carotid bifurcates (divides) into an internal carotid artery for the brain and an external carotid artery for the face and scalp. Turbulent blood flow at any arterial bifurcation predisposes to local thrombosis. When the thrombus becomes large enough to narrow the arterial lumen by about 70%, blood flow through the artery begins to slow. A thrombus at the bifurcation may also break off, embolize downstream into the middle cerebral artery causing a stroke or, if the embolus then breaks apart, a transient ischemic attack.[11]

Many people handle complete internal carotid occlusion without difficulty because of adequate collateral supply from alternative arteries like the opposite internal carotid through the Circle of Willis (see chapter 31). Those who don't have sufficient collateral arteries suffer a stroke when the internal carotid occludes.

Arrhythmia: Some arrhythmias, especially atrial fibrillation, may cause strokes by embolizing clots which have formed in the non-contracting atria.[12]

Mitral Valve Disease: A scarred, stenotic mitral valve (a common complication of rheumatic fever) may serve as a source of emboli for two reasons: thrombi may adhere to its scarred surface, or thrombi may form in the dilated left atrium.[14]

Mitral Valve Prolapse: A common (2–5% of population?) abnormality of the mitral valve which causes it to bulge backwards into the left atrium during systole. Very rarely, associated with emboli to the brain.[15]

Mural Thrombus: After a heart attack, the infarcted ventricular wall repairs itself with scar tissue. During the repair process, platelets adhere to the new collagen tissue being deposited in the ventricular wall, especially if that part of the ventricle doesn't contract well. Circulating clotting factors immediately deposit on the clumped platelets, forming a mural (wall) thrombus which may later embolize to the brain.[16]

SBE (Subacute Bacterial Endocarditis): A smoldering infection of a heart valve (the term endocarditis is a misnomer; the endocardium is the inner layer of the ventricular wall). Because there's no blood supply to the valve itself, white cells cannot reach the bacteria to kill them. Friable vegetations subsequently form on the valve, vegetations which frequently embolize to the brain.

Bacteria are continuously shed from the valve. Once in a while, these bacteria infect the wall of a cerebral artery, weaken it, and produce a 'mycotic' aneurysm. (Mycotic, which means fungal, is another misnomer.)

Marantic Endocarditis: Heart valve vegetations mysteriously caused by distant cancers, especially longstanding cancers.[17]

Atrial Myxoma: A benign tumor which grows inside the left or right atrium from a stalk attached to the atrial wall. By swinging on its stalk, the tumor may acutely block the tricuspid or mitral valve. Bits of the tumor may embolize to the lung from a right atrial myxoma, or embolize to the brain and body from a left atrial myxoma.[18]

Paradoxical Embolus: Since the lungs do not breathe during fetal development, every fetus is equipped with a foramen ovale in the heart—a hole in the interatrial septum that allows venous blood to bypass the right ventricle and lungs and flow directly into the left atrium. If the foramen ovale fails to close at birth, emboli from the legs and pelvis may slip through the patent foramen ovale into the arterial circulation.[19]

Migraine: A type of headache in which arteries supplying the brain are speculated to go into spasm (in response to something occurring within the brain?[20]), followed by painful dilation of arteries supplying the scalp.[21] If the initial vasospasm is severe enough, no blood gets through, causing temporary ischemia or permanent strokes.[22]

ORGAN DYSFUNCTION:

Hypotension: Any diffuse cerebral insult, including hypotension, may bring out the signs of an old stroke. In addition, if hypotension somehow deprives a local area of brain of sufficient blood (implying a preexisting arterial stenosis), hypotension may precipitate a fresh stroke.

Todd's Paralysis: Sometimes a seizure confined to one area of the body is followed by prolonged weakness of the involved limb, typically lasting one or two days. Todd's paralysis usually implies prior injury to the corresponding area of brain.

Hypoglycemia: Low blood sugar may re-evoke signs of a previous cerebral abnormality (such as a hemiparesis), signs which were undetectable when the blood sugar was normal. Like sudden hypoxia and hypotension, a *rapid* drop in blood sugar will produce symptoms that a more gradual drop would not. Severe hypoglycemia may, like severe hypoxia and hypotension, cause a frank cerebral infarction.

Eclampsia: A complication of pregnancy consisting of marked hypertension, proteinuria (spillage of protein into the urine), and widespread edema. Severe cases may progress to coma, convulsions, and strokes. Though eclampsia disappears after delivery, no one knows precisely how the fetus and/or placenta cause eclampsia.

As discussed in chapter 5, the exact organization of the differential diagnosis depends on your outlook. For example, it's perfectly reasonable to insert Ruptured AVM and Ruptured Aneurysm under 'Genetic' insults to the vascular system. Or Arrhythmia, Mitral Valve Prolapse, Mural Thrombosis, SBE, Marantic Endocarditis, and Atrial Myxoma under 'Organ Dysfunction: Cardiac' for the Neuromuscular system. I prefer to think of all these insults as directed against the vascular system, but you may prefer to omit the vascular intermediary. As long as you *consider* the etiologies in your differential diagnosis, the pigeonhole you choose is not terribly important. It's more important that you be consistent, so that your etiologic differential diagnosis will always be consistent and comprehensive.

During the history-taking, as you filter through the list of etiologic insults, ask the necessary questions to rule out each diagnostic possibility. It may take some practice for you to translate medical pathophysiology into symptoms and signs, and then to translate those symptoms and signs into everyday English, the kind of English *patients* understand.

Diagnostic Possibility	Question
IV Amphetamine	Have you ever shot up drugs?
Oral Contraceptives	Are you taking any hormones?
Brain Abscess,	Do you have a headache? Fever? Have you had any
Bacterial Meningitis,	recent dental work* or recent infections?
Fungal Meningitis,	Any fever? Headache? (Ask the family about seizures
Herpes Encephalitis	and confusion.)
Syphilis	Have you ever been told you had 'bad blood'**?
AVM (unruptured)	Have you ever had seizures or convulsions?
Multiple Sclerosis	Have you ever had a spell of blindness, double vision, incoordination, or gait difficulty?
SLE	Have you had any trouble with joint pains or swelling? How about unexplained fevers? Rashes?
Temporal Arteritis	Any trouble with headaches, fevers, or transient blindness?
Rheumatoid Arthritis	Joint pains? Morning hand stiffness? Swollen joints?

Fever, Dental Work: You're looking for a source of infection. Dental work frequently sends a shower of mouth bacteria into the bloodstream.

Bad Blood: A colloquial term for syphilis. The blood test which detects syphilis is the VDRL, the same test you must have prior to being granted a marriage license. Some normal people have 'false positive' VDRL's, meaning the test is positive, but not because the patient has syphilis. Some of those people later develop autoimmune diseases like lupus erythematosus. The FTA, a more specific test for syphilis, usually clears up the uncertainty.

A false negative test means that a test is negative even though the patient has the disease.

Glioma, Meningioma	Have you had any seizures or convulsions? Are you sure your strength returned to normal after the first episode of weakness? Have you felt confused at all? Headaches? If so, are they worse during the day or in the middle of the night and early morning*?
Metastatic Tumor	Do you have cancer anywhere? Do you smoke? Any trouble with a new cough? Have you coughed up any blood or blood-tinged sputum? Have you noticed any recent breast lumps? Any change in bowel habits? Have you lost any weight?
Leukemia	Any trouble with fever? Any excessive fatigue? Bleeding gums?
Lymphoma	Have you noticed any lumps or enlarged glands?
Polycythemia Vera	Has your skin felt prickly or burning? Any headaches?
Multiple Myeloma	How about excessive fatigue or bone pain?
Thrombocytosis	Have you had any trouble with blood clots anywhere in your body?
Aortic Dissection	Did you have any chest or back pain when you became weak this morning?
Ruptured AVM, Ruptured Aneurysm, Hypertensive Hemorrhage	Did you have any headache when you got weak? Did you develop a headache after your weakness began? Is your neck stiff or painful*?
Subdural Hematoma	Have you banged your head recently or been knocked out? Headaches?
Middle Cerebral Artery Thrombosis Internal Carotid Artery Thrombosis	Are you sure you haven't had brief spells of weakness either before or between the two big episodes of weakness?
Embolus: Mural Thrombus	Have you had a recent heart attack?
Embolus: Arrhythmia	Have you felt your heart skipping about, dropping beats, turning over, or racing unexpectedly?

Early Morning Headache: An intracerebral tumor may become symptomatic in a recumbent patient for two reasons. When we stand up, gravity helps drain venous blood from the brain. In a recumbent position, higher cerebral venous pressure prevents edema in and around a brain tumor from escaping into the veins. Also, when we lie down at night, fluid which had collected in the legs (because of gravity) reenters the vascular system. The extra blood volume further compresses the already tight intracerebral contents, hence, the headache.

Neck Stiff or Painful: Blood in the subarachnoid space around the brain causes a 'chemical' meningitis which the patient notices as a stiff and painful neck.

Subacute Bacterial Endocarditis	Any fever, chills, night sweats? Recent dental work or recent infections? Ever had rheumatic fever* or been told of a heart murmur*?
Migraine	Have you had trouble with headaches throughout your life? Are you absolutely certain you never had a spell of weakness* on one side of your body before the first one six weeks ago?
Hypotension	Did you feel faint before either of these spells of weakness? Did anyone say you turned pale*?
Seizure*	Did your hand jerk either before or after you got weak?
Hypoglycemia*	Has anyone told you you had diabetes? Have you had spells of weakness or near fainting if you go without food? Did you become weak, nauseated, or sweaty, or feel your heart race just before your weakness this morning?
Eclampsia (if pregnant)	Have you noticed your feet swelling? Headaches? Seizures?

Rheumatic Fever: An autoimmune attack against the patient's own heart valves precipitated by a streptococcal throat infection. The damaged heart valves are thereafter susceptible to SBE, especially during extensive dental procedures.

Murmur: Blood rumbling across an abnormal heart valve is audible with a stethoscope. Murmurs sound like pulses of low-pitched, hissing steam.

Spell of Weakness: Some people with 'hemiplegic migraine' suffer recurrent bouts of either hemiparesis or homonymous hemianopia during the initial phase (intracerebral vasospasm?), before the second (headache) phase of extracerebral vasodilation in the dura and scalp.

Pale: When the blood pressure drops, the body responds by sacrificing blood flow to the skin (turning the skin pale) and diverting it instead to the internal organs, especially the brain.

Seizure: In some patients, each seizure is followed by focal weakness lasting hours to days, called Todd's paralysis.

Hypoglycemia: Early diabetes often begins with a sluggish insulin response to a sugar load. As insulin reaches its maximal output, the serum glucose may have *already* returned to normal by other means (uptake by the brain, spillage into the urine, etc.) resulting in a further suppression of the serum glucose by insulin, a situation called reactive hypoglycemia.

In response to the hypoglycemia (which causes the weakness and nausea), the body responds with an outpouring of adrenalin causing tachycardia and diaphoresis (sweating). Hypoglycemia may also (rarely) be caused by an insulin-secreting tumor of the islets of Langerhans.

Let's suppose, for the purposes of this discussion, that the woman admits to spells of her heart jumping about, raising the possibility that an arrhythmia caused her left hemiparesis by flipping an embolus* to the right middle cerebral artery. This Distant Domino, the heart, now removes its mask as victimizer and dons a new mask as victim. By joining the anatomic differential diagnosis, the heart is thereby promoted to the top of its own DIG IT TOM column. Run through the list of etiologic possibilities again, this time considering the heart—specifically, heart rhythm—as a victimized primary site of pathology. Such a list would be as follows:

	Heart Arrhythmia	Question
Drugs:	Digoxin toxicity, amitriptyline*, etc.	What medicines do you take regularly?
Infection:		
Genetic:	Congenital heart disease	When did you first notice your heart skipping about? Has a doctor ever told you that you had a heart murmur?
Immunologic:	Mitral stenosis or regurgitation* from rheumatic fever	Ever had rheumatic fever or been told of a murmur?
Tumor:		
Trauma:		
Mechanical:		
Organ Dysfunction		
Systemic:		
Skin:		
Neurologic:		
Eyes:		
Ears:		
Endocrine:	Hyperthyroidism*	Any weight loss, recent excessive nervousness, tremor, heat intolerance, diarrhea?

Embolus: Certain rhythm disturbances of the heart like chronic atrial fibrillation, intermittent atrial fibrillation due to hyperthyroidism, and tachy-brady arrhythmia ('sick sinus syndrome') raise the risk of emboli from the heart.[23] Rhythm disturbances that make the heart pause produce global symptoms like dizziness, syncope, gait unsteadiness, but not (or at least very rarely) focal neurologic signs.[24]

Amitriptyline: An antidepressant which may cause arrhythmias in too high a dose.

Mitral Stenosis or Regurgitation: A stenotic or regurgitant mitral valve backs up blood into the left atrium, eventually distending the atrium. Sluggish blood flow through an enlarged left atrium predisposes to mural thrombi, especially if the atria are also fibrillating (firing so rapidly that they don't have time to contract).

Hyperthyroidism: By causing atrial fibrillation, hyperthyroidism can predispose to cerebral emboli from the heart.[25]

	Heart Arrhythmia	Question
Cardiac:	Congestive heart Failure (CHF*)	Any excessive shortness of breath on exertion? How many pillows do you sleep on? Do you have any trouble waking at night with shortness of breath? Any trouble with feet swelling?
GI:		
RE:		
Urologic:	Hypokalemia	Are you sure you take no potassium pills or potassium liquids?
Genital:		
Vascular:	Myocardial infarction*	Have you had any bouts of severe chest pain?
Hematologic:		
Bone:		
Coverings & Connective Tissue:		

With the history alone we have sorted through the anatomic and etiologic differential diagnosis to what we believe are the top choices. Separating the anatomic differential diagnosis from the etiologic differential diagnosis allowed us to compile a comprehensive list of etiologies. And by considering etiologies for *each* anatomic site, the long list of etiologies was kept from becoming unmanageable. For each site we were able to list the etiologic differential diagnosis, consider each disease individually, and then ask the appropriate questions for each disease.

Postulating individual diseases and asking the appropriate questions is what separates doctors from reporters. This becomes even more apparent when you want to present the case, the topic of the next chapter.

Congestive Heart Failure (CHF): Being too weak to pump the necessary volume of blood demanded by the body's tissues, failing ventricles compensate by enlarging (becoming "congested") which improves ventricular contraction. Congestive heart failure predisposes to arrhythmias.

Myocardial Infarction: Heart attack. An acute occlusion of one coronary artery infarcts part of the ventricle. The ventricular scar after a heart attack may serve as an irritable focus of arrhythmias. Heart failure and ventricular aneurysms may also develop after a heart attack.

PRESENTING THE HISTORY

DEPENDING ON YOUR PATIENT'S RESPONSES to your questions, you ought to have narrowed down all the possible etiologic diagnoses to five or ten likely ones. The upcoming physical exam should confirm the disturbance of the presenting organ system and perhaps a Distant Domino organ system. The exam may even uncover the telltale constellation of signs for a specific illness, but once you've examined the patient, with or without the laboratory data, comes the moment of truth—your oral presentation of the case to a peer or your written presentation in the chart.

Before you open your mouth or pick up a pen, however, you must get off the fence and make a clinical decision about the cause of your patient's illness. This means you must decide the site of primary organ system dysfunction, the etiologic insult to the primary organ system, and the pathophysiology—how the primary organ system dysfunction affected the presenting organ system. Your presentation will not simply be a smorgasbord of historical and physical facts from which the listener picks and chooses the pertinent ones to make a cogent medical analysis. If that's all there were to a presentation, my secretary could take the history and record all the facts. Your presentation has two functions—it should keep the listener from staring out the window winding his watchstem in abject boredom, and it should lead the listener along to the 'obvious' diagnosis which you've have already arrived at.

When presenting the case you are no longer a doctor, but a lawyer arguing and defending your diagnostic impression before a judge and jury. To 'win your case' you must first capture their interest by stating what you think is the central issue of the case, an issue which you shall now unravel with your presentation. By stating the clinical* problem first—before the chief complaint—you give your audience a reason to listen, something that will help focus their attention. People need to know where you're leading them before they'll follow.

Once you've captured their interest with the central issue of the case, state the patient's chief complaint (if it isn't already obvious from your description of the central issue of the case) so that everyone knows what's bothering the patient. After that, keep your audience awake by smoothly presenting the history, breaking it up into chapters of symptoms, signs, lab, impression, treatment, and response to treatment. Lead them to your diagnosis by emphasizing aspects of the case that support your diagnosis while de-emphasizing aspects that support other diagnoses. This may strike you as unscientific, but in reality, the *last* thing a scientist does is walk into a lab and start randomly knocking test tubes together. He goes in with a purpose—a point of view—a hypothesis to prove or disprove.

Clinical: A shorthand term for 'symptom-and-sign-wise;' the problem as seen in the clinic, not the laboratory.

Before presenting the case you need to draw defensible conclusions so that you feel confident about your diagnosis as you plan your investigation and initiate treatment. Reserving the prerogative to change your mind, you must be prepared to defend your conclusions, to make it clear to other physicians how you arrived at your diagnosis. This requires that you emphasize certain points in the history and de-emphasize other ones. Sure another doctor may take those same facts and assemble them differently. That's fine, in fact the other doctor may be right, but at least I know where you stand and what you're thinking. You can always change your mind, but make your position clear.

There will be two kinds of facts in a history: positives and negatives. Positive facts are symptoms, signs, laboratory data, and responses to treatment actually experienced by the patient. Negative facts are those he didn't experience. Those positive facts that support your diagnosis are 'Good Positives,' and those positive facts that refute your diagnosis and support another are called 'Bad Positives.'

Likewise there are Good and Bad Negatives. Bad negatives are facts which are characteristic of your diagnosis, but which are absent in this case. Good negatives are facts characteristic of another diagnosis but, by their absence, favor your diagnosis.

Suppose you make a diagnosis of a heart attack. Symptoms characteristic of a heart attack are sudden chest pain, shortness of breath, weakness, diaphoresis[8], and pallor. If the patient denied shortness of breath, that negative symptom would be a Bad Negative. Examples of Good Negatives (symptoms characteristic of another disease but absent in this case) would be no hemoptysis (pulmonary embolus), no weakness of the legs or bladder incontinence (aortic dissection with spinal cord ischemia), no hematemesis (peptic ulcer), no fever (pneumonia), and so on.

The actual presentation of the history is given in a structured order. Within the framework of chapters (symptoms, signs, lab, impression, treatment, and response to treatment), focus on *your* diagnosis. Present those characteristic symptoms, signs, laboratory data, and responses to treatment that were present AND those that weren't—the Good Positives and the Bad Negatives. By placing the Bad Negatives up front for all to see, you make it clear that you still favor your diagnosis despite the absence of certain characteristic, supportive facts.

In the patient you thought had a heart attack despite no chest pain, your presentation might begin: "This 60 year-old man was walking home yesterday when he suddenly became short of breath, weak, pale, and diaphoretic, all without chest pain." Waiting until the end of the presentation to mention that he had no chest pain would only draw attention to that fact and detract from your diagnosis.

At the end of your presentation, include 'Pertinent Negatives' and 'Of Interest.' Pertinent negatives are the Good Negatives: symptoms, signs, laboratory data, and responses to treatment characteristic of other diagnosis, but which were absent in your patient's history. Pertinent negatives keep the listener from straying to other diagnostic possibilities, away from the one you favor.

'Of interest'—Bad Positives—are those symptoms, signs, laboratory data, and responses to treatment that were present in the history and suggest other possible diagnoses, but which you feel are not strong enough to deter you from your diagnosis.

Diaphoresis: Sweating.

In the case of our woman with a stroke in the previous chapter, suppose you put the story together in this way: three months prior to admission she had a transient ischemic attack, was discovered to have hypertension, and was begun on diuretics without potassium supplements*. She then developed hypokalemia and a subsequent cardiac arrhythmia (secondary to hypokalemia while on digoxin) which flipped an embolus from the heart, causing the second hemiparesis. This may not be the correct interpretation, but if *you* believe it to be so, you must emphasize symptoms and signs supporting the diagnosis of hypokalemia and arrhythmias, and defuse other diagnostic possibilities in your differential diagnoses, like a brain tumor (primary or metastatic), subdural hematoma, arteriovenous malformation, arteritis, embolus from a carotid bifurcation plaque*, in-situ thrombosis*, small intracerebral hemorrhage, and subacute bacterial endocarditis, all of which may present with this woman's clinical history.

Your presentation might then go as follows: "This is a 55 year-old right-handed Black female bookkeeper who has suffered two episodes of left hemiparesis within three months. She was admitted yesterday following the second episode which began in the morning and was partially resolving by the time of admission six hours later. The patient had been on digoxin for several years to control mild congestive heart failure and was neurologically asymptomatic until three months prior to admission when she awoke with numbness and weakness of her left hand and face, symptoms which resolved over several hours. Examination by her physician the following day revealed a blood pressure of 190/105, a regular pulse, no carotid bruit, and a normal sedimentation rate and platelet count. The diagnostic impression was transient ischemic attack and hypertension for which the patient was given two aspirin tablets per day and hydrochlorothiazide 50 mg per day without potassium supplementation.

"Over the ensuing three months, while on digoxin and hydrochlorothiazide without potassium supplements, she noted increasingly frequent spells of dropped heart beats and periods of rapid heart rate lasting two to three minutes. During the week prior to admission an irregular heart rhythm was occurring at a frequency of three to four times per day. On the morning of admission while fixing coffee, she abruptly developed a profound left hemiparesis (involving the face, hand, and foot) which gradually resolved over the next six hours to approximately 50% of its worst disability. The patient specifically denied headaches, head trauma, focal jerking of the left hand or foot, seizures as a child, fever, or recent infections. Of interest is that she noted a mass in her left breast one week prior to admission."

It should be clear from this history that the examiner thought a hypokalemic induced arrhythmia played an important etiological role in this woman's stroke. If, on the other hand, he had felt that the stroke was simply a garden variety embolus from the carotid artery bifurcation, he would have put the symptoms of arrhythmia into the 'of interest' section at the end of the history, thereby de-emphasizing it, but not obscuring it. The breast mass was included in 'of interest,' because the mass could conceivably be breast cancer and the stroke, metastatic breast cancer.

Potassium Supplements: Diuretics like hydrochlorothiazide cause urinary loss of both sodium and potassium. Without potassium supplementation, hypokalemia may ensue.

Plaque: A site of roughened arterial endothelium where a thrombus has formed.

In Situ Thrombosis: A thrombus which *forms* at a specific site, as opposed to thrombosis upstream with embolic obstruction downstream.

This presentation is anything but a bland and stodgy compilation of historical facts. It has a definite point of view about this woman's illness, a point of view the listener may disagree with, but one that states clearly what the presenter is thinking. A crisp, directed presentation is a joy to listen to. Instead of *my* having to analyze all the scattered clinical facts, you've done it for me. Instead of asking me to do your job for you—namely, to analyze the clinical data—you've challenged me with an interesting proposition: to come up with a better explanation than yours. My interest is piqued, I'm attentive, and I respect that you've given the problem some thought and had the courage (and knowledge) to make a clinical judgment. Don't worry if your judgment is wrong. Judgment improves with experience, but only if you *force* yourself to draw conclusions and make judgments. You can always change your opinion, but at least have one.

If you are quite certain that a particular clinical fact, be it a symptom, sign, laboratory data, or treatment, is irrelevant to the current problem but may still need investigation, either approach it as a second clinical problem or slip it under the review of systems[8] later. Do not include it in your presentation of the chief complaint. To do so would only muddy the waters and prevent the listener from a clear, logical arrival at your diagnosis.

RECAP

Before leaving the history-taking, let's recap the steps. First, firmly establish what is bothering the patient most, his chief complaint. Determine how many medical problems he has by asking whether he would be perfectly okay if you fixed his chief complaint. If he listed several chief complaints, determine the truly chief complaint by asking him "If I could only fix one problem, which one would you prefer I fix?"

Then bring the patient back to the very onset of the symptom, or to the very onset of symptoms for that organ system. Elicit the symptoms which occurred prior to his first visit to a physician. Continue the patient's story through signs, laboratory data, diagnosis, therapy, and then start a new chapter with response to therapy.

When you think you've located the presenting organ system, try to narrow the anatomic differential diagnosis to a few sites within the presenting organ system. Then list the Trojan Horse organ systems to complete the anatomic differential diagnosis. Slowly walk through the etiologic categories to jog your thoughts about specific illnesses. Think of any Drug (that is, any external, non-traumatic, inanimate insult like drugs, radiation, electric shock, vitamins, heavy metals, transfusions, food, etc.) which might have affected the presenting organ system or any of the Trojan Horse organ systems. Next, say to yourself, "if such and such a 'drug' caused the problem, the patient should have the following symptoms because this illness affects such and such organ systems." You then return to the patient with the appropriate symptoms, signs, and laboratroy data that you'd expect to find if the patient had the proposed illness. Any other question which might confirm or deny a proposed 'drug' would also be appropriate.

Review of Systems: The laundry list of symptoms for each organ system (chapter 2), symptoms which were neither complained about nor asked about in the present illness. Sought at the end of the history-taking, the review of systems may uncover a potentially important medical problem unrelated to the present illness.

Next consider Infectious etiologies, and as each infectious agent is considered for each site in the anatomic differential diagnosis, ask the patient about symptoms characteristic of that postulated illness. Continue through the etiologic categories: Genetic/Degenerative, Immunologic, Tumor, Trauma, Mechanical, and Organ Dysfunction, asking the necessary questions for each postulated illness. Remember that for the category Organ Dysfunction, there are specific functions performed normally by each organ system which, if not done, affect distant organ systems. The questions for this etiologic category reflect those specific functions. If one of the Distant Domino organ systems turns out to be a probable etiologic agent, look for the cause of *its* malfunction by graduating the Distant Domino to the head of its own column for a DIG IT TOM etiologic analysis.

Why are the Trojan Horses necessary? Why not simply list, say, all vascular etiologies under the category 'Organ Dysfunction: Vascular,' like this?



If you could consistently list all the vascular etiologies by doing it this way, fine. But by graduating 'vascular' to the top of its own DIG IT TOM column, you subject 'vascular' to the same systematic thinking that you used for the presenting organ system.

Moreover, a dysfunctioning Distant Domino may manifest in the presenting organ system by first affecting a Trojan Horse embedded within the presenting organ system. When taking a history it's virtually impossible to sort out whether the primary insult was directed against the presenting organ system or against one of its Trojan Horses. By automatically making each Trojan Horse part of the anatomic differential diagnosis, you force yourself into recognizing this fact. Each Trojan Horse, being part of the anatomic differential diagnosis, *always* gets its own DIG IT TOM column; in this way you automatically consider Distant Domino insults directed against each Trojan Horse.

This cross indexing of anatomy and etiologies enables you to assemble a thorough differential diagnosis *before* initiating laboratory investigations and medical therapy. It's so important to begin with a comprehensive differential diagnosis, because certain diseases are so malicious that, regardless of their rarity, they *have* to be ruled out now—not tomorrow, not next week. By constructing a thorough differential diagnosis at the onset, you need only glance over your differential diagnosis to pick out those explosive diseases. The doctor in the trenches first seeing the patient must construct his differential diagnosis not according to likelihood, but according to *danger*. Once he's bought a little breathing room by ruling out the dangerous diagnoses first, he can then restructure the differential diagnosis according to statistical likelihood, ease of diagnosis, and treatability.

PAST MEDICAL HISTORY, SOCIAL HISTORY, FAMILY HISTORY, REVIEW OF SYSTEMS

BETWEEN THE PRESENT ILLNESS AND THE PHYSICAL EXAMINATION lie the past medical history, social history, family history, and review of systems. Unless these areas bear directly on the present illness, they usually don't require the effort and concentration you devoted to the present illness. The *social history* (where the patient lives, whom he lives with, his job, smoking and drinking habits) should already have been probed in the present illness for a number of reasons. Taking a social history at the very beginning of the patient's history tells you the effect the illness has had on the patient's life (and vice versa), establishes a social bond between you and the patient, and helps you remember his history. The *past medical history* is simply those past operations, allergies, and prior illnesses unrelated to the present illness—all of which are extraneous to his current medical problems. The *family history* inquires into illnesses which appear to run in the family, but like the past medical history, anything pertinent should have been mentioned in the present illness.

The *review of systems* is a roll call of symptoms that were not specifically addressed in the present illness. The review of systems can often be a bag of worms. There are so many depressed, lonely people out there and so many people exquisitely sensitive to their own bodies, that you may find more symptoms than you know what to do with. You'll have enough trouble trying to figure out symptoms the patient complains about, let alone trying to find things he doesn't actively complain about. Besides, hospitalizations are not the time to be fishing around for medical problems that don't bear directly on the present illness. Hospitalizations are just too expensive to pursue clinic-type problems. You're going to be under pressure to diagnose the patient's present illness, treat it, and then discharge the patient. Don't disregard secondary medical problems, but don't get overly involved with them either. The great advantage to following patients in clinic is that the pressure is off to uncover and solve the patient's every medical, social, and sexual problem at one sitting.

There are, however, certain 'E. F. Hutton' symptoms[*] that should be asked of every patient, symptoms which, because they were transient or so gradual, did not prompt the patient to seek medical advice, like gradual hearing loss, or spells of hemiparesis, unconsciousness, blindness, double vision, dyspnea, hemoptysis, irregular or rapid heart beats, orthopnea, angina, hematemesis, melena, and hematuria.

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*E.F. **Hutton' Symptom:** A symptom which, even if heard across a crowded room, would still catch your ear.

ANATOMIC TERMINOLOGY

OVER THE YEARS, DOCTORS have developed a shorthand vocabulary to sharpen their descriptions of signs and symptoms. Two general types of terms have evolved: ones describing anatomic sites, and ones describing the relation of one body part to another.

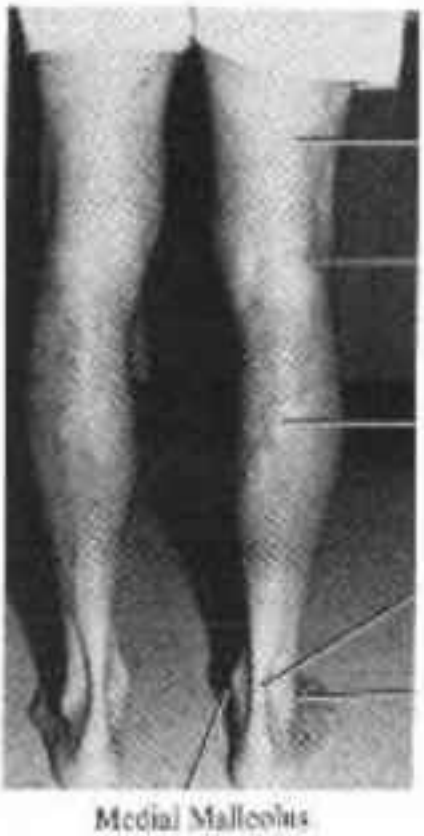
Anatomic sites are demarcated here:






Sternocleidomastoid Muscle
Posterior Triangle
Submandibular Region


Retroauricular Area
Cervical Region
Suprascapular region
Scapular Spine
Infrascapular Region
Loin


Hamstring Muscle
Popliteal Fossa
Gastrocnemius Muscle
Achilles Tendon
Lateral Malleolus
Medial Malleolus





There are three planes, one for each dimension: sagittal, frontal, and horizontal. Sagittal planes pass through the midline front to back; planes parallel to the sagittal, but off midline, are parasagittal. The frontal plane is parallel the front of the body. There are no 'parafrontal' planes; all planes parallel to the frontal are still called frontal. In the head, the frontal plane is also called the coronal plane.

Terms describing the relation of body parts to other another are divided into fixed positions and movements:

Position	Movement
Medial	Adduction
Lateral	Abduction
Unilateral	
Bilateral	
Ipsilateral	
Contralateral	Decussation
Proximal	Afferent
Distal	Efferent
Ventral	
Dorsal	
Anterior	Anterograde
Posterior	Retrograde
Rostral	
Caudal	
Supine	Supination (Eversion, External Rotation)
Prone	Pronation (Inversion, Internal Rotation)
Superior	
Inferior	
Flexed	Flexion
Extended	Extension
	Circumduction



Any point to the right or left of midline is lateral. Another, second point closer to midline is medial to the first point. In the arms, medial is defined with the palms facing forward. The ulnar side is medial; the radial side, lateral.

A single lateral structure is unilateral relative to midline. Two structures, one on each side of midline, are bilateral relative to midline, but contralateral to each other. Two structures on the same side of midline are ipsilateral to each other.

A single structure simply crosses the midline, but two contralateral structures crossing the midline through each other *decussate*.

If any structure has a beginning and an end, a source and a sink, then a point near the beginning is proximal to a point further downstream, or distal. So, the wrist is distal to the elbow, the aortic arch proximal to the renal arteries.

Afferent and efferent refer to movement toward or away from a reference point. Because *you* decide the reference point, the same structure can be afferent to one structure and efferent from another. For example, blood in the renal artery is afferent to the kidney but efferent from the aorta.

Posterior means behind; anterior means in front of. Dorsal means toward the backside; ventral, toward the abdominal side. Rostral means toward the head; caudal, toward the legs. Superior means on top of; inferior, below. When combined with another word, superior becomes supra, like supravalvular stenosis. Likewise, inferior becomes infra, or sub, as in infracostal or subhepatic.

Rostral/caudal, ventral/dorsal, anterior/posterior, and medial/lateral are all relative to the body, regardless of the body's position in space. Superior/inferior are relative to Earth, like up/down.

A patient lying on his stomach is prone, and supine when lying on his back.

Flexion and extension refer to any movement that, respectively, shortens or lengthens the trunk or a limb. In the foot *dorsi*flexion means to pull the foot up and *plantar* flexion means to step on the gas. The thumb flexes by sliding across the palm, and extends as the hand is opened wide.

*Ab*duction is any movement laterally, away from midline; *ad*duction is any movement medially, toward midline. The two exceptions to this rule are in the hand. For the fingers, the midline is the long finger. So when you spread your fingers, you abduct them; when you close your fingers, you adduct them (even though the ring and little fingers move away from the body's midline). The thumb abducts forward, away from the palm, and adducts back to rest against the palm and index finger. The thumb's fifth direction of movement is opposition—rotation across the palm to touch the tip of the little finger.

Flipping the palm over into a prone (palm down) position is called pronation; rotating the palm up is supination ('more soup please'). Rotation of the sole inward is inversion; outward, eversion.

To circumduct is to swing a limb in a circular orbit, like a softball pitcher making his windup.

SIGNS

Signs, the objective evidence of organ dysfunction, are, like symptoms, grouped according to organ systems. Each system's signs *must* be memorized. There is nothing more fundamental to being a doctor than knowing what signs to look for and knowing how to elicit them. It was no accident that the inspiration for history's greatest detective, Sherlock Holmes, the master of diagnostic acumen, was based on a real-life physician, Dr. Joseph Bell, himself a master of perceptive observation and attention to detail.[1] Recognize those smooth outcroppings, tiny bumps, and gentle ridges that make the human body so characteristic. What was once a casual bulge should become a familiar bone, or a real muscle innervated by a traceable nerve and fed by a palpable artery.

Instead of examining the body geographically—head, neck, chest, abdomen, and extremities—examine it by organ systems. Take each organ system one at a time. What signs *anywhere* in the body would you expect if that organ system malfunctioned? Below are the signs to expect for each organ system.

	Signs
Systemic:	blood pressure*, orthostatic hypotension*, pulse rate, respiratory rate, fever*, diaphoresis*, dry mouth*, diminished skin turgor*
Skin:	macule*, papule*, mole*, nodule*, plaque*, petechia*, vesicle*, bulla*, pustule*, ulcer*, constricted skin*, laceration*, abrasion*, contusion*, vitiligo*, alopecia*, erythema nodosum*, desquamation*
Neurologic:	see Chapters 13–26
Eyes:	corneal opacity, lens cataract*, Kayser-Fleischer ring*, chemosis*, conjunctival injection*, proptosis*, disc*, fundus*: cotton wool spots*, pigmentary clumping*
Ears:	discharge*, tympanic membrane*
Endocrine:	*Pituitary*—(Acromegaly*): prognathism*, frontal bossing*, large hands/feet. (Excessive Prolactin): galactorrhea* *Thyroid*—(Hyperthyroid): tachycardia, weight loss*, warm moist plethoric skin*, fine thin hair, pretibial myxedema*, hypervigilance*, nervousness, tremor*, proximal weakness*, exophthalmos*, stare*, lid retraction*, lid lag*, thyromegaly*, thyroid hum*, atrial fibrillation*, congestive heart failure*, diarrhea* (Hypothyroid): bradycardia, course hair, doughy skin*, puffy face (especially eyelids), loss of lateral eyebrows, slowed thinking, hoarseness, cerebellar ataxia*, hung up reflexes*, thyromegaly, distant heart sounds*, macroglossia* *Adrenal*—(Cushing's Syndrome*): purple striae*, round plethoric face, truncal obesity*, hirsutism* (Addison's Disease*): hypotension, hyperpigmented scars, excessively dark skin*

Islets (Diabetes): fundus dot/blot hemorrhages*, waxy exudates*, microaneurysm*, cotton wool spots
Gonads—(Feminization): loss of beard, loss of axillary* and pubic hair, gynecomastia*
(Masculinization): hirsutism, loss of subcutaneous fat, male pattern baldness, loss of breast tissue

Respiratory: nasal obstruction, epistaxis*, hoarseness, cough, hemoptysis*, tachypnea*, use of accessory respiratory muscles*, lip pursing*, stridor*, cyanosis*, clubbing*, subcutaneous crepitus*, deviated trachea*, thoracic contour*, dullness to percussion*, hyperresonance (tympany*), vocal fremitus*, rales*, rhonchi, diminished breath sounds, tubular breath sounds, whispered pectoriloquey, wheezes, auscultatory percussion, diaphragm movement*

Cardiac: pulse rhythm*, pulse character*, pulsus paradoxus*, splinter hemorrhages*, Roth spots*, cyanosis, basilar rales*, hepatomegaly*, jugular venous distension*, venous pulse waves*, pedal edema*, left ventricular heave*, right ventricular heave, apex*, S1*, S2*, inspiratory split S2*, S3*, S4*, opening snap*, click*, murmur*

GI: cheilosis*, glossitis*, macroglossia, melanin pigmentation* of lips/buccal mucosa, mouth ulcer, tongue induration*, parotid enlargement, hepatomegaly, nodular liver*, jaundice*, fluid wave*, shifting dullness, spider angioma*, gynecomastia*, dilated venous collaterals*, purpura*, palmar erythema*, testicular atrophy*, asterixis*, abdominal mass, abdominal guarding*, absent bowel sounds*, tinkling bowel sounds*, rectal mass, rectal blood*

RE: lymphadenopathy*, splenomegaly*, tonsils, lymph streaks*

Urologic: sallow complexion*, nephromegaly*, costovertebral angle tenderness*, asterixis*

Genital: testicular mass, scrotal mass, hernia*, prostate enlargement, prostate induration*, pelvic exam, breast mass, gynecomastia

Vascular: blood pressure asymmetry*, radial pulse asymmetry, carotid/thoracic/abdominal/femoral bruit*, radial-femoral pulse delay*, thrill*, pulsatile abdominal mass*, dorsalis pedis pulse*, posterior tibial pulse*, capillary filling time*, swollen-tender non-pulsatile* superficial temporal artery, retinal emboli*, cotton wool spots, waxy exudates*, diminished A-V ratio*, A-V nicking*, arteriolar hemorrhages*, arcus senilis*, telangiectasia*, varicose veins*, deep venous tenderness/cord*, Homan's sign, hemorrhoids*

Hematologic: pallor*, plethora*, petechia*, purpura*, ecchymosis*, xanthelasma*, xanthoma*

Bone: and Joint: Joint: deformity*, erythema*, swelling, tenderness, warmth, crepitation*, diminished range of motion, instability. Kyphosis*, scoliosis*, pectus carinatum*, pectus excavatum*, arachnodactyly*, loss of lumbar lordosis*

Coverings & Connective Tissue: periarticular* swelling, meningismus*, pleural friction rub*, pericardial friction rub*, rebound tenderness*, psoas test*

SYSTEMIC:

Blood Pressure: A regular blood pressure cuff on a large arm will record a spuriously high blood pressure.[3] Use a wide cuff to avoid this problem.

Orthostatic Hypotension: A drop in blood pressure on arising from a supine position. More than a 30mm drop in blood pressure is often associated with feeling faint or dizzy on standing. Orthostatic hypotension is either due to not enough blood in the vascular tree (like gastrointestinal hemorrhage), or not enough venous constriction on standing, a vascular reflex that normally prevents venous blood from pooling in easily distensible veins inferior to the heart, like the inferior vena cava, abdominal veins, and leg veins.[3]

Fever: Fever is caused by a special protein released by white cells during inflammation.[4]

Diaphoresis: In response to hypotension, the autonomic nervous system tries to constrict arteries and veins, but also ends up stimulating the sweat glands. So a patient about to faint looks pale and sweaty, and his skin feels cool (due to poor skin perfusion and the evaporating perspiration).

Dry Mouth: If the patient isn't mouth breathing, a dry mouth often signifies dehydration.

Skin Turgor: Poor skin turgor (usually due to dehydration) is present when skin over the extremities won't bounce back after being pinched.[5]

SKIN:

Macule: A flat, colored spot on the skin, undetectable by running your finger across it (like a freckle).

Papule: A small, raised lesion of the skin.

Mole: A small, raised, usually pigmented lesion, often containing a small tuft of hair.

Nodule: A small mass.

Plaque: A broad raised lesion.

Petechia: A tiny red dot of blood from a burst capillary.

Vesicle: A small bubble of usually clear fluid. Typically appears as a crop, as in a vesicular rash.

Bulla: A sizeable collection of fluid in the skin, like a large blister after a burn.

Pustule: A vesicle filled with cloudy, inflammatory fluid. A zit.

Ulcer: A hole at the surface walled off by inflammation. A boil (an abscess under the skin) that bursts open and continues to weep and drain is a good example of an ulcer. An ulcer does not have to be on the skin surface, nor does the inflammation have to be in response to infection; a stomach ulcer eroded by gastric acid is a good example.

Constricted Skin: Tight, deeply lined skin around the mouth or tight shiny skin on the hands may suggest collagen deposition in the skin, commonly seen in an immunologic disease called scleroderma.

Laceration: A tear or cut.

Abrasion: What happens to your thigh when you slide into home on a concrete playground.

Contusion: A black and blue mark caused by a direct blow. Meaning the blow was severe enough to burst some blood vessels and leak blood into the skin.

Vitiligo: A patch of skin depigmentation.

Alopecia: Hair loss.

Erythema Nodosum: A red, tender nodule associated with chronic infections and immunologic diseases.

Desquamation: Dead skin peeling off.

EYES:

Cataract: Opacity.

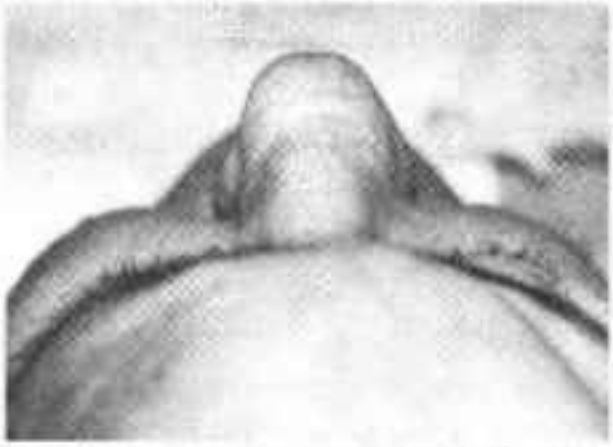
Kayser-Fleischer Ring: A brownish ring around the periphery of the iris, usually beginning at 12:00 high and over months to years extending circumferentially. Virtually pathognomonic of Wilson's Disease (chapter 34).

Chemosis: Wet (edematous) conjunctiva bulging from the upper or lower eyelids. Often due to obstruction of venous outflow from the eye.

Conjunctival Injecton: Red eye.

Proptosis:[5] Bulging eye. Synonymous with exophthalmos. Often easier to detect by looking down on the eyes while standing behind a seated patient.

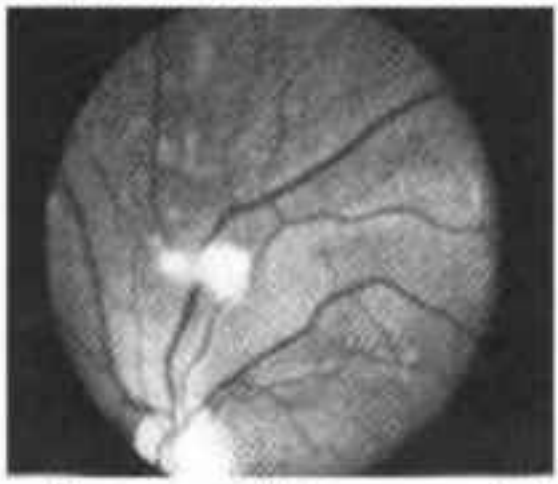




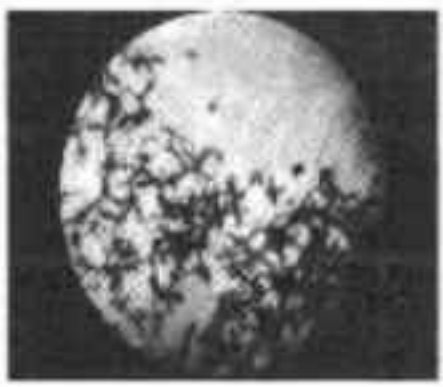
Disc: The tip of the optic nerve, where the optic nerve inserts into the eyeball. The disc is visible with an ophthalmoscope, an instrument invented in 1850 consisting of about twenty small lenses of increasing refractive strength that permit a direct view of the retina and disc.

Fundus: The retina as seen through the ophthalmoscope.

Cotton Wool Spot: A small, whitish, fuzzy-bordered area of infarcted retina. Due to obstructed axoplasmic flow in retinal axons (chapter 20).[7]



Pigmentary Clumping: The retina begins to look as if someone sprinkled pepper over it. In advanced cases, the black speckles accumulate to the size of small spicules.



Spicules of Degenerating Retinal Pigment

EARS:

Discharge: Any fluid oozing out of a hole.

Tympanic Membrane: The major landmarks as seen through an otoscope are:



Picture courtesy
Dr. William Gray

ENDOCRINE:

Acromegaly: Caused by a benign pituitary tumor secreting excessive growth hormone.

Prognathism: An exceedingly large jaw.

Frontal Bossing: Large supraorbital ridges due to enlarged frontal sinuses.

Galactorrhea: Milk seeping from the breasts.

Weight Loss: Thyroid hormone 'uncouples' mitochondria by diverting Acetyl CoA into heat instead of ATP. Glucose and fat, the sources of Acetyl CoA, are used up in the process. If it weren't for its ill effects on other organ systems, thyroxine might be a good diet pill (forget it, it's already been tried and abandoned).

Warm Moist Plethoric Skin: To rid itself of hyperthyroid heat, the body sweats and dilates blood vessels in the skin to carry excess heat to the body surface, making the face look flushed, or plethoric.

Pretibial Myxedema: Even though myxedema means hypothyroidism, this skin condition occurs in hyperthyroidism. The skin over the shins (tibial bones) becomes thickened, like orange skin.

Hypervigilance: Like birds sitting on a fence, these easily distractable patients dart their attention around the room, briefly giving notice to everything.

Tremor: The rapid, fine (small amplitude) tremor of hyperthyroidism is best seen with the patient's hands held out in front of him with the fingers spread apart. The tremor is finer and more rhythmic than typical 'morning after' tremulousness.

Proximal Weakness: Excess thyroid hormone weakens muscles around the shoulder and pelvic girdles.

Exophthalmos: Bulging eye. Synonymous with proptosis.

Stare: Infrequent blinking.

Lid Retraction: The eyelids are pulled back slightly; white sclera can be seen above and below the iris. Lid retraction is probably due, in part, to overstimulation of Mueller's muscle (chapter 20).

Lid Lag: When the eyes glance downward, the upper eyelid lags because of an overactive Mueller's muscle.

Thyromegaly: Enlarged thyroid (goiter). Normally, you should barely be able to palpate (feel) thyroid tissue surrounding the base of the thyroid cartilage (Adam's apple).

Thyroid Hum: A continuous whishing sound heard with a stethoscope signifying excessive blood flow through an overactive thyroid.

Atrial Fibrillation: Instead of the S-A node firing the atria, widespread areas of the atria simultaneously try to pre-empt the S-A node. The atria fire so rapidly that no effective atrial contractions take place. Instead, the atria remain in a quivering, almost paralyzed state. Thyroxine appears to stimulate all the atrial 'pretenders' to the S-A throne.

Meanwhile, the A-V node, bombarded by atrial impulses, responds randomly. The result is a highly irregular, often rapid, ventricular heartbeat.

Congestive Heart Failure: A heart whipped by thyroid hormone may eventually fail.

Diarrhea: Like most everything else innervated by the sympathetic nervous system, the gut too is stimulated by thyroid hormone.

Doughy Skin: Imagine pinching the Pillsbury Dough Boy.

Cerebellar Ataxia: The pathophysiology of hypothyroid ataxia is unknown. See chapter 18 for a description of cerebellar ataxia.

Hung Up Reflexes: After a tendon is tapped, the muscle attached to it contracts and then relaxes. In hypothyroidism the relaxation phase is prolonged; the muscle glides back to its resting position instead of smartly snapping back.

Distant Heart Sounds: The hypothyroid heart doesn't contract vigorously, so the valves don't snap shut. Distant heart sounds may also be due to a pericardial effusion, an occasional complication of hypothyroidism, as are joint and pleural effusions.

Macroglossia: Enlarged tongue. Like thickening and effusions elsewhere in the body, macroglossia is due to fluid and mucopolysaccharide accumulation in the tongue (see chapter 35 for more about mucopolysaccharides).

Cushing's Syndrome: Excessive cortisol production by the adrenal gland, due either to an adrenal tumor or to an ACTH producing pituitary tumor. Named after the eminent neurosurgeon, Harvey Cushing, who, during the early 1900's, pioneered the entire field of neurosurgery, especially the surgery of pituitary tumors.

Purple Striae: Purple stretch marks.

Truncal Obesity: Cortisol increases fat storage in the face, neck, and trunk.

Hirsutism: Excessive hair on the face, trunk, and limbs.

Addison's Disease: Adrenal gland failure, after Sir Thomas Addison, a renowned physician in the mid-nineteenth century.

Hyperpigmented Scars and Dark Skin: Due to erroneous production of melanocyte stimulating hormone (which darkens the skin) by the pituitary during its enthusiastic attempts to stimulate a sluggish adrenal with ACTH. (ACTH also has its own melanocyte stimulating properties.) Look for dark skin along the inner forearm, which is normally a lighter color than the sun-exposed outer side. Uniform darkening on both sides of the forearm suggests true hyperpigmentation.

Dot/Blot Hemorrhages: Tiny hemorrhages in deeper layers of the retina, as opposed to more superficial 'splinter' hemorrhages (chapter 20).

Waxy Exudate: A sharply demarcated clump of lipid from a burst retinal capillary.



Microaneurysm: A tiny venous aneurysm before it has leaked a dot hemorrhage.

Axilla: Arm pit.

Gynecomastia: Enlarged breasts.

RESPIRATORY:

Epistaxis: Nosebleed.

Hemoptysis: Coughing up blood.

Tachypnea: Rapid breathing. Though tachypnea strictly refers to rapid, shallow breathing (hyperpnea means rapid *deep* breathing), tachypnea is used to mean hyperpnea, too. Hyperventilation is what happens to the patient's blood during hyperpnea: the overventilated lungs raise the blood pO_2 and wash out the CO_2 (lowering the serum pH).

Accessory Muscles: Not used in normal breathing, the accessory neck muscles help expand the chest wall during labored breathing.

Lip Pursing (on expiration): By providing back pressure to small bronchioles during expiration, lip pursing prevents weakened (by cigarette smoke) bronchiolar walls from collapsing during expiration and so trapping air within alveoli. Lip pursing is almost always a sign of emphysema.

Stridor: Coarse wheezing from upper airway obstruction like food in the trachea, a swollen epiglottis, etc.

Cyanosis: Blue fingernails and lips, usually from poorly oxygenated arterial blood.

Clubbing: Enlargement and softening of the nailbed. Though seen in many chronic lung diseases, the pathophysiology of clubbing is uncertain.

Subcutaneous Crepitus: Blebs of air under the skin. Usually seen when a lung leaks air into the subcutaneous tissue.

Deviated Trachea: Usually means one lung is overexpanded or the other lung has collapsed.

Thoracic Contour: A badly misshapen chest may impair lung expansion.

Dullness to Percussion: Percussing (thumping) the thorax normally produces a deep, rich, hollow resonance. A pleural effusion or a consolidated lung (a lung filled with inflammation) produces a flat, dull sound.

Tympany: If the thoracic percussion sound is *too* hollow and resonant, it means there's too much air on that side of the chest. This happens when rupture of a lung alveolus or puncture of the chest wall allows air to penetrate the pleural space, disrupting the bond of surface tension between the two pleurae. The lung collapses leaving a large, empty, hyperresonant hemithorax, called a pneumothorax. Conversely, blood in the pleural space is called a hemothorax, which, like any pleural effusion, causes *dullness* to percussion.

Tympany is a very hyperresonant sound ('bell-like'), commonly elicited by percussing over the stomach or other hollow internal organ.

Vocal Fremitus: Vibrations (fremitus) felt on the chest wall as the patient talks. Since these vibrations are conducted to the chest wall by lung tissue, a collapsed lung, or an effusion between the lung and chest wall, reduces vocal fremitus. Conversely, since sounds travel better through solids than air, *increased* fremitus suggests lung consolidation or compression of lung tissue (atelectasis).

Atelectasis—collapse of alveoli—occurs in three major circumstances: 1) when a lung is compressed above a pleural effusion, 2) whenever air cannot reach alveoli because of bronchial obstruction (by a tumor, mucous plug, or an aspirated (inhaled into the trachea) foreign body), and 3) when a pulmonary artery is occluded (typically by an embolus); without a steady supply of CO_2, alveolar air becomes rapidly depleted of CO_2, which stimulates bronchiolar and alveolar constriction. The other reason for alveolar collapse after a pulmonary embolus is the absence of blood-borne nutrients

necessary to make surfactant, a crucial lipid lining all alveolar walls. Surfactant helps small alveoli remain open by reducing surface tension inside the alveolus. Without surfactant, small alveoli would empty into larger ones. Because surfactant isn't made until 4–6 weeks before delivery, premature infants frequently suffer 'respiratory distress': stiff, poorly distensible lungs due to absent surfactant.

Stethoscope Sounds:

Vesicular Breath Sounds are normal. You're hearing air flowing into nice, dry alveoli.

Rales sound like crinkling tissue wrapping paper, as the edematous, sticky alveoli smack open.

Rhonchi are long, coarse, multi-pitched sounds due to partially obstructed large bronchi, usually obstructed by pus or mucus.

Diminished Breath Sounds are due to insufficient air either reaching the alveoli (because of bronchial obstruction) or entering the alveoli (which have collapsed from infection, edema, pleural effusion, or previous bronchial obstruction).

Tubular Breath Sounds resemble the harmonious sound of air flowing through the trachea (place your stethoscope over the trachea). Tubular breath sounds reflect normal air flowing through normal bronchial tubes, well-heard because the sounds are conducted to the chest wall through solid (consolidated) lung tissue instead of aerated lung tissue.

Whispered Pectoriloquy are (normally inaudible) whispered words heard clearly through the chest wall because of lung consolidation.

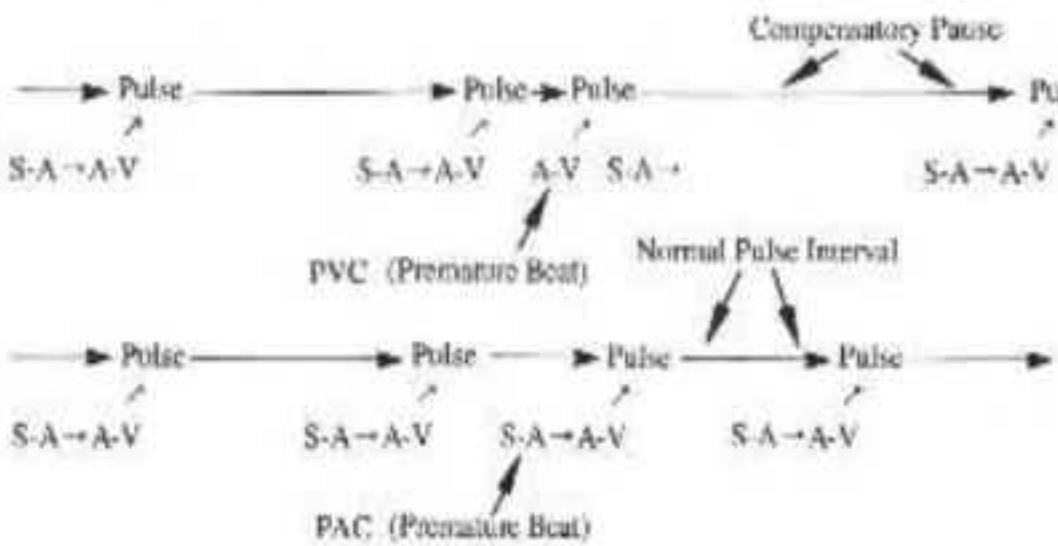
Wheezes are high pitched whistles of air squeaking through tightly constricted bronchioles.

Auscultatory Percussion: percuss the upper sternum while listening over the lung or along the vertebral column. Diminished resonance is highly significant, indicating a mass between the stethoscope and sternum.[3]

Diaphragm Movement: The lower level of the lung corresponds to the diaphragm. This level can be found along the back by noting where percussion sounds change from resonant to dull. If this level descends when the patient takes a deep breath, the diaphragm has moved. Normal movement is about three fingerbreadths. Be sure to check both sides, because each side is innervated separately by the right or left phrenic nerve, nerves which begin high in the neck and travel through the mediastinum to reach the diaphragm.

CARDIAC:

Pulse Rhythm: The cadence of the heart beat. A chaotically irregular pulse varying in both amplitude and rhythm is almost always atrial fibrillation. A regular rhythm with premature beats may represent an atrial or a ventricular premature contraction depending on the interval between the premature beat and the next palpable one. A premature beat followed by a 'compensatory' pause is a premature ventricular contraction (PVC). Without the compensatory pause, it's probably a premature atrial contraction (PAC).



The reason for the compensatory pause is that the A-V node needs time to repolarize before it can fire again. That is, if a premature ventricular contraction has already discharged the A-V node from below, the A-V node won't fire when the normal S-A impulse arrives from above. Instead, the A-V node must wait for the next S-A impulse. A premature atrial (or supraventricular) beat discharges the A-V *and* S-A node, thereby resetting the S-A node. The interval to the next pulse beat is simply the normal pulse interval.

Many times you won't feel a premature heart beat at the radial artery because the premature beat contracts too soon after a normal contraction for enough blood to fill the left ventricle. What you feel instead is a missed ('dropped') heart beat. You'll have to tap out the pulse: if the pulse after the dropped beat arrives with your toe tap, the dropped beat is probably a PVC. If the next pulse arrives before it should, then the S-A node must have been reset (i.e., a premature atrial contraction). In addition, the first pulse after a PVC is much stronger, because that particular heart beat also pumped the blood that should have been pumped by the PVC.

Pulse Character: Concentrate on the initial rise of the pulse. Does it tap your finger (normal) or slowly bulge into your finger (suggesting aortic stenosis)? Or does it rap your finger forcefully to suggest a widened pulse pressure (systolic minus diastolic = pulse pressure) as in aortic insufficiency or hyperthyroidism?

Pulsus Paradoxus: During normal inspiration the lungs become a very large reservoir of blood, sucking blood forward from the right ventricle and withholding pulmonary venous blood returning to the left atrium. The resulting drop in left ventricular output can easily lower systolic blood pressure during inspiration by 10–12mm.

When pericardial constriction becomes tight enough, or when a pericardial effusion becomes large enough to tamponade (squeeze) the heart, the inferior and superior vena cavae cannot fill the heart with adequate blood, a dangerous situation because the cardiac output drops. This situation is worsened during each inspiratory breath because: 1) blood flow through the right ventricle increases (encroaching on already limited elbow room within the pericardial sac), and 2) right ventricular blood on its way to the left ventricle is sequestered in the lungs, accentuating an already tenuous blood supply to the left ventricle. The result is a serious drop in systolic blood pressure with each inspiration, which you hear as an exaggerated pulsus paradoxus. (Pulsus paradoxus actually occurs less commonly with pericardial constriction than with tamponade.[9])

Pulsus paradoxus is also seen in severe asthma when desperate inspiratory efforts against a 'tight' chest (severe bronchial constriction) may raise intrathoracic pressure enough to restrict venous return to the right atrium by compressing the superior and inferior vena cavae.

To detect pulsus paradoxus, pump the blood pressure cuff well above systolic and slowly lower the pressure until you hear the very first systolic pulse; this will be heard during expiration. Not every single heart beat will be heard until you lower the cuff pressure still further. The difference in systolic blood pressure between the point at which you first hear any systolic pulses and the point at which you hear *all* the systolic pulses is the pulsus paradoxus. Normal is less than 12 mm.

Also check the neck veins during inspiration (when the right ventricle is demanding additional blood from the inferior and superior vena cavae); neck vein distension during *inspiration* implies the same as an exaggerated pulsus paradoxus—obstruction to right ventricular filling.

Splinter Hemorrhages: A sign of emboli from the heart, these sliver-like hemorrhages usually appear in the nail beds and mucosa of the eye or mouth.

Roth Spot: A splinter hemorrhage in the retina containing a tiny white spot in its center where the emboles obstructed the arteriole. (Roth actually described only the white spot, not the surrounding hemorrhage.[10])



Basilar Rales: Elevated back pressure behind a failing left ventricle forces fluid into dry alveoli. The pulmonary edema is audible during inspiration as the sticky alveoli pop open—rales.

Hepatomegaly: Enlarged liver. The liver is normally not palpable below the right costal margin (lower edge of the rib cage). Hepatic distension may result from venous engorgement behind a failing heart.

Jugular Venous Distension: Just as venous blood dams up behind a failing heart into the liver, venous blood also backs up into the neck. At a thirty degree incline, the neck veins should be collapsed. Distension implies heart failure (or obstruction to right ventricular filling from tricuspid stenosis or pericardial tamponade). It's best to concentrate on the internal jugular vein, because the external jugular vein may be distended by local kinking as it rounds the clavicle and first rib.

Early heart failure can be suspected by the hepatojugular reflux. With the patient propped up at thirty degrees, firm pressure on the liver forces extra venous blood out of the liver into the neck. If jugular venous distension persists while you maintain hepatic compression, early heart failure is present.[11]

You can measure your own venous pressure by noting when veins on the back of your hand collapse as you lift your hand to heart level. Be sure you're well hydrated so that your blood volume is expanded enough to include the peripheral hand veins.

Venous Pulse Waves: Jugular veins in the neck pulsate, something you can discern in a patient lying propped up at thirty degrees. 'Cannon waves' exploding up the jugular vein with each heartbeat indicate tricuspid insufficiency; less prominent cannon waves suggest high right atrial pressure (pulmonary emboli, pulmonic or tricuspid stenosis, etc.) Occasional cannon waves are seen with 'A-V block' in which the atria, beating independently of the ventricles, occasionally pump against a closed tricuspid valve.

Pedal Edema: Firm thumb pressure will leave a pit which gives pedal edema its alias, pitting edema.

Heave: Visible or palpable bulging of the chest wall with each heart beat due to an enlarged ventricle.

Apex: Tip of the heart. Should normally be felt as a gentle tap in the 4th intercostal rib space underneath the breast in the mid clavicular line. An apex beat too far lateral or too low usually means an enlarged heart.

S1: The first heart sound occurs when the mitral and tricuspid valves snap shut. The resulting vibrations of the myocardial wall and intraventricular blood create the first heart sound.[7]

S2: The second heart sound stems from audible shock waves of the myocardial wall and intraventricular blood when the aortic and pulmonic valves snap shut.[7]

Inspiratory Split S2: The second heart sound (S_2) normally splits into a doublet during inspiration and merges again into a single sound during expiration. The reason for the inspiratory split is that it takes longer for the right ventricle to empty during inspiration when there is increased right ventricular blood flow. So during inspiration, the pulmonary valve component (P_2) of the second heart sound lags slightly behind the aortic component (A_2). During expiration P_2 merges again with A_2 to form a single S_2.

Fixed splitting of S_2 (split during both inspiration *and* expiration) occurs in atrial septal defects (ASD), because blood flow through the right ventricle is *already* maximal; inspiration cannot further augment blood flow through the right ventricle. S_2 is already split during expiration and remains split during inspiration.

S3: A sign of congestive heart failure. Heard after the 2nd heart sound, not quite midway to the first heart sound. Due to blood pouring through the mitral valve into an enlarged, failing left ventricle (like dumping water into an empty bucket).[4]

The heart enlarges during congestive heart failure to increase its cardiac output. The heart has only two ways to increase its cardiac output. It can increase its heart rate or increase the amount of blood ejected per beat (the stroke volume). Normally, only about ½–⅔ of left ventricular blood is ejected during any one beat. Athletic hearts increase this ejection fraction, i.e., empty the ventricles more completely, a feat made easier by not having to pump against a head of high arterial pressure. A failing heart, unable to pump with the heightened vigor of an athletic heart, increases the amount of blood ejected per heart beat by pumping the usual ½–⅔ (or less) of its ventricular contents, but from a *larger* left ventricular volume—i.e., the heart enlarges when it fails.

S4: Heard just before S1. Probably due to a left atrial kick forcing blood into a stiff left ventricle.

Opening Snap: A normal mitral valve opens silently at the beginning of diastole. A stiff, stenotic mitral valve *snaps* open, producing an audible snap immediately after S2.

Click: A backward billowing of the mitral valve during systole, audible as a click.

Murmur: Same as a bruit. Means turbulent blood, in this case from blood tumbling over an abnormal heart valve or through an atrial or ventricular septal defect. Sometimes the blood tumbles when an exceptionally healthy heart pumps blood extra vigorously past a normal valve or when too much blood is flowing. Too much blood flow occurs when an abnormal channel between the right and left side of the heart (an atrial or ventricular septal defect) allows blood to recirculate through the right ventricle instead of being pumped down the aorta.

GASTROINTESTINAL:

Cheilosis: Splitting of skin at the corners of the mouth; a sign of vitamin deficiency.

Glossitis: An inflamed, bright red, smooth tongue.

Melanin Pigmentation: Dark pigmented macules along the lips and buccal (cheek) mucosa. Associated with Peutz-Jeghers syndrome: buccal pigmentation and intestinal tumors.

Induration: Hardness. Suggests cancer of the tongue.

Nodular Liver: A sign of scarring within the liver (cirrhosis). Usually not palpable because the scarred liver is shrunken up behind the ribcage.

Jaundice: Best seen in the conjunctiva of the eye.

Fluid Wave: A small, scarred (cirrhotic) liver obstructs intestinal venous blood returning to the heart. Venous back pressure causes fluid to weep from the liver surface into the abdomen, filling the belly with ascites. The presence of fluid is detected by tapping one side of the abdomen and feeling the wave of fluid break against the other side. The level of fluid in the abdomen can be determined by percussing (tapping) up the abdominal wall while listening for a change in sound from flat to resonant. Since some normal people have this change without ascites, the patient is shifted to his left or right side and the percussion repeated. If a similar change in resonance occurs, it means the belly is partially filled with fluid which shifts as the patient shifts—called shifting dullness. You can also hear ascitic fluid with a stethoscope by rapidly pressing the abdominal wall while listening for a 'succussion splash.'

Spider Angioma: Small, spider-shaped capillary dilations on the trunk; associated with liver failure.

Gynecomastia: Male breast enlargement occurs in liver failure because the liver normally 'detoxifies' estrogen in men.

Dilated Venous Collaterals: Venous obstruction through a small cirrhotic liver forces the blood to detour through veins in the abdominal wall, visible as dilated venous collaterals.

Purpura: Large bruises due to inability of the liver to synthesize the coagulation factors necessary for normal clotting.

Palmar Erythema: Red palms associated with liver dysfunction. Commonly seen in alcoholics.

Testicular Atrophy: Like gynecomastia, testicular atrophy results from elevated estrogen levels in liver failure.

Asterixis: Inability to maintain muscles in active contraction against gravity (see chapter 13). Also called 'liver flap' because asterixis is frequently seen in liver failure.

Guarding: Reflex spasm of the abdominal wall as you press over an area of tenderness.

Absent Bowel Sounds: With a stethoscope you can normally hear occasional grumbling sounds as the intestines move (peristalsis). Absent bowel sounds imply paralysis of the intestines, called ileus.

Tinkling Bowel Sounds: Very high pitched tinkling sounds, like rapidly tapping an expensive wine glass, suggest partial obstruction of the bowel.

Rectal Blood: Invisible amounts of blood ('occult blood') can be detected by mixing a small patch of stool with a special tablet that turns blue when moistened in the presence of blood. Checking every patient for occult blood is a very useful screening test for asymptomatic rectal and colonic cancer.[15]

RETICULOENDOTHELIAL:

Lymphadenopathy: Enlarged lymph glands. Important places to look for lymphadenopathy are high up in the axilla, supraclavicular fossa, base of the neck, groin, and deep in the abdomen.

Splenomegaly: Enlarged spleen.

Lymph Streaks: Red streaks usually along the forearm signifying an ascending infection in the lymphatic canals, common in infections around the nail bed, called paronychia.

UROLOGIC:

Sallow Complexion: The color of gray-yellow candle wax.

Nephromegaly: Enlarged kidney.

Costovertebral Angle (CVA) Tenderness: Tenderness to thumping over the costovertebral angle (the middle of the back where the lower ribs join the vertebrae). CVA tenderness, a sign commonly indicating a kidney infection (pyelonephritis), can be exquisite enough to provoke a chandelier sign—the patient leaps off the bed onto the chandelier.

Asterixis: Same sign as in liver failure; occurs in kidney failure or after a bout of severe hypoxia.

GENITAL:

Hernia: In order for the testes, which originally formed in the fetal abdominal cavity, to descend into the scrotum, they must pass through a hole in the lower abdominal wall. If the hole enlarges during later life, intestines can herniate into the scrotum.

Prostate Induration: Usually a sign of prostate cancer. The prostate is palpated through the rectum.

VASCULAR:

Asymmetry: A lower blood pressure in one arm suggests stenosis of either the subclavian or brachial artery. Confirm the stenosis by simultaneously palpating both radial pulses: the abnormal radial pulse will be fainter and will arrive a split second later than the normal side.

Bruit: Sounds just like a systolic heart murmur.

Radial-Femoral Delay: Since both the radial and femoral arteries are the same distance from the heart, a delayed femoral pulse suggests aortic coarction. The amplitude of the femoral pulse should also be diminished, and you may hear a bruit over the back.

Thrill: Palpable vibration. Implies turbulent blood tumbling through a stenotic artery.

Pulsatile Abdominal Mass: Large, bulging aneurysm of the abdominal aorta.

Dorsalis Pedis Pulse: Felt on top of the foot.

Posterior Tibial Pulse: Felt behind the medial malleolus (ankle).

Filling Time: If it takes too long for capillaries to reperfuse skin you pinched white, the circulation is impaired.

Swollen-Tender-Non-Pulsatile: These are the signs of temporal arteritis.

Retinal Emboli: Bits of cholesterol, fibrin, or clumps of platelets in retinal arterioles imply embolization from either the carotid bifurcation or the heart.

Waxy Exudates: A small puddle of lipid that leaked from an abnormal blood vessel. The circumference of a waxy exudate is sharp, unlike that of a fuzzy bordered cotton wool spot.

A/V Ratio: Arterioles react to the increased pressure of hypertension by constricting which you see (with an ophthalmoscope) as a lowered arteriole/venule (A/V) ratio in the retina.

A/V Nicking: Chronic hypertension causes scarring at points in the retina where arterioles cross veins. These scars cause local narrowing ("nicking") of arterioles as they cross the veins.[9]

Hemorrhages: Severe hypertension causes retinal arterioles to bleed, producing splinter hemorrhages (chapter 20).

Arcus Senilis: A white ring around the iris often associated with atherosclerosis. Absence of arcus senilis in one eye implies stenosis of the ipsilateral internal carotid artery (preventing high blood pressure from reaching the eye.)[1]

Telangiectasia: Dilation of capillaries, like the spider angiomas of liver failure. Scleroderma often produces telangiectasias on the fingers.

Varicose Veins: Veins (usually in the legs) dilated by gravity sucking venous blood backward through incompetent venous valves. Venous valves normally allow blood to flow in only one direction—toward the heart. Venous return from the legs is aided by muscular contractions squeezing the veins coursing through the leg muscles.

Tenderness/Cord: By not exercising their calf muscles, patients lying in bed are particularly susceptible to stasis (stagnation) of venous blood in the legs, a situation which predisposes to venous thrombosis and thrombophlebitis (inflammation of the blood clot). Deep venous thrombophlebitis is palpable as a tender cord deep within the gastrocnemius (calf muscle). Pushing upward on the ball of the foot stretches the already inflamed vein and causes a sudden sharp pain in the calf, called Homan's sign. The danger of a deep venous clot is that it may dislodge and embolize through the right ventricle into the pulmonary artery, fatally obstructing it.

Hemorrhoid: A varicose vein in the rectum.

HEMATOLOGIC:

Pallor: Pale skin. If you have trouble telling where the lips end and the surrounding skin begins, the patient is pale. Also check for pallor in the conjunctival blood vessels by pulling down the lower eyelid. Pinch the nail: does it turn white, or is there no change (i.e. it was pale to begin with)?

Plethora: Red skin from too much blood flowing through it.

Petechia: When capillaries burst, the tiny leakage of blood is manifest in the skin as a petechia.

Purpura: A purple macule due to blood in the skin.

Ecchymosis: A large purpura.

Xanthelasma: Yellowish deposits of cholesterol in the skin, usually seen around the eyelids.

Xanthoma: Deposits of cholesterol and triglycerides, best seen in the Achilles tendon.

BONE:

Deformity: For example, a valgus deformity everts a joint (knock knees); a varus deformity inverts the joint (bowlegged).

Erythema: Redness.

Crepitation: Grinding of a joint when it's moved.

Kyphosis: Forward curvature of the upper spine; frequently seen in old age.

Scoliosis: Sideways curvature of the spine.

Pectus Carinatum (pigeon breast): A triangular shaped chest in which the sternum (breast bone) sits too far anteriorly.

Pectus Excavatum: The sternum sits too far inward, forcing the ribs to curve backward to attach to the sternum.

Arachnodactyly: Long spidery fingers associated, most commonly, with Marfan's disease, a genetic abnormality of bones and connective tissue affecting many different organ systems: lens displacement, retinal detachment, aortic insufficiency, dilation of the proximal (ascending) aorta, pectus carinatum, pectus excavatum, hyperextensible joints, kyphoscoliosis, joint dislocations (hip, clavicle, etc), arm span longer than height, and a lower than normal head-to-pelvis/pelvis-to-feet ratio.

Arachnodactyly is also seen in homocystinuria, a genetic defect of homocysteine (amino acid) metabolism—see chapter 35. Besides looking Marfanoid, homocystinurics also suffer from mental retardation and thrombotic strokes.

Lumbar Lordosis: Lumbar muscle spasm straightens the normal lumbar lordosis (the backward curve in the small of the back).

COVERINGS & CONNECTIVE TISSUE:

Periarticular: An articulation is where two bones join. Periarticular means next to the articular area.

Meningismus: As you flex the patient's head forward, his neck responds with sudden involuntary resistance. If severe, you should be able to lift the patient's trunk off the bed by simply lifting the occiput (back of the head).

Pleural Friction Rub: A coarse, leathery sound (like a creaking saddle) due to inflamed parietal and visceral pleura rubbing together.

Pericardial Friction Rub: The same leathery sound as a pleural friction rub, but audible with each heart beat.

Rebound Tenderness: When the abdominal wall is pressed inward and suddenly released, the patient experiences a severe, painful spasm of the abdominal wall. A sign of peritonitis.

Psoas Test: Hyperextending the patient's hip stretches the peritoneum overlying the psoas muscle. If this maneuver elicits reflex pain and involuntary resistance, there is inflammation in the posterior peritoneum or psoas area.

Two things should be readily apparent from the above list of signs. First, the list varies with the type of specialty practice. A cardiologist, for example, may include other, more sophisticated cardiac and vascular signs while deemphasizing parts of the GI exam. Second, like overlapping symptoms, some signs can fit into more than one organ system. Analogous to the problem of overlapping symptoms, proper placement of an overlapping sign into the correct organ system demands that you know, stone cold, the constellation of physical signs for each organ system. For example, testicular atrophy may be a sign of primary testicular failure, or—if you had also found hepatomegaly, jaundice, telangiectasias, and asterixis—a sign of liver failure.

Signs must become second nature to you, nothing less. They are the fundamental tools to diagnose the anatomic site of a patient's complaint. As you postulate diseases you will immediately know which signs to expect, because every disease affects a characteristic constellation of organ symptoms. Even when two diseases affect the same organ systems, the constellation of signs for each disease will still be distinctive, because any two diseases affecting the same organ system do so in different ways. This means you must not only know the signs of each organ system and which organ systems a disease attacks, but also which subset of signs to expect for each disease.

For example, a patient complains of back pain. From anatomy you know which organ systems are in or adjacent to the back, so your anatomic differential diagnosis will include the following organ systems (in parentheses are likely etiologies): Neuromuscular (root compression*), Gastrointestinal (pancreatitis*), Urologic (pyelonephritis*), Genital (pelvic infection), Vascular (aortic aneurysm or dissection*), Bone (cancer, infection, etc.), and Coverings & Connective Tissue (tumor lying against the dura surrounding the spinal cord). If, after questioning, you suspect the urologic system, what signs will you look for? What if you suspected the neuromuscular, vascular, GI, bone, or coverings & connective tissue organ system? If you do find signs that confirm your suspicions, you'll still look for the *absence* of signs in the other organ systems, but your approach is the same: postulate an abnormal organ system and look for specific signs to confirm or refute it. And if you consider a specific illness, such as lung cancer metastatic to a lumbar vertebral body, then you must know the potential signs in each of the sixteen organ systems for metastatic and nonmetastatic lung cancer so that these signs can be specifically sought.

Root Compression: The spinal cord sits behind the vertebral bodies which are stacked one atop the other with cartilaginous discs between them. Nerve roots exiting and entering the spinal cord are vulnerable to compression by a bulging, herniated disc, a condition which often radiates pain from the back into the hip or leg (chapter 22).

Pancreatitis: Though gallstones may obstruct the pancreatic duct, the most common cause of pancreatitis is alcoholism.

Pyelonephritis: Kidney infection—almost always due to a bladder infection which ascends the ureters to the kidneys. Recurrent pyelonephritis can eventually scar the kidneys badly enough to render them useless.

Aortic Aneurysm/Dissection: A dilated aorta pressing on a vertebral body or a nerve may cause back pain. Sudden aortic dilation or sudden dissection of the aortic wall may precipitate acute, severe back pain.

The examination of the body is not a Sunday stroll from head to neck to chest to abdomen admiring whatever comes to view. You are on a hunt; you know exactly what you are looking for because you have postulated that a particular organ has malfunctioned and you know before touching the patient what signs you're specifically looking for. Do not just look at the body, look *for* something. It's almost almost guaranteed that you won't find what you're not specifically looking for. You simply have to know what you are doing before you do it.

ORGANIZING THE PHYSICAL EXAM

ONCE YOU'VE ORGANIZED ALL THE PHYSICAL SIGNS into the sixteen organ systems, it naturally follows that those signs should be sought by examining one organ system at a time instead of examining part of each organ system geographically (head, neck, chest, abdomen, extremities). The only drawback to examining by organ systems is that it entails checking various body regions more than once. For example, in suspected hepatic failure you would look for jaundice, spider telangiectasias, gynecomastia, ascites, liver enlargement or nodular atrophy, testicular atrophy, purpura, etc. You would again look at the testicles later when examining the genital system. Don't worry about the minor amount of extra time spent examining the same organ twice. The improved organization of your thinking will more than make up for the few extra minutes.

Since different organ systems must be examined with the patient in either the sitting or lying position, you (and the patient) will grow tired of having him repeatedly sit up and lie down. Instead, you'll begin to check more than one organ system at a time when the patient changes to a new position. It is important, however, in the beginning to perform the physical exam strictly by organ systems. In this way, as you later, for efficiency's sake, evolve your own compromise geographical/organ system exam, you will continue to *think* in terms of organ systems. When an abnormal sign is discovered, it is simply pigeonholed into the appropriate organ system.

Naturally, each patient's physical exam will differ depending on the clinical problem and physical limitations of the patient. As a rough guideline, the following might be a typical systems exam on a routine patient. For a more in-depth examination of each organ system, refer back to the signs discussed in chapter 10.

'BASIC SYSTEMS EXAM'

Systemic:	Blood pressure, orthostasis, pulse rate, respiratory rate, temperature.
Skin:	Suspicious moles, cafe-au-lait spots
Neuro-muscular (see chapters 13–26)	Mental status: Level of consciousness, orientation, aphasia, confusion. Cranial nerves: Field cut, discs, fundi, extraocular movements, pupil size and reaction to light, facial touch sensation, facial weakness, hearing deficit, dysarthria. Motor: Gait, tone, strength, coordination. Sensory: Vibration. Tendon reflexes: Biceps, knees, ankles, Babinski.
Eye:	Conjunctiva, cornea, fundi.
Ears:	Tympanic membranes.
Endocrine:	Prognathism, hand size, thyromegaly, exophthalmos, stare, lid retraction, lid lag, eyelid puffiness, eyebrow loss, hung up reflexes, Cushinoid face or trunk, hyperpigmented skin, diabetic fundus changes, secondary sexual characteristics.
Respiratory:	Labored respiration, cough/sputum, dullness to percussion, rales and rhonchi, diminished breath sounds.
Cardiac:	Pulse rhythm, character of radial pulse, jugular venous distension, hepatic jugular reflux, basilar rales, apex beat, LV/RV heave, S1, S2, S3, S4, murmurs.
GI:	Glossitis, spider telangiectasias, jaundice, palmar erythema, purpura, hepatomegaly, abdominal mass or tenderness, ascites, bowel sounds, rectal mass, rectal blood.
RE:	Splenomegaly, lymphadenopathy.
Urologic:	Nephromegaly.
Genital:	Testicular mass, breast mass.
Vascular:	Blood pressure asymmetry, carotid, femoral, dorsalis pedis, and posterior tibial pulses, carotid, abdominal, and femoral bruit, superficial temporal artery tenderness or swelling, fundus changes.
Hematologic:	Pallor, plethora, xanthelasma.
Bone:	Joint inflammation, diminished range of motion.
Coverings & Connective Tissue:	

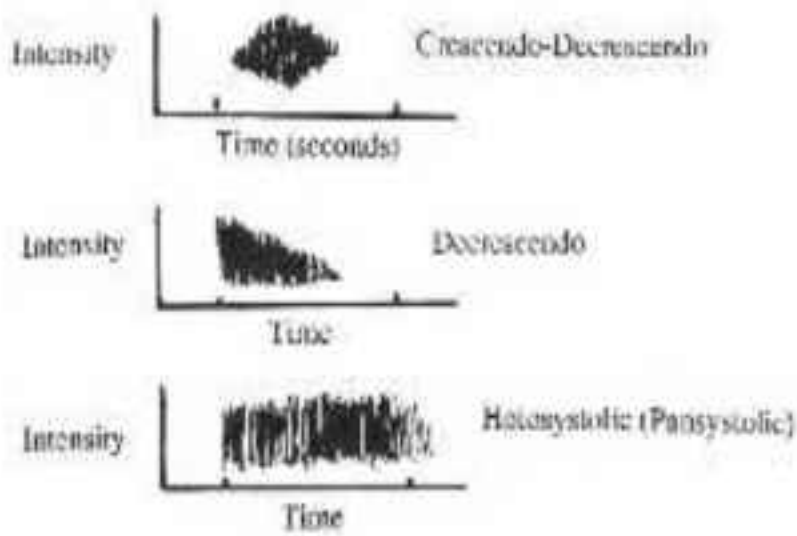
The neurologic exam will be greatly amplified in subsequent chapters. The cardiac exam, perhaps the next most complicated part of the physical, is best approached by first looking for the peripheral manifestations of heart malfunction: pulse rhythm, pulse quality, jugular venous distention, hepatomegaly, basilar rales, and pulsus paradoxicus.

The heart itself is examined in three steps: look, feel, and test. Look first for the apex impulse and for a right or left ventricular heave. Next palpate for a right or left ventricular heave, or the presence of thrills. Finally, organize your auscultation according to the heart sounds, concentrating on the quality of one heart sound at a time in each auscultatory area.

Listen for the quality of S1 in the aortic, pulmonic, left sternal border, and apical areas. Return to the aortic area and repeat the auscultation in each of these areas while concentrating on S2. Return again and repeat the procedure for S3, S4, systolic click or murmur, and finally, diastolic murmur. Don't try to listen to all the heart sounds in each auscultatory area. You'll find it easier to recall your findings if you concentrate on how the character of each individual sound changed as you moved your stethoscope through the four auscultatory areas. Instead of reporting that along the left sternal border you heard a soft S1, loud systolic murmur, soft S2, and a questionable S3, it's more meaningful to say that S1 was particularly loud over the apex and aortic areas, and S2 was normally split over the pulmonic area but was somewhat soft over the aortic area, etc.

When listening to a murmur, the specific qualities to concentrate on are: the grade (loudness), pitch (high or low), quality (coarseness or peculiar quality, like the call of a seagull), timing relative to the heart sounds (early, late, or middle systole or diastole), shape[3] (crescendo, decrescendo, pansystolic), point of maximal location, areas of radiation, and changes with respiration and position (inspiration, expiration, valsalva[4], squatting, standing up, and strong hand grip).[1] Naturally, do not confine yourself to the four standard listening areas; murmurs often radiate into the axilla, into the back, and across to the right side of the sternum.

Shape: There are three typical shapes to a murmur:



Valsalva: Forceful expiration against a closed epiglottis ("Bear down like you're having a bowel movement.")

ADVANTAGES OF THE ORGAN SYSTEM APPROACH

Predicting the Symptoms and Signs of Disease

THE SYSTEMS APPROACH GUIDES YOUR THINKING. Each physical exam is a directed hunt for specific signs because you will have postulated an abnormal organ system or even a specific diagnosis before examining the patient. If you've already organized diseases according to which organ systems they affect, for each postulated DIG IT TOM disease you can rapidly search: "systemic, skin, neuro; eyes, ears, endo; respiratory, cardiac, GI; RE, uro, genital; vascular, heme, bone, and coverings & connective tissue" for the affected organ systems and therefore the expected signs. What, for example, are the clinical manifestations of sarcoid? You can carry around a memorized list, or you can trot through the organ systems like this:

	Clinical Effects of Sarcoid
Systemic	Fever, weight loss, fatigue
Skin	Erythema nodosum, pigmentary changes, alopecia
Neuromuscular	Seizures, facial palsy, granulomatous neuropathy and myopathy
Eyes	Anterior uveitis*, keratoconjunctivitis sicca*, lacrimal gland enlargement
Ears	
Endocrine	Hypercalcemia, diabetes insipidus*
Respiratory	Sinusitis, interstitial pulmonary changes*
Cardiac	Arrhythmias
GI	Parotid enlargement, hepatomegaly, intrahepatic cholestasis*
RE	Splenomegaly, lymphadenopathy
Urologic	
Genital	
Vascular	Pulmonary hypertension
Hematologic	
Bone	Punched out lesions in digits (on xray)
Coverings & Connective Tissue	Periarticular inflammation, granulomatous meningitis

Anterior Uveitis: The uvea is the choroid, iris, and ciliary body. Anterior uveitis (inflammation anterior to the lens: in the ciliary body and iris) is usually due to immunologic conditions. Posterior uveitis (in the retina) is more likely infectious (toxoplasmosis, bacteria (SBE), tuberculosis, fungi).

Keratoconjunctivitis Sicca: Dry eyes, dry mouth due to inflammation within the tear and salivary glands. Etiology usually immunologic, like sarcoid.

Diabetes Insipidus: Dramatic polyuria (2–3 gallons or more per day) due to absent antidiuretic hormone (or, rarely, insensitivity of the kidney to antidiuretic hormone). Usually results from malfunctioning of the posterior pituitary where ADH is released.

Interstitial Pulmonary Changes: The interstitial region is the lung tissue between alveoli.

Cholestasis: Stagnant bile flow through the liver.

Presenting the Physical Exam

When summarizing a case, either in the chart or before the attending physician, you'll find it much easier to remember the abnormal signs if you've already filed them into organ systems. Similarly, it'll be much easier for the listener to organize his own thoughts since he hears all the signs pertaining to a particular organ system at one time.

Thinking During Emergencies

In emergencies, the systems approach will help you consider urgent diagnoses without having to carry around impossible-to-remember lists of etiologic diagnoses for each and every conceivable situation. The organ systems help you to think anatomically, to imagine the actual organs. Say a chest trauma patient is rapidly losing his blood pressure. Considering each organ system separately, you can systematically, consistently, and calmly run through a list of possibilities for your deteriorating patient:

Neuromuscular	cord transection*
Endocrine	Addisonian crisis*
Respiratory	bronchial tear*, pneumothorax, tension pneumothorax*, hemothorax
Cardiac	myocardial infarction
GI	esophageal or intestinal perforation*, pancreatitis
Vascular	aortic tear, pulmonary embolus
Bone	flail chest*

Cord Transection: Cutting (transecting) the cord prevents the sympathetic nervous system from constricting arteries and veins, a reflex that helps maintain the blood pressure.

Addisonian Crisis: Acute adrenal failure—inadequate cortisol, epinephrine, and aldosterone—causes hypotension and hypoglycemia.

Bronchial Tear: Inhaled air leaks into the mediastinum instead of coursing through the bronchial tubes to the alveoli.

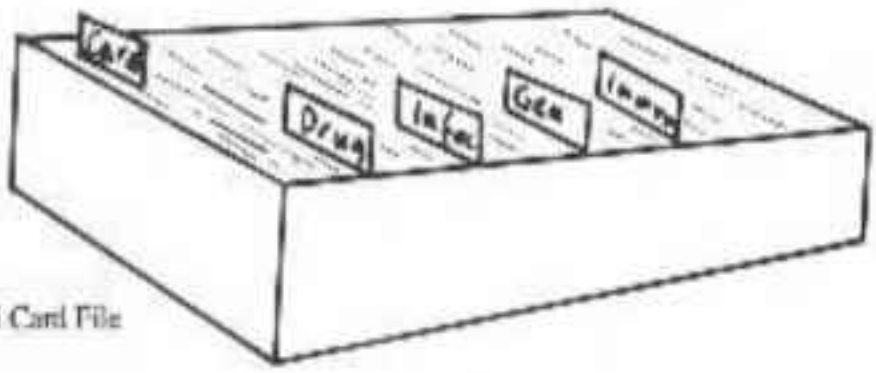
Tension Pneumothorax: A small flap of tissue over a hole in the lung or thoracic wall may allow air to enter the pleural space during inspiration, but prevent escape of that air during expiration. Eventually, enough air accumulates in the pleural space to shove the lung to the opposite side of the thorax, compressing the heart and the superior and inferior vena cavae. The immediate treatment is to make another sizeable hole in the chest wall (with a large bore needle) to allow the high intrathoracic pressure to escape.

Intestinal Perforation: Intestinal bacteria and digestive juices loose in the mediastinum or abdomen may cause rapid sepsis and shock.

Flail Chest: If a rib is fractured in two places, the free-floating piece may be sucked into the thorax with each inspiration, preventing expansion of that section of the lung.

Literature Retrieval

There is nothing more frustrating than trying to locate an article you *know* you've read, but can't locate because it could be in umpteen different folders. The systems approach facilitates the retrieval of articles you've read. Each article is first listed under the appropriate organ system and then subclassified under the type of DIG IT TOM insult to that organ system.



3x5 Card File

Progress Notes

Cross-referencing the organ systems against symptoms, signs, lab, diagnosis, therapy, and response to therapy fits naturally into hospital progress notes. Notwithstanding the risk of viewing a patient as the sum of sixteen different organ systems, by focusing your attention on each malfunctioning organ system separately, you can think more clearly about the patient's problems, and can summarize (and remember) the patient's progress more succinctly. Anyone reading your progress notes will be quickly able to judge the clinical status of each malfunctioning organ system, the investigations which may still need to be done, and the adequacy of therapy.

I. Respiratory System
  A. Symptoms
    1. Feels less dyspneic this morning
  B. Signs
    1. Fever ranging 101°–103°
    2. Cough and yellow sputum persist, but diminished
    3. No further accessory muscle usage
    4. Respirations 18/min
    5. Dullness to percussion persists right base
    6. Rales improved
  C. Lab
    1. Chest Film
      a. Right lower lobe infiltrate persists
      b. Effusion disappearing
    2. Blood gases on 40% inspired O_2 (FIO_2 40%):
      pO_2 70mm, pCO_2 34mm, pH 7.44, HCO_3 23 meq/l
    3. Sputum and blood cultures growing pneumococcus, sensitive to penicillin
  D. Diagnosis
    1. Pneumococcal pneumonia with effusion
    2. Mild hypoxia and respiratory alkalosis

E. Treatment
1. Penicillin 1 million units IV per day
2. FIO_2 40% face mask
3. Chest percussion and drainage

II. Cardiac
A. Symptoms—none
B. Signs
1. Fever 101°-103°
2. Jugular venous distension gone; hepatojugular reflux persists
3. Bibasilar rales gone
4. High pitched grade II/VI diastolic murmur maximal aortic area radiating down left sternal border, increased by leaning forward—no change from yesterday
5. S3 gone
6. Occasional dropped beat
7. No new splinter hemorrhages or Roth spots
C. Lab
1. Chest film this morning
a. Heart size smaller
b. Upper lobe vasculature redistribution improved
2. Central venous pressure 12cm
3. EKG unchanged
D. Diagnosis
1. Aortic insufficiency
2. Subacute bacterial endocarditis?
3. Resolving congestive heart failure
E. Treatment
1. Continue pencillin for 1 week. If murmur worsens during this time, treat for SBE

Doctor's Orders

When it comes time to write your orders* for patient care, concentrate on the diagnostic tests and therapies for each organ system individually.

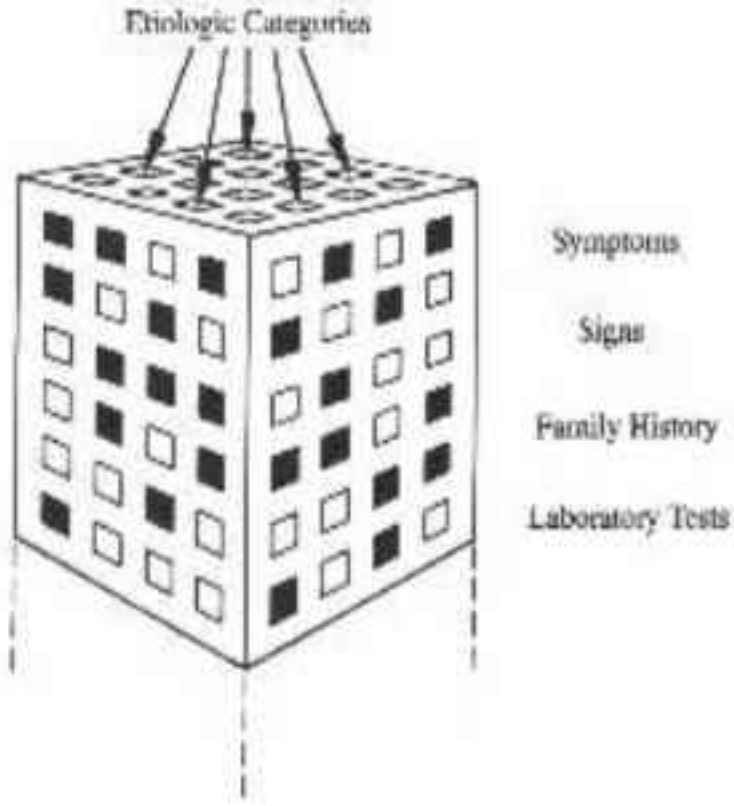
Conceptualizing Physical Diagnosis

Schematically, physical diagnosis begins on the roof of an apartment building on which all diseases are grouped according to etiologic category. Each floor of the building represents a particular symptom, sign, piece of laboratory data, item of family history, or associated illness. Beneath each diagnosis is a room on each floor of the building. If an item is true for the illness overhead, a light in the room is turned on. Each diagnosis, then, has a characteristic vertical pattern of room lights beneath it.

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*Orders: Written instructions to the nursing and paramedical staff regarding tests and therapy for the patient.

A patient may present at any level of the building with a symptom, a sign, an abnormal laboratory test, a relative with a genetic disease, etc. By scanning that entire floor of the building, you can quickly see which room lights are on. Since each room (lighted or unlighted) represents a disease overhead, you immediately have the etiologic differential diagnosis (all the lighted rooms on that floor). All you have to do now is compare your patient's vertical constellation of symptoms, signs, laboratory data, family history, and past illnesses against what's expected for each disease in the differential diagnosis.



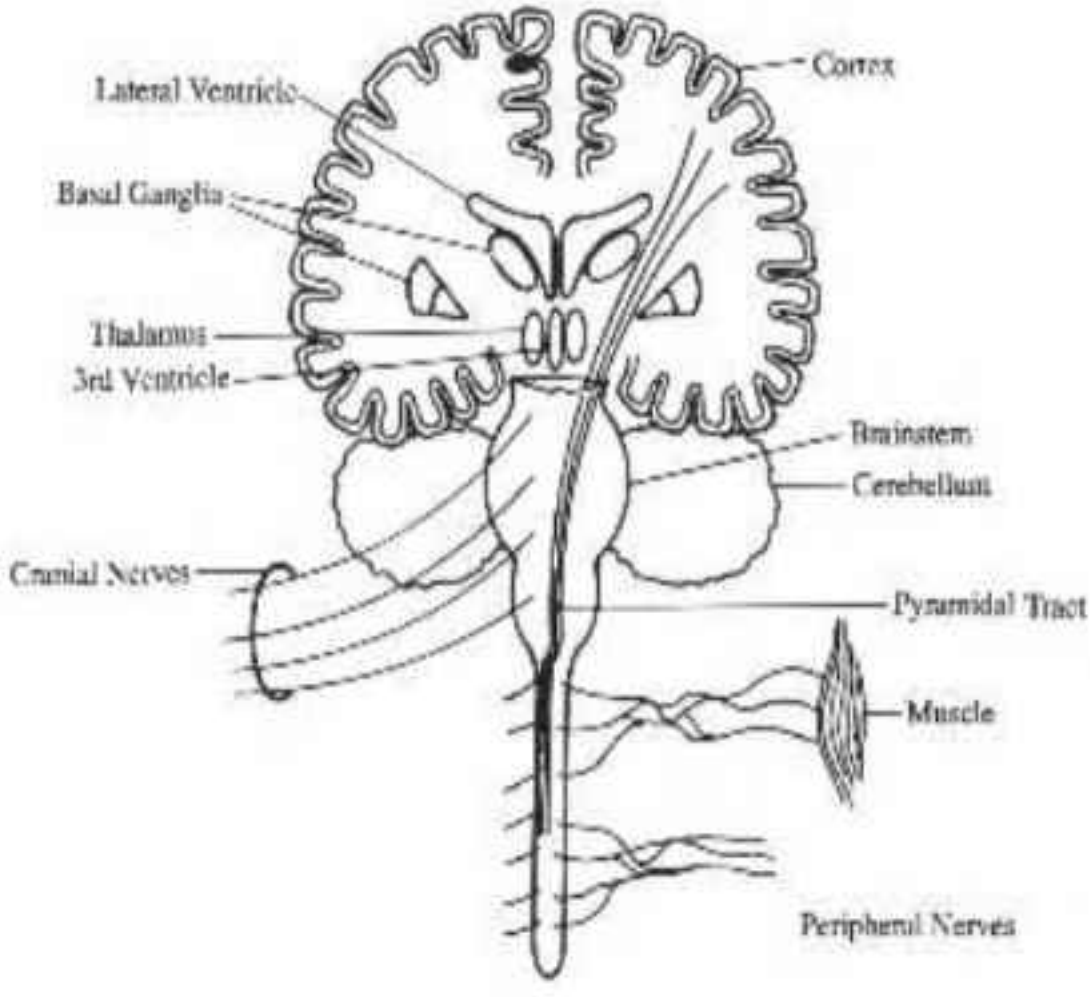
All *I* ask is that you first narrow the etiologic differential diagnosis by constructing an anatomic differential diagnosis. And all DIG IT TOM does is help you organize the entire differential diagnosis into sensible groups, ones that you can consistently remember, before comparing your patient's clinical picture (constellation of room lights) against each disease's characteristic clinical picture.

The hard part of physical diagnosis is knowing whether the presence or absence of a particular symptom, sign, laboratory data, family history, or past illness *categorically* rules in or out the disease overhead. And if not categorically, with how much assurance can you discard or embrace a diagnosis based on the presence or absence of a particular symptom, sign, laboratory data, family history, or past illness? The reason for this uncertainty is that not every room light is fully lit. That is, some symptoms (or signs or lab data or genetic facts) are not present in every patient. Should you accept a diagnosis when most of your patient's symptoms and signs match up to only dimly lit rooms? The most powerful symptoms and signs, then, are those whose lights are either fully on or fully off—they're either always present in that disease, or never present.

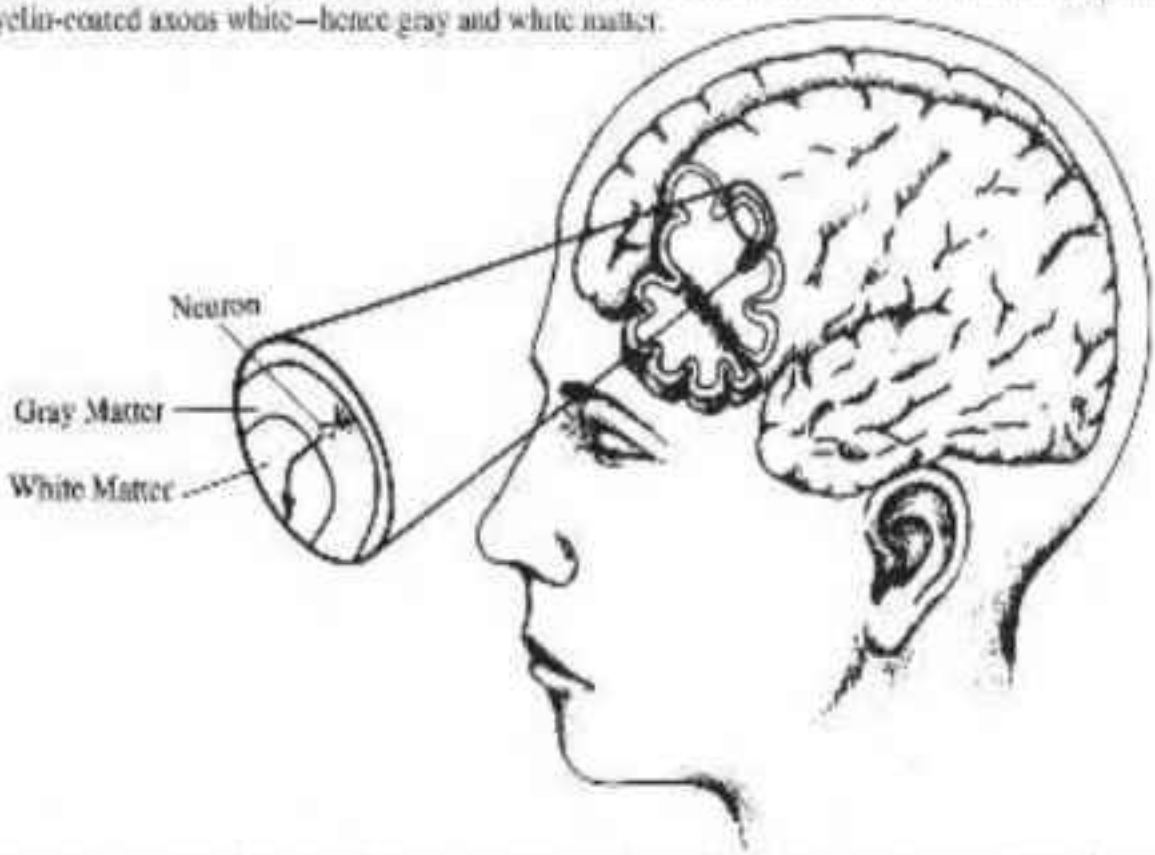
NEUROLOGIC DIAGNOSIS

> There are only two mysteries in this world worth talking about. One is the nature of the origin of the universe, and the other is how the hell the brain works.

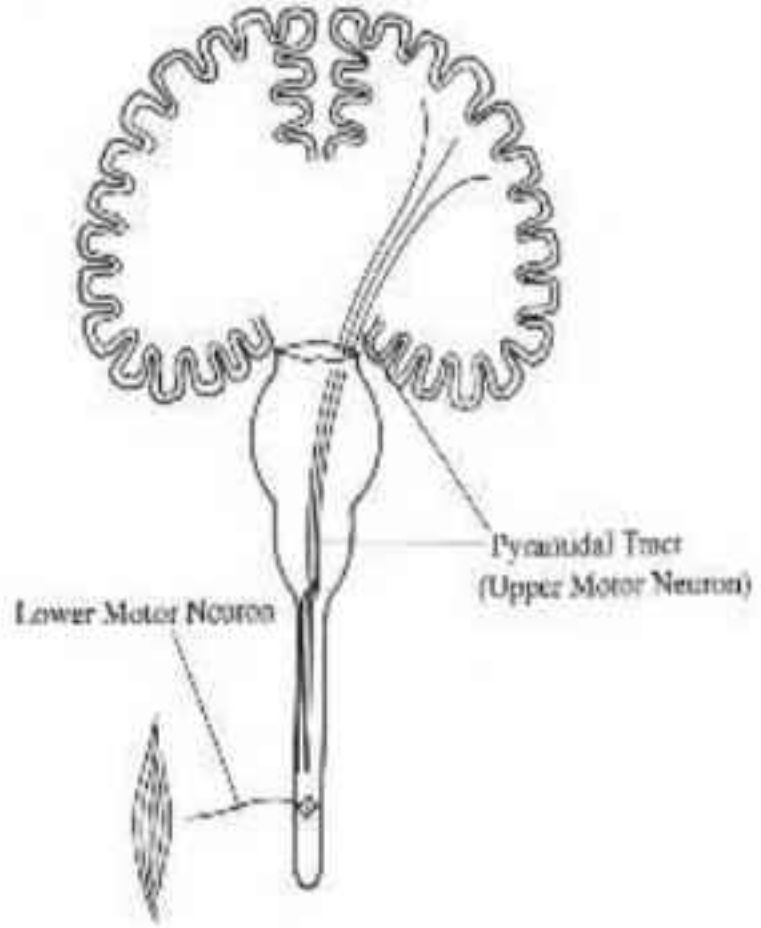
LET'S TURN OUR ATTENTION to the nervous system where neurologic diagnoses are constructed in the same manner we've already discussed: first, an anatomic diagnosis, and then an etiologic diagnosis. Unfortunately, anatomic localization in the nervous system is fundamentally different, and definitely more difficult, than in internal medicine. There are a number of reasons for this. First, and most importantly, the nervous system is composed of ten subsystems, each of which is as complex as any internal organ. These subsystems are the cortex*, pyramidal tracts*, basal ganglia*, cerebellum*, brainstem*, cranial nerves*, spinal cord*, roots*, peripheral nerves, and muscle.



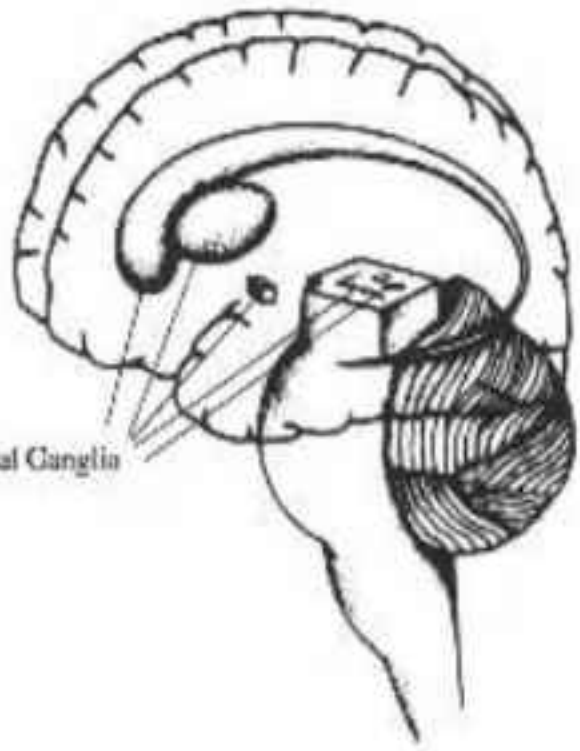
Cortex: The rind of gray matter covering the surface of the brain. In the cortex neuronal cell bodies are lined up alongside each other with their dendrites pointing like antennae toward the cortical surface, and their axons pointing south to carry instructions to other parts of the brain and spinal cord. Brains are routinely preserved in formaldehyde, a solution which turns cell bodies gray and myelin-coated axons white—hence gray and white matter.



Pyramidal Tract: Whenever you decide to move a muscle, the instruction to that muscle is first carried south from the cortex along a large dense bundle of axons called the pyramidal tract to a second neuron lying in the brainstem or spinal cord. This second neuron, the *lower* motor neuron, then carries the instruction outward from the brainstem or spinal cord to the muscle. The first neuron, the one descending from the brain to the lower motor neuron, is called the upper motor neuron.



Basal Ganglia: A ganglion is a cluster of cell bodies. The basal ganglia are a group of ganglia lying deep within the brain. Phylogenetically older than cortex, the basal ganglia help govern the speed and spontaneity of movements.



The Basal Ganglia

Cerebellum: 'Small cerebrum.' Once the pyramidal tract initiates a movement, the cerebellum—discreetly nestled behind the brainstem—functions like a rocket computer, keeping that pyramidal movement locked on target. Movements without cerebellar assistance are ataxic—clumsy, incoordinated, and choppy.

Brainstem: Sitting beneath the two cerebral hemispheres like the cone part of an ice-cream cone, the phylogenetically ancient brainstem controls the primitive functions shared by all animals: consciousness, sleep, eye movements, facial movements, chewing, swallowing, head turning, respiration, and heart rate.

Cranial Nerves: The cranial nerves innervate the scalp, face, and neck. Cranial nerves contain 1) lower motor neurons exiting the brainstem to direct eyeball, face, throat, and neck movements, and 2) brainstem-bound sensory neurons carrying sensation of the scalp, eyes, mouth, face, ears, and throat.

Spinal Cord: The spinal cord sends lower motor neurons to the limb and trunk muscles, and receives sensory neurons from the skin and internal organs. *Vertical* columns (tracts) of axons within the cord carry sensations upward to, and motor instructions downward from, the brain to the *horizontal* sensory and motor neurons entering and exiting the spinal cord.

Roots: Nerves entering and exiting the spinal cord are called roots. Soon after leaving the spinal cord, roots join into a plexus from which they exit as peripheral nerves.

The nervous system is not an internal organ! You may say that there is something wrong with the heart, but you may not say that there is something wrong with the brain. Instead, you must say there is something wrong with the cortex, or basal ganglia, or brainstem, etc. Before we even approach the nervous system, you've got to expand your concept of it. Each subsystem of the nervous system is equivalent to an entire internal organ! And just as you have been learning the pathognomonic symptoms and signs* of each internal organ system, your job now is to learn and be able to elicit pathognomonic signs of each subsystem of the nervous system.

The second reason neurology is a unique specialty is that many of the subsystems stretch over long distances, which complicates accurate anatomic localization. For example, proprioception* of the big toe is carried from its origin in the big toe through the peripheral nerve, up the posterior column* of the spinal cord to the brainstem, and then up to the cortical sensory strip*, a distance in some people of six feet or more. If someone has absent proprioception, where along the six foot path is the lesion? The answer to that question often requires detection of dysfunction in a second neurologic subsystem. The lesion is then inferred to be where these two subsystems intersect. This method of localization is unique to the nervous system and, naturally, requires an accurate knowledge of neuroanatomy and an accurate neurological exam.

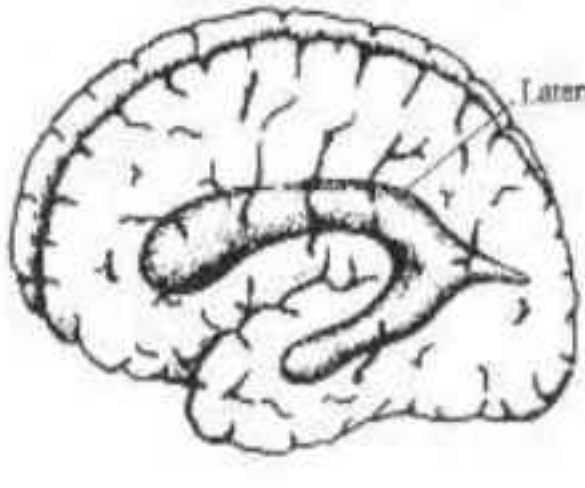
Moreover, when it comes time to consider vascular etiologies, mere anatomic localization won't be enough. To diagnose ischemic vascular disease, you must be sure that all the signs lie within the distribution of a single artery, a frustrating task at times because widely separated areas of the brain may be supplied by the same artery. Neuroanatomy includes *neurovascular* anatomy.

Pathognomonic Signs: Many of the signs that we've already discussed are pathognomonic of an anatomic site, like rales for the lungs, bruit for the vascular system, etc. (Few if any signs are indicative of a specific etiology.) Because of intimate interdependence between the neuromuscular subsystems, neuromuscular signs are less pathognomonic than signs in general medicine. The exceptions, fortunately, are relatively uncommon, but still common enough that it pays to cultivate friendships with experienced neurologists.

Proprioception: Ability to tell where your limbs and digits are in space.

Posterior Column: Peripheral sensory nerves are capable of detecting five sensory modalities: touch, vibration (rapidly repeated touch), proprioception (joint position sense), pain, and temperature. After reaching the spinal cord, these five modalities sort themselves out so that vibration and proprioception ascend in the posterior columns of the cord, while pain and temperature ascend together in the anterolateral columns. Touch goes up both the posterior and anterolateral columns.

Sensory Strip: Sensations are analyzed by the cerebral cortex in the sensory strip.



Another difficult area in neurology is the expansion of Distant Domino etiologies to include other neurologic subsystems. Like any other organ system, each neurologic subsystem is vulnerable to any one of the body's Distant Domino organ systems. But in addition, many neurologic subsystems can also be affected by other neurologic subsystems by way of the ventricular system*, subarachnoid spaces, and direct electrical connections. Only well grounded knowledge of cerebral physiology—reviewed in the next thirteen chapters—will allow you to confidently diagnose first the *presenting* neurologic subsystem, then the site of *primary* dysfunction, and finally the primary etiology.

The final reason neurology takes a while to learn is that the etiologic diagnosis depends not only on what neurologic subsystem is affected, but also on the time course of the disease. You cannot make an etiologic diagnosis based on the neurologic signs alone, because the neurologic exam only reveals the site of the problem; you need the history to diagnose the etiology. My boss used to summarize this observation with a catchy little aphorism: "Anything can cause anything." For example, a hemiparesis that came on while watching TV is a stroke, but if the hemiparesis started several months ago and was gradually worsening, it's a tumor. Or, if the hemiparesis came on abruptly but was preceded a year ago by a two month bout of diplopia, the diagnosis is multiple sclerosis* (probably). So more than in any other specialty, the history assumes major significance, and to make matters worse, the history may not even be obtainable from the patient because of coma or confusion.

With this overview of the nervous system, we're going to review whatever neuroanatomy is necessary to understand the pathognomonic signs of each subsystem of the Neuromuscular system. The subsystems include the cortex, pyramidal tracts, basal ganglia, cerebellum, cranial nerves, brainstem, spinal cord, roots, peripheral nerves, and muscles. Neurologic symptoms are less important right now because they're usually obvious once the signs are understood.

DIVISIONS OF THE NERVOUS SYSTEM

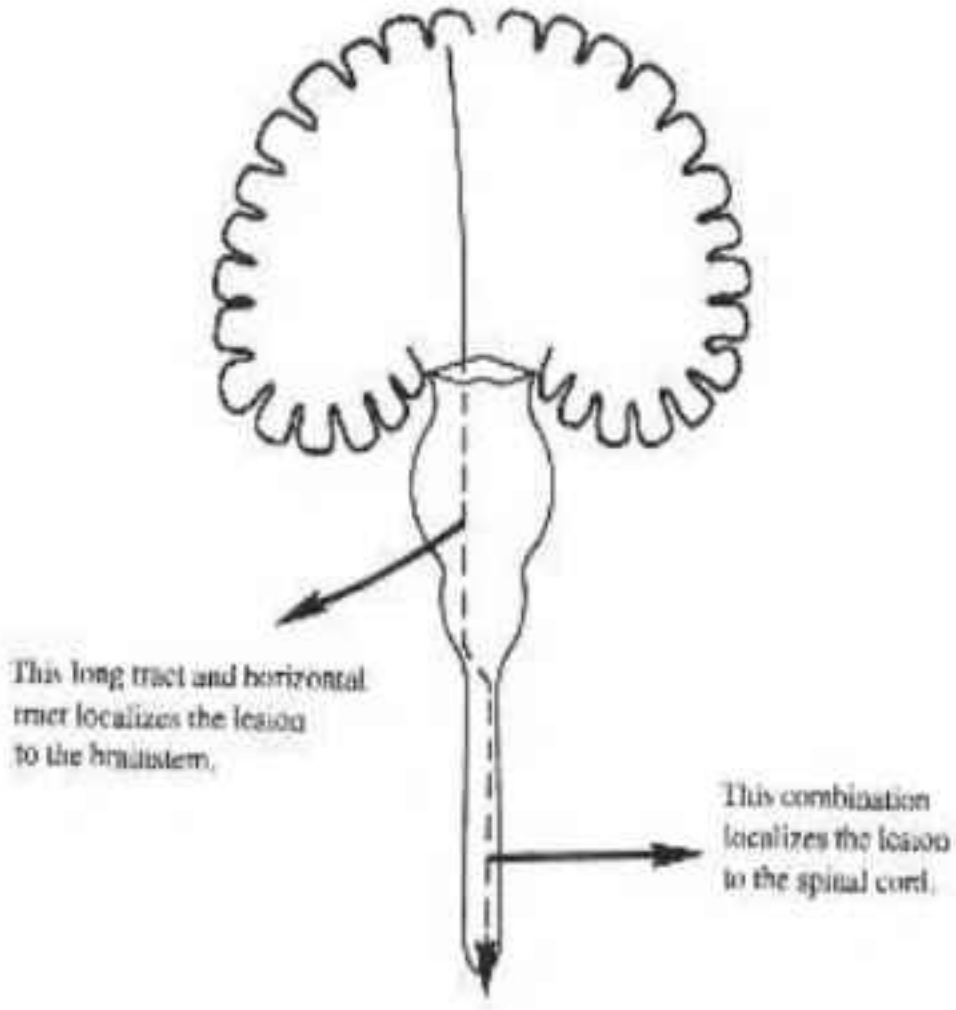
From an anatomic standpoint, the nervous system is divided into the central nervous system (brain and spinal cord) and a peripheral nervous system (roots and peripheral nerves). From a physiologic standpoint, any nerve that begins *and* ends in the brain* or spinal cord is part of the central nervous system. If a neuron begins in the brain or spinal cord but terminates outside them, the neuron is part of the peripheral nervous system. Similarly, a neuron that begins in the periphery and terminates in the brain or spinal cord is also in the peripheral nervous system.

Ventricular System: The brain is actually hollow (ventricle means 'belly' in Latin). The central cavities, the ventricles, contain a crystal clear fluid called cerebrospinal fluid (CSF).

Multiple Sclerosis: Multiple sclerosis attacks by stripping myelin off a small patch of axons in the brain or spinal cord. Over the ensuing weeks and months the body imperfectly repairs the myelin damage.[1] Months to years later this unpredictable disease demyelinates another patch of axons, causing new symptoms and signs. (Even though it seems intuitively obvious that remyelination is what improves a patient's function after an attack of MS, improvement may actually depend on something else.[2])

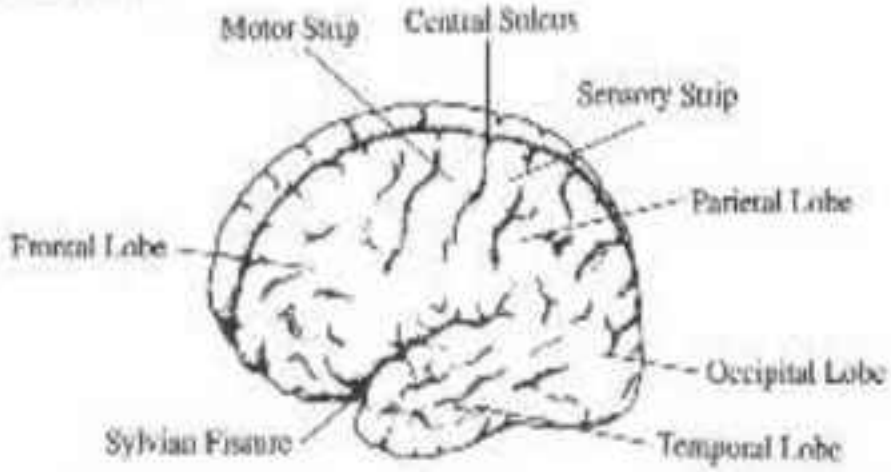
Brain: This includes the eye which formed during fetal development as an outpouching of the brain.

From a clinician's standpoint, the nervous system is divided into a vertical and a horizontal nervous system. The vertical systems, known as the 'long tracts,' are the pyramidal tracts, posterior columns, and spinothalamic tracts (anterolateral columns). The horizontal systems are ones which intersect the long tracts: the cortex, basal ganglia, brainstem, cranial nerves, cerebellum, and roots. The reason for dividing the nervous system this way is that localizing a lesion to the pyramidal tract, posterior column, or spinothalamic tract is not exact enough. Long tract signs do not tell you *where* along the long tract the lesion is. If you can also find a horizontal sign that intersects one of the three long tracts, then you've pinpointed the lesion to the point where the long tract and horizontal subsystem intersect.



FOCAL CORTICAL SIGNS

LET'S BEGIN WITH THE CEREBRAL CORTEX AND SUBCORTICAL WHITE MATTER. The cortex is a thick ribbon of gray matter composed of neuronal cell bodies, while the white matter is composed of axons and insulating myelin. Each cerebral hemisphere is made up of four lobes. The frontal lobe extends back to the central sulcus* (also called the Rolandic fissure*) which divides the frontal motor strip (or motor gyrus*) from the parietal sensory strip (or sensory gyrus). The parietal lobe begins at the central sulcus and merges without a distinct border into the occipital lobe posteriorly, and laterally into the temporal lobe, again without a distinct border. The temporal lobe is separated from the frontal lobe by the Sylvian* fissure. The frontal lobe is larger than you might think; the medial end of the central sulcus actually lies about even with the external ear canal.



There are two major types of pathognomonic cortical signs: focal and bihemispheric. Focal cortical signs direct you to a specific area of cortex in *one* hemisphere. Bihemispheric cortical signs tell you there is something wrong in *both* hemispheres, either in multiple focal areas (multifocally) or throughout the entire cortex diffusely. Focal cortical signs imply a unilateral lesion; bihemispheric cortical signs imply bilateral lesions.

Beginning in the left hemisphere, we'll now review the pathognomonic signs* for each focal cortical area.

Sulcus: Groove.

Fissure: A large sulcus, a cleft.

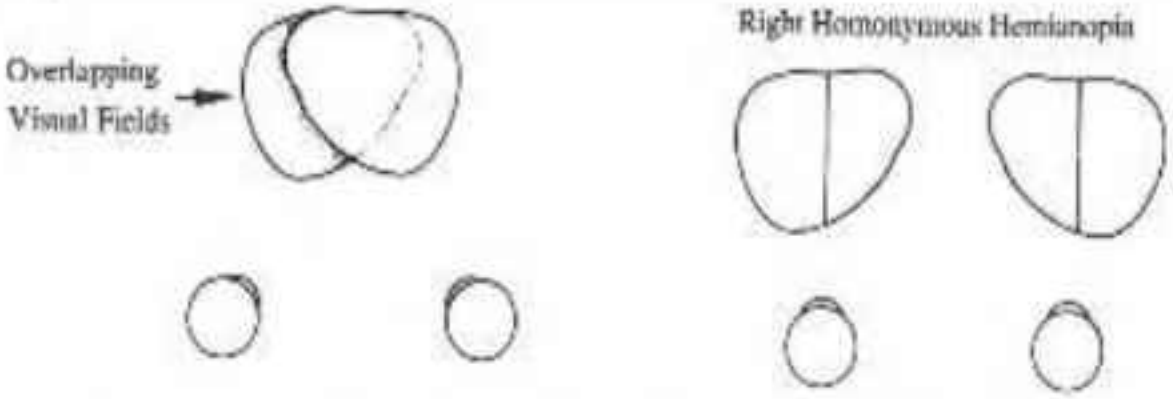
Gyrus: The rounded peaks of cortex on either side of a sulcus or fissure.

Sylvius: A Dutch Professor of Medicine during the mid-1600's.

Pathognomonic Signs: By pathognomonic, I mean that if you find the sign, you can be sure of the lesion's location, sure enough to put a bank loan on it. The converse – if the sign is absent, the lesion cannot be there—is most definitely not true!

LEFT OCCIPITAL LOBE

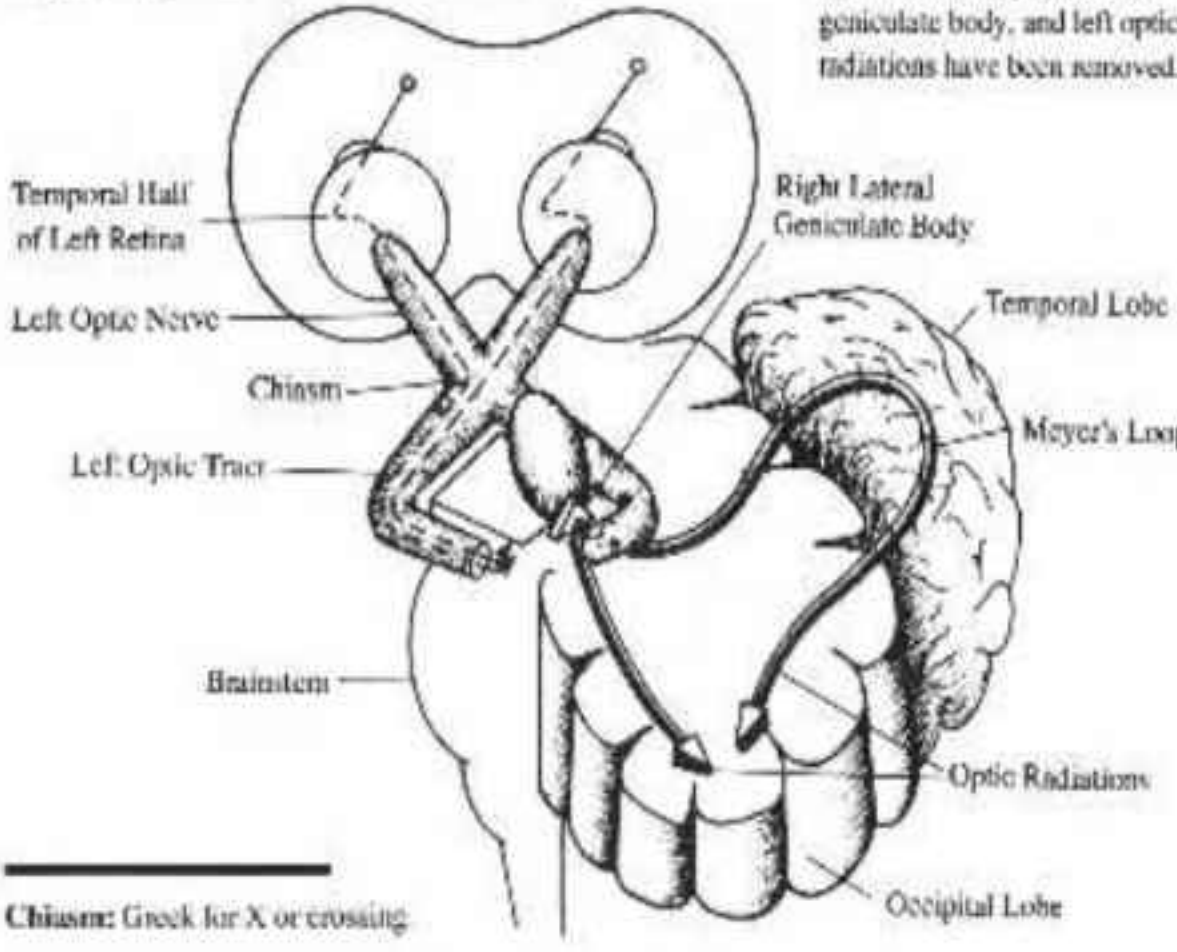
Focal cortical signs are not always readily predictable. Suppose, for example, we surgically ablate the left occipital lobe. The result is a right homonymous hemianopia; the person cannot see to the right of midline with either eye.



Even though removal of the left occipital lobe produces a right homonymous hemianopia, this field cut is not necessarily pathognomonic of left occipital lobe dysfunction because it can theoretically result from a lesion of the left optic tract or the left lateral geniculate body. Let's look at the anatomy of the visual system to be sure you understand why a right homonymous hemianopia is not pathognomonic of the left occipital lobe.

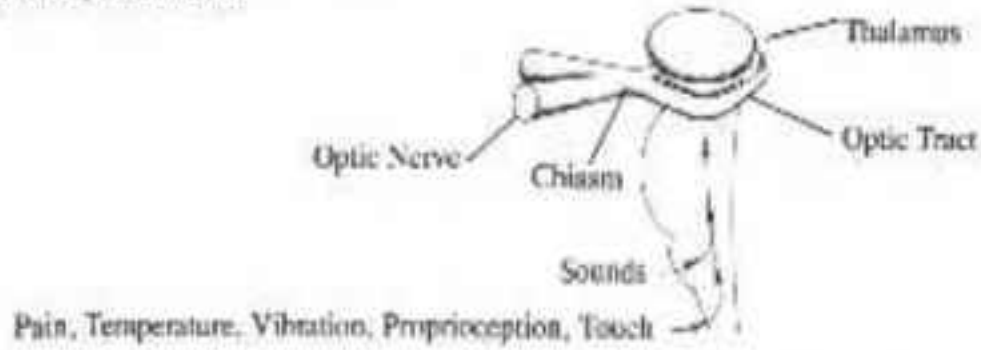
The right visual world is seen by the left half of the retina of each eye. Retinal nerve fibers from the left half, or temporal half, of the left retina course back through the left optic nerve to the optic chiasm* where they are joined by crossing fibers from the left half, or nasal half, of the right retina. This union becomes the left optic tract which wraps *around* the upper brainstem (midbrain), ending up in the left lateral geniculate body sitting at the back end of the thalamus.

The left thalamus, left lateral geniculate body, and left optic radiations have been removed.



*Chiasm: Greek for X or crossing

The thalamus, in fact, intercepts *all* sensory information except smell. After analyzing each arriving sensory impulse, the thalamus decides—based on what the cortex has told it—which new information is important enough to alert the cortex about. The thalamus is appropriately situated for this job, lying in the dead center of the brain right on top of the brainstem. In this central location the thalamus can simultaneously intercept the horizontal optic tracts sweeping back to the occipital lobes, and all the ascending vertical tracts carrying sounds, vibration and proprioception, pain and temperature, and touch.

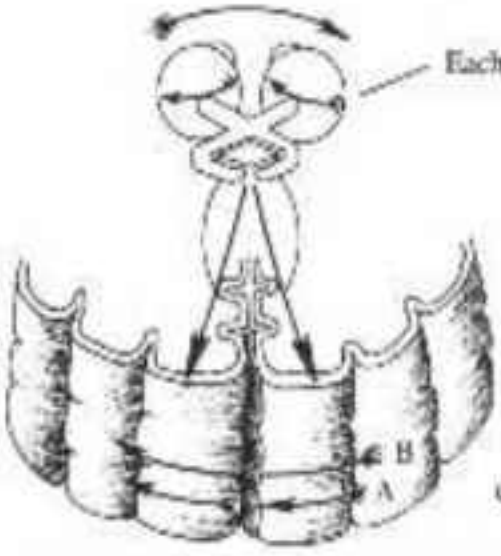


The lateral geniculate body is the first synapse* for retinal ganglion neurons, neurons which began back in the retina. Second order* neurons begin in the lateral geniculate body, a tiny shower head that sprays the optic radiations diffusely through the temporal and parietal lobes back to the ipsilateral occipital cortex*. So, the only thing you can safely say about a right (or left) homonymous hemianopia is that it is retrochiasmal (behind the chiasm).

Synapse: The junction of an axon onto another neuron's dendrites, cell body, or axon.

Second Order: For order, read 'neuron-in-a-chain-of-neurons.'

Ipsilateral Occipital Cortex: Criss-crossing of retinal fibers in the optic chiasm provides a selective advantage for survival, because the criss-crossing allows each occipital lobe two slightly different views of the world, one from each eye. This clever arrangement gives *each* occipital lobe three-dimensional perspective, like binoculars instead of a telescope. The optic chiasm was probably an inevitable evolutionary development anyway. As pointed out by Ramon y Cajal, the brilliant Spanish anatomist at the turn of the century, the optic chiasm was necessary for panoramic vision.[1] If there were no decussation through the chiasm, the cortical picture would be disjointed.



If each retina projected its entire retinal image to the ipsilateral occipital lobe (A), the image would be duplicated. If, however, each retina projects the left half of the image to the left occipital lobe (and right half to the right occipital lobe), as in B, the occipital lobes would, together, 'see' a continuous image.

Decussation provides a panoramic view. From a decussated visual system stemmed, Cajal believed, the evolution of decussated motor and sensory fibers, explaining why each hemisphere controls all motor and sensory function of the opposite side of the face and body.

Nevertheless, there are times when you can localize a right homonymous hemianopia to the left occipital lobe. Lesions of the optic tract, lateral geniculate body, and optic radiations produce incomplete homonymous hemianopias. Dense homonymous hemianopias* occupying the entire right (or left) visual field are almost always occipital.

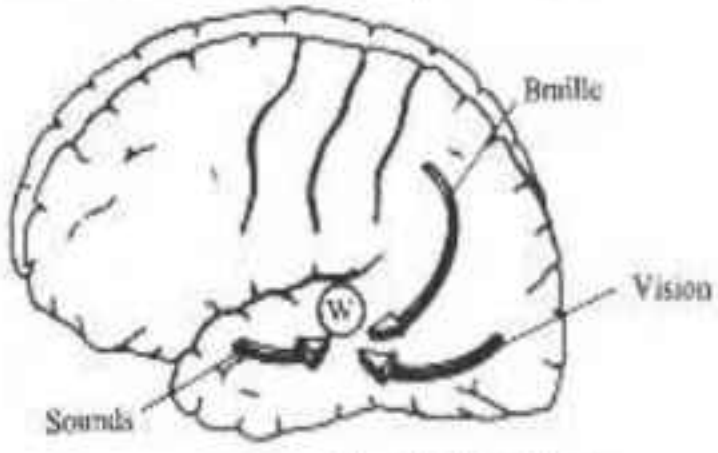
Sometimes incomplete homonymous hemianopias are associated with other phenomena indicative of parieto-occipital pathology. Palinopsia is a good example: the patient complains that images persist in the right hemianopic field minutes to hours after having looked at them.[2]

Probably the best sign of left occipital cortical dysfunction, a sign about as rare as palinopsia, is a seizure that begins in the left occipital cortex. During the period in which the discharge is confined to the left occipital lobe, the patient will say he sees colored sparks or simple images in the right visual field of each eye, sensations he may feel compelled to look at.[3] This is called a focal seizure* emanating from the left occipital cortex.

LEFT TEMPORAL LOBE

Wernicke's Aphasia

Let's move on to the left temporal lobe, to a vitally important structure here called the comprehension center, or Wernicke's area, named after Carl Wernicke, the great German neurologist of the late 1800's. All language must pass through this area to be understood, including the spoken word, the written word, lip reading, braille, even sign language.[4] In 98% of right-handed people Wernicke's area is located in the left temporal lobe.[5] In most left-handed people Wernicke's area is located in either the left temporal lobe alone or in both temporal lobes; in only a minority of left-handed people is Wernicke's area confined to the right temporal lobe.[6]



W = Wernicke's Area

Dense Homonymous Hemianopia: Density and size characterize field cuts. A complete hemianopia means the entire hemi-field is affected. A dense field cut means the patient cannot even sense a waving target.

Focal Seizure: Neurons communicate with each other by sending orderly electrical discharges to one another. A renegade neuron (or group of neurons) discharging too frequently may convince its neighbors to join in. Clinically, this manifests as an abrupt onset of symptoms or signs of that neighborhood—a focal seizure. Once beyond the neighborhood, the seizure rapidly converts the whole brain into an anarchy of wildly discharging neurons—a grand mal convulsion.

A lesion of Wernicke's area produces Wernicke's aphasia*. The simplest definition of aphasia is speech that has either spelling or grammatical mistakes* (over and above the patient's usual speech). Uncertainty arises in two circumstances: acquired stuttering and sudden mutism. Acquired stuttering in the adult—even without spelling or grammatical errors—is probably a form of aphasia (Broca's aphasia—see below).[7] Sudden mutism—the absence of speech—is usually Broca's aphasia, too, but not always. The distinction between mutism and aphasia is usually not difficult. A truly mute person cannot utter any sounds; a mute aphasic can. A mute person can mouth the words; a mute aphasic cannot. And a mute aphasic almost always has an associated right hemiparesis and inability to write.*

Location of Wernicke's area on the sensory side of the Rolandic fissure gives Wernicke's aphasia its alternative names: sensory or receptive aphasia. The speech itself is fluent with good cadence and modulation, but it's filled with gibberish words. When you and I speak, we constantly monitor our own speech for errors. Since a person with Wernicke's aphasia cannot understand the spoken word, including his own, he doesn't recognize when he has mispronounced a word or chosen an incorrect one*. He keeps talking as if nothing were wrong, generating the proper tone but not the proper words. The speech sounds like this: "I am going to the kreedisfran for a preeble." When you find yourself leaning forward poised like the RCA Victor dog, straining to understand what the patient is saying, trying to decide if the words are even English, you're probably listening to Wernicke's aphasia. Because of the normal rhythm and modulation, the speech sounds like it ought to make sense, but it doesn't.

If you suspect Wernicke's aphasia, the first step is to determine if the patient can understand the spoken word. Ask him (in a loud voice, if necessary, to overcome deafness) to perform a simple task, such as touching his nose. If he doesn't carry out your instruction, be sure he is looking you in the eye and concentrating on what you're saying. Otherwise you may be dealing with inattention or confusion, or even deafness. Also, keep your hands at your side when giving instructions to avoid giving visual cues. If he doesn't touch his nose, despite good concentration, either he has difficulty understanding the spoken word or he is incapable of carrying out the command because of a rather rare and strangely fascinating condition called apraxia*.

Aphasia: Phasis is Greek for speech.

Spelling or **Grammatical Mistakes:** Paraphasia is a general term for any misspoken word. Spelling mistakes involving single letters, like 'sreef' for street, are called literal paraphasias. Phonemic paraphasias involve a whole syllable. Verbal (or semantic) paraphasias are mischosen (but correctly spelled) words like 'cat' for dog. A totally incomprehensible word is called a jargon paraphasia.

Grammatical mistakes (lexical errors) occur when the patient leaves out syntactical words like pronouns (he, she), articles (a, an, the, that), conjunctions (and, because), participles (the, that), and prepositions (of, from).

Incorrect One: Normal people will also make 'aphasic' mistakes when they are prevented from monitoring their own speech by special earphones that delay auditory feedback.[8] But they do recognize their mistakes. What's so puzzling about Wernicke's aphasia is that the patients still think they're speaking correctly.

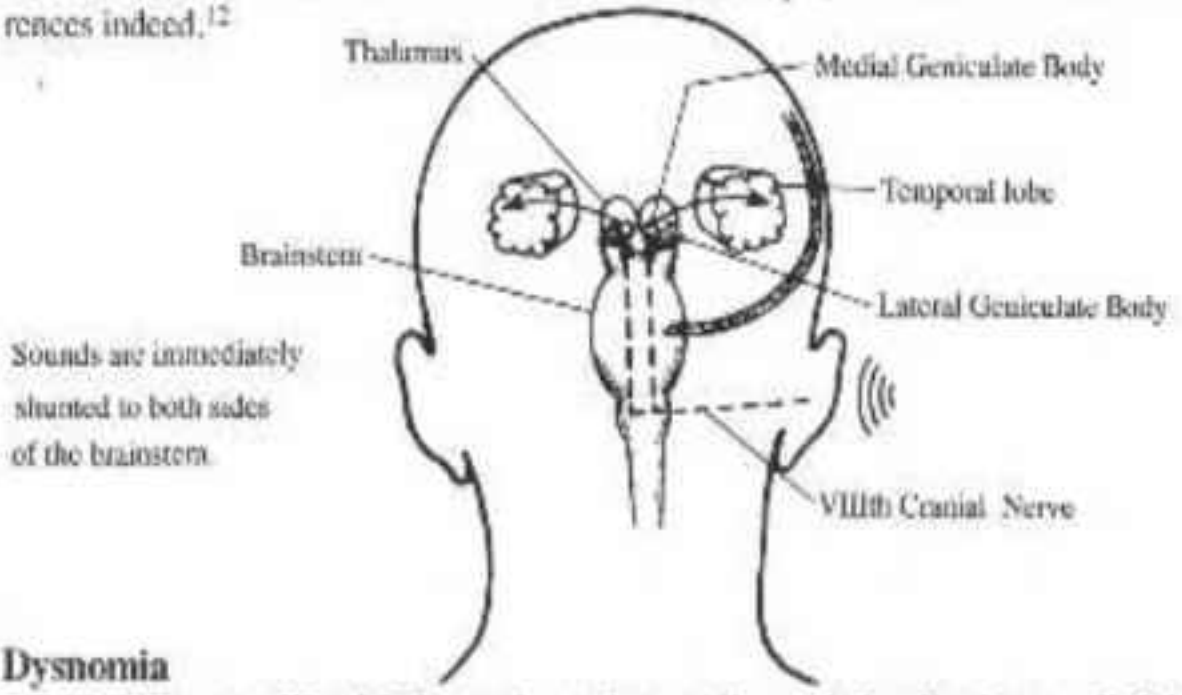
Why Wernicke's aphasics make so many spelling mistakes is unclear. Besides being unable to monitor their own speech, they also seem unable to choose correct sounds and assemble them into words.

Apraxia: From praxis, Greek for action.

Despite normal comprehension, strength, and coordination, the apraxic patient cannot carry out a command, because he cannot get the understood instruction from Wernicke's area to the motor cortex that controls the limb (because of a lesion in the white matter connecting Wernicke's area to the motor strip).[10] In the presence of adequate strength and coordination, however, inability to follow commands is almost always due to comprehension difficulties, not apraxia. Confirm this by eliciting incorrect answers to yes-no questions which do not require a motor response, like "Am I a flower?" or "Do helicopters eat their young?" If he's alert enough, check his handwriting; disturbances of written grammar and spelling generally parallel the disturbance of speech.

On occasion a patient with Wernicke's aphasia may not understand the spoken word, but may understand the written word.[11] Although this clinical point is interesting anatomically, to the patient it's vital, because the written word may be his only means of language communication with those around him. The anatomic reason for this unusual situation is that the pathway into Wernicke's area for written words differs from the pathway for spoken words. Written words come from the occipital cortex while spoken words come from *both* temporal lobes. As long as the lesion doesn't damage connections between Wernicke's area and the occipital lobes*, he may still be able to understand written commands.

It's worth emphasizing that sounds come from both temporal lobes. Unilateral temporal lobe lesions do not produce hearing loss. In fact, it is extremely rare for any central nervous system lesion to produce deafness. Immediately after entering the brainstem (via the eighth cranial nerve), spoken words are shunted to both sides of the brainstem before ascending to both temporal lobes. So central deafness* must be due to a lesion on both sides of the brainstem or both temporal lobes—both rare occurrences indeed.[12]



Dysnomia

Somewhere near Wernicke's area is another small, poorly localized area called the dysnomia center.[13] A lesion here produces difficulty finding the names of objects without any other disturbance of speech. When shown a pencil, he may tell you it's to

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Occipital Lobes: Though words are seen by the occipital lobes, the visual images must first be sent to Wernicke's to be deciphered as language.

Central Deafness: Deafness due to a central nervous system lesion; lesions in the ear or in the auditory nerve leading to the brainstem cause 'peripheral' deafness.

write with, or that he uses it all the time, but the term pencil will elude him*. At other times, he may respond with a paraphasic term. Unfortunately, unless dysnomia is the only finding, you can't attribute dysnomia to temporal lobe pathology because almost any aphasia—temporal, parietal, or frontal—has a component of dysnomia.[15]

Temporal Lobe Seizures

Another pathognomonic sign of temporal lobe dysfunction is a focal, temporal lobe seizure. These are fits consisting of a sense of fear, pleasure, or deja vu*, an unusual smell or sound, a forced memory, or spells of automatic purposeless behavior.[16] How strange that epilepsy can be a forced memory or a foul odor or a feeling of fear instead of the usual convulsion one normally conjures up when epilepsy is mentioned. The reason for this is the same as for the visual phenomena of occipital lobe seizures. During the time a focal seizure discharge remains confined to the temporal lobe, those structures normally found in the temporal lobe are being stimulated to 'do their thing*' (or stop doing their thing, like speech arrest[15]). The reason temporal lobe epilepsy produces a smell, an emotion, or a memory is that the neurons controlling these phenomena lie in the temporal lobe.

Let's take emotions* first. Emotions manifest themselves in two ways: with an internal *feeling*[*], and a *response*. Responses are carried out under the direction of the hypothalamus by the autonomic and neuroendocrine systems*.[17]

Elude Him: Long-winded, roundabout descriptions of an object (without actually naming it) are called circumlocutions. Why dysnomic patients can't find the name is unclear: have they damaged their 'dictionary' of names, or have they simply forgotten how to use the "dictionary"?[15]

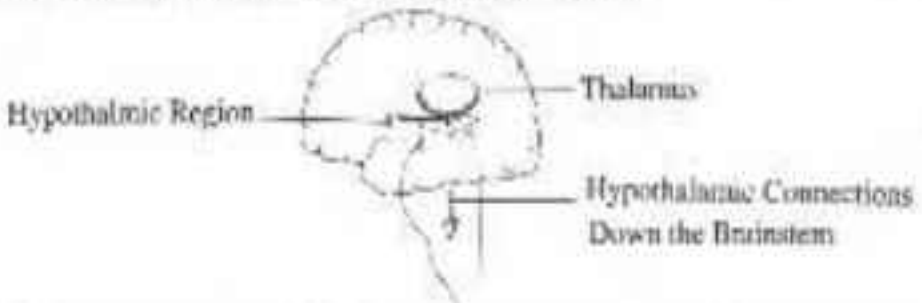
Deja Vu: A sense of undue familiarity, of having experienced the situation before. The opposite of deja vu is jamais vu, a sense of strangeness and unfamiliarity.

Do Their Thing: So far, however, it's been somewhat difficult to elicit consistent temporal lobe phenomena by stimulating individual structures in the human temporal lobe.[17]

Emotions: How in the world can the brain feel emotions? How did Mother Nature assemble a dense feltwork of electrical connections so that one set of neurons and neurotransmitters make you feel jealous, and another set, disdain, or sympathy, or spite, or any of the innumerable subtleties of human emotions? Granted, the brain is no Heathkit, but still, how did she do it?

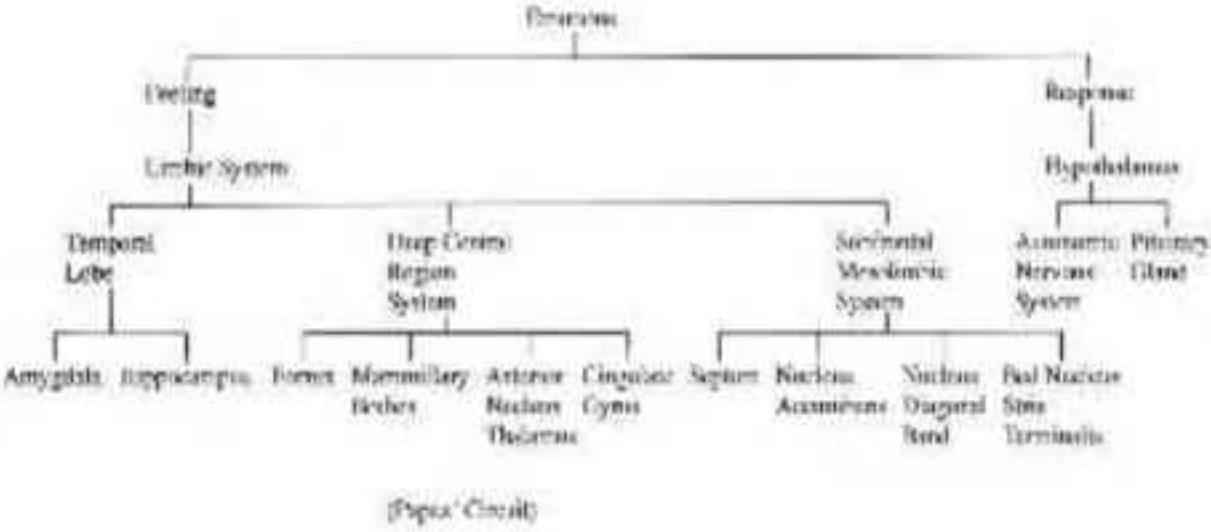
Internal Feeling: Like happiness, sadness, love, anxiety, hate, jealousy, envy, etc.

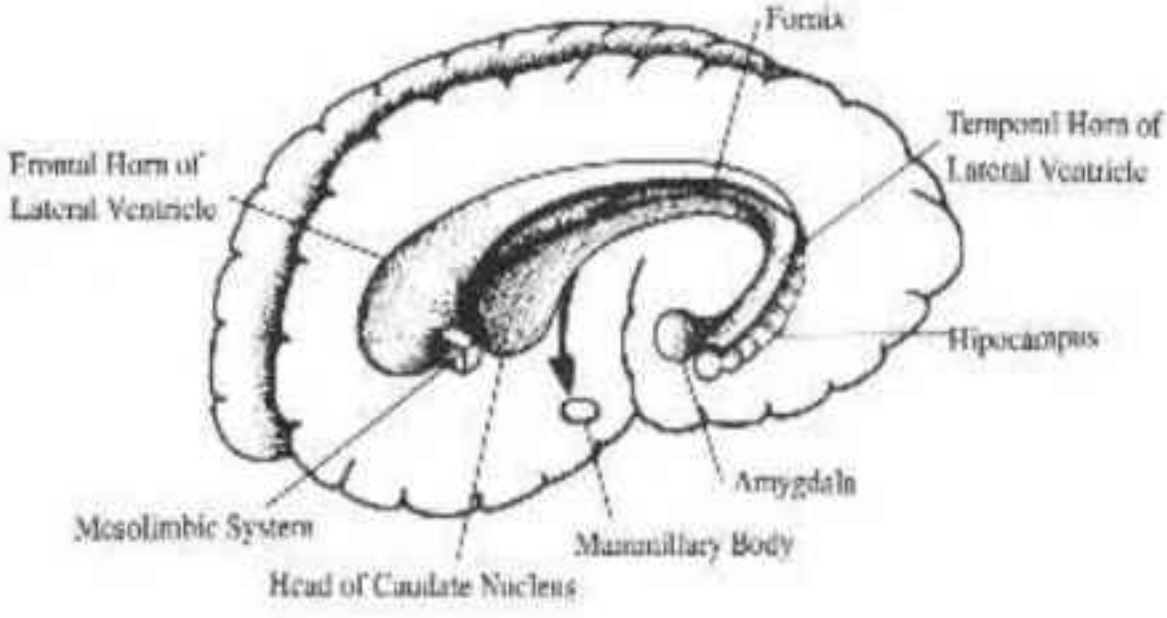
Autonomic and Neuroendocrine Systems: The hypothalamus expresses its autonomic responses—change in blood pressure, facial flushing, tachycardia, sweating, and tachypnea—via direct connections down the brainstem and spinal cord to the internal organs.



Neuroendocrine responses consist of changes in serum cortisol, antidiuretic hormone, thyrotropin releasing hormone, etc. In addition to stimulating the pituitary below, hypothalamic releasing hormones (like thyrotropin releasing hormone) may also flow *upward* to influence brain activity during stress.[20] Pituitary hormones, too, may flow upward to influence the brain before being diluted in the systemic circulation.[21]

Internal feelings are felt by the limbic system, a collection of very old phylogenetic structures devoted to the basic emotions and drives shared by all mammals: fear, anger, sex, curiosity, caution, joy, sadness, and so on. Buried underneath the cortex, the limbic system includes: 1) the amygdala and hippocampus in the temporal lobe, 2) the fornix, mammillary body, anterior nucleus of thalamus, and cingulate gyrus deep within the center of the brain, and 3) the subfrontal* mesolimbic system: septal nucleus, nucleus accumbens, nucleus of the diagonal band, and bed nucleus of stria terminalis.[22] Mesolimbic structures are situated just anterior to the caudate nucleus.





Subfrontal: Underneath or deep within the frontal lobe.

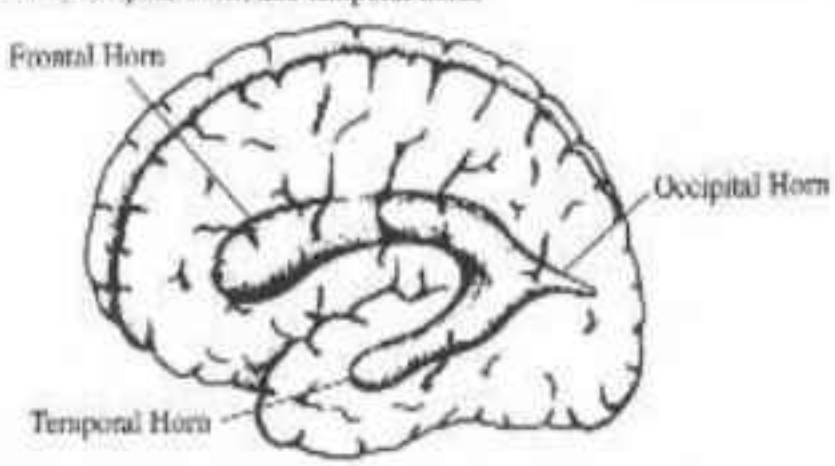
The temporal lobe has direct access to all these deeply situated centers of emotion by way of three temporal lobe structures: hippocampus*, amygdala*, and temporal lobe cortex. The *hippocampus* lies smack in the temporal lobe abutting the undersurface of the temporal horn of the lateral ventricle*. A thick cable of fibers, the fornix*, arches gracefully upward from the hippocampus* through the lateral ventricle, forward above the roof of the third ventricle, and then downward to the mesolimbic system, hypothalamus, and mammillary bodies* below.[36] The *amygdala*, a large grey matter structure in front of the temporal tip of the lateral ventricle, projects two major fiber tracts to the hypothalamus and mesolimbic system. One is the ventral amygdalofugal pathway, and the other, stria terminalis. Even the *temporal lobe cortex* projects unnamed fibers throughout the neighborhood of the mesolimbic system.[37]

At the beginning of a temporal lobe seizure, the sensations of fear, anxiety, pleasure, or anger probably stem from these direct-access fibers connecting the temporal lobe to emotional centers in the hypothalamus and limbic system.[38] In fact, since electrical stimulation of the temporal lobe can exaggerate rage reactions,[39] an occasional legal defense for rage attacks is that they are, in fact, temporal lobe seizures. However, unless the patient is forceably restrained during the seizure or during the confused postictal* state, he is very unlikely to attack another person, and certainly not in an organized or premeditated way.[36]

Hippocampus: Hippo means horse. In cross section the hippocampus is shaped like a sea horse.

Amygdala: Means almond in Latin.

Lateral Ventricle: The ventricular system is composed of four separate ventricles, the lateral being one of them. Horns (extensions) of the lateral ventricle are named according to the surrounding lobe: frontal horn, occipital horn, and temporal horn.

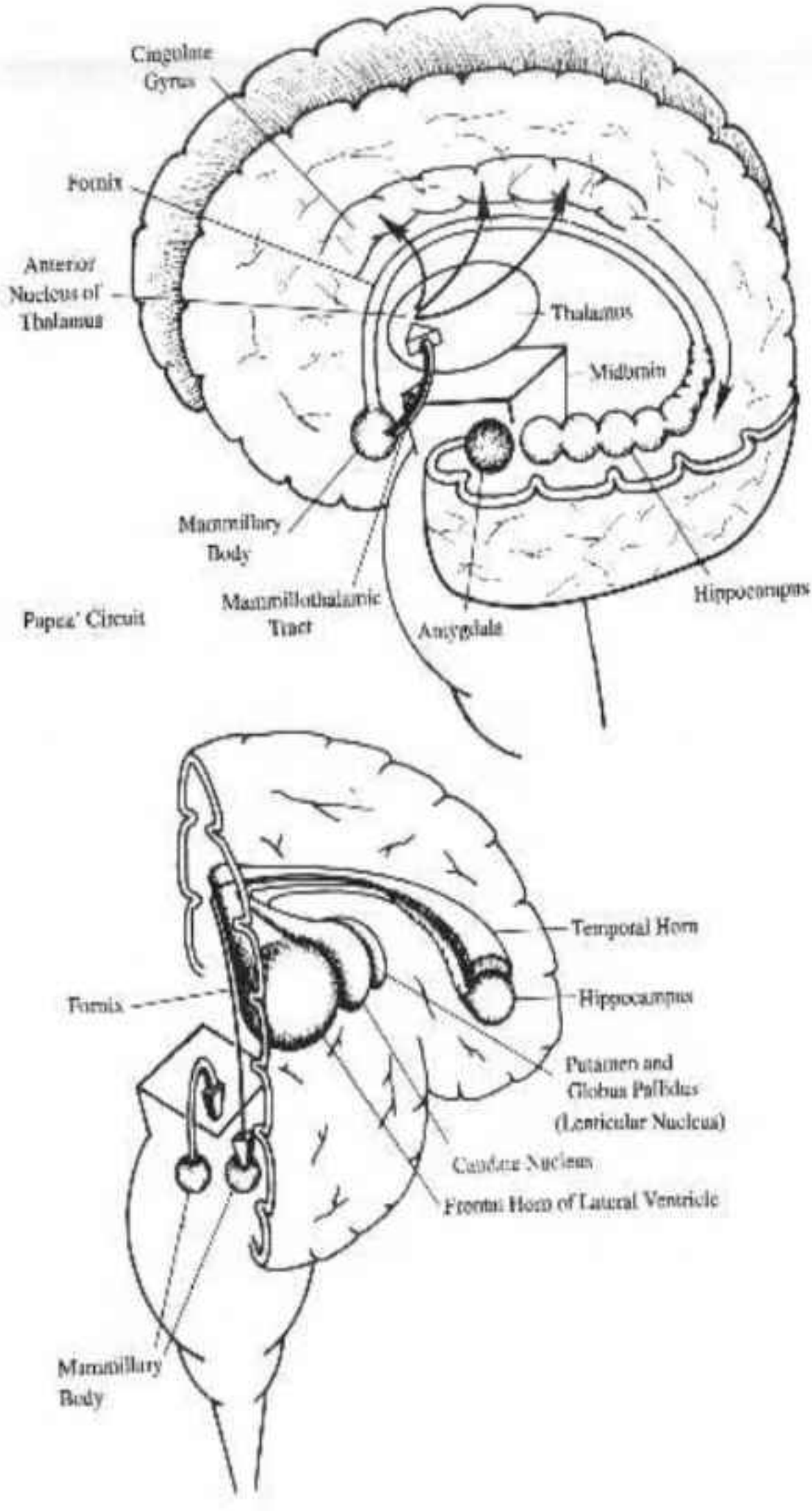


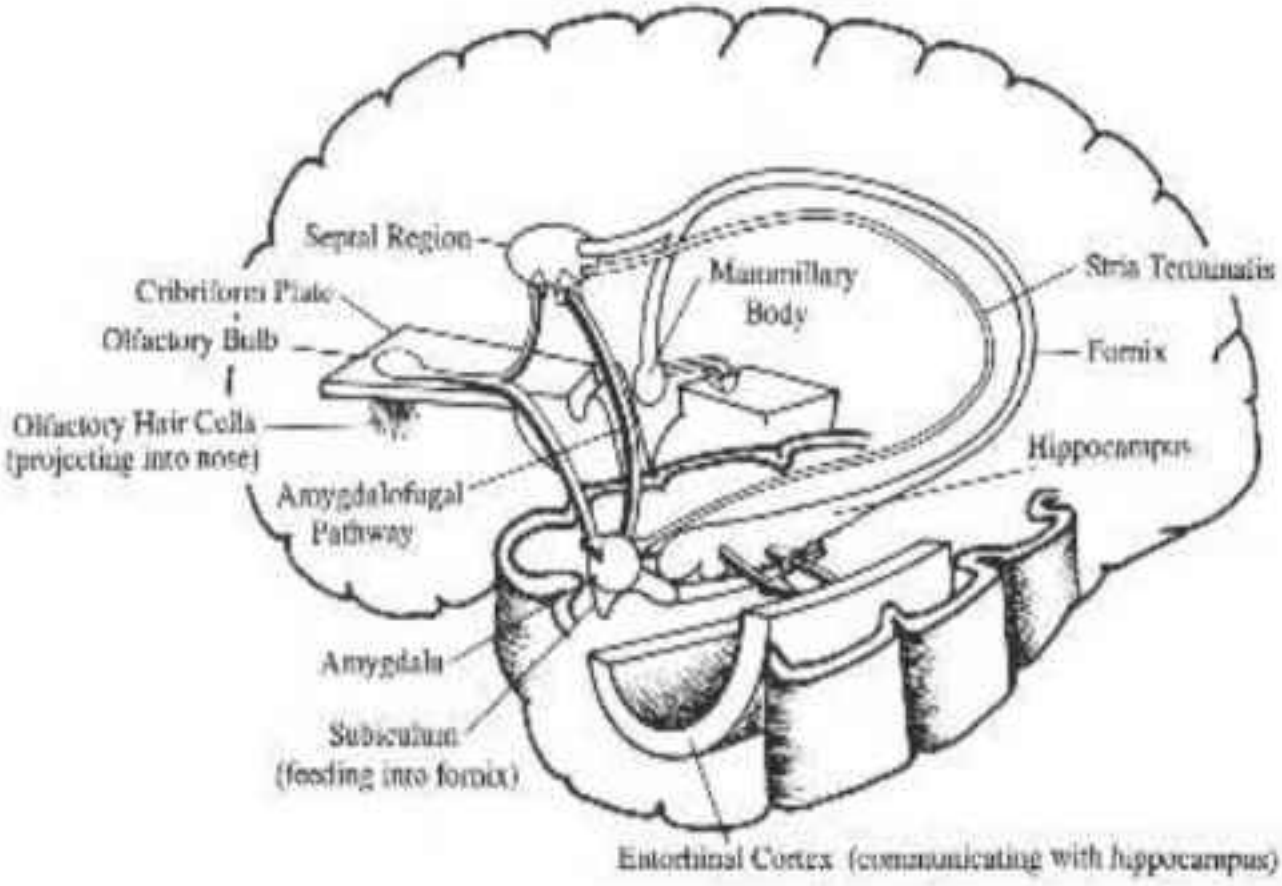
Fornix: Archway. Archways into Roman brothels spawned 'fornicate.'

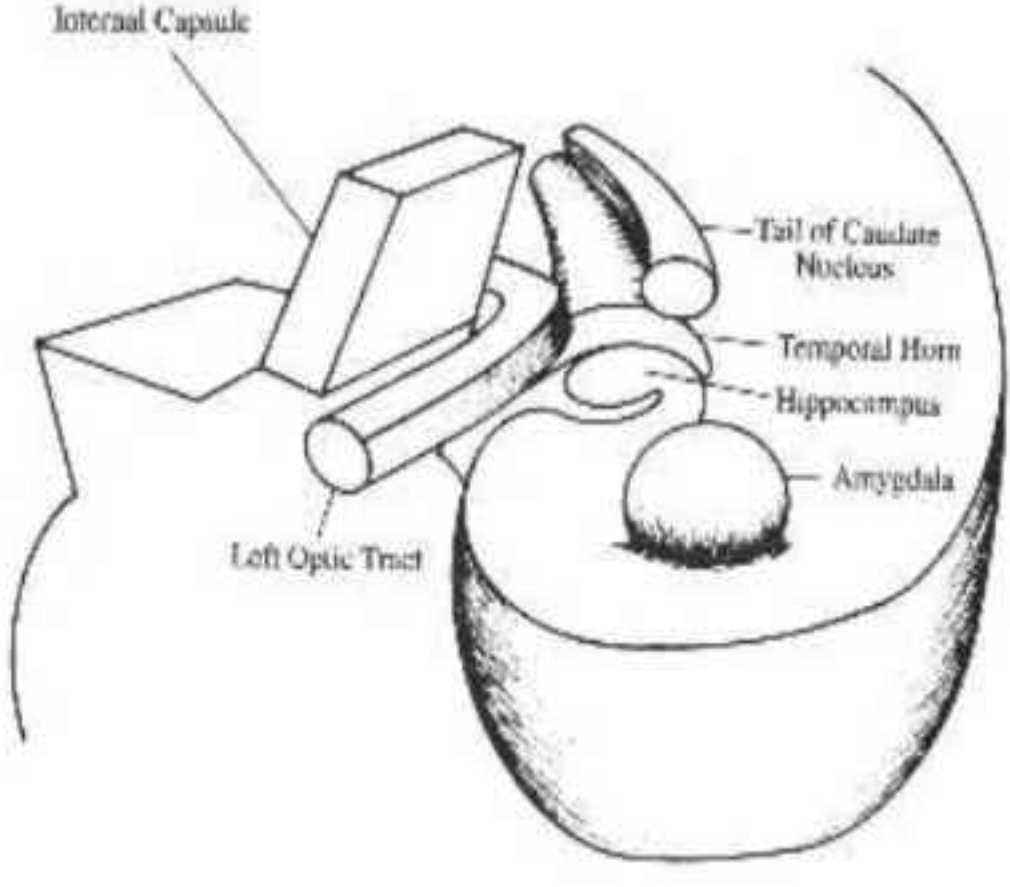
From the Hippocampus: Most of the fibers in the fornix do not, in fact, originate from the hippocampus proper, but rather from an adjacent temporal area called the subiculum.[23] In addition, many fibers in the fornix are actually traveling retrograde—from the septal region toward the temporal lobe. Perhaps the septal region—the probable pleasure center of the brain—is trying to reinforce whatever the temporal lobe is doing (like learning a new memory).[24]

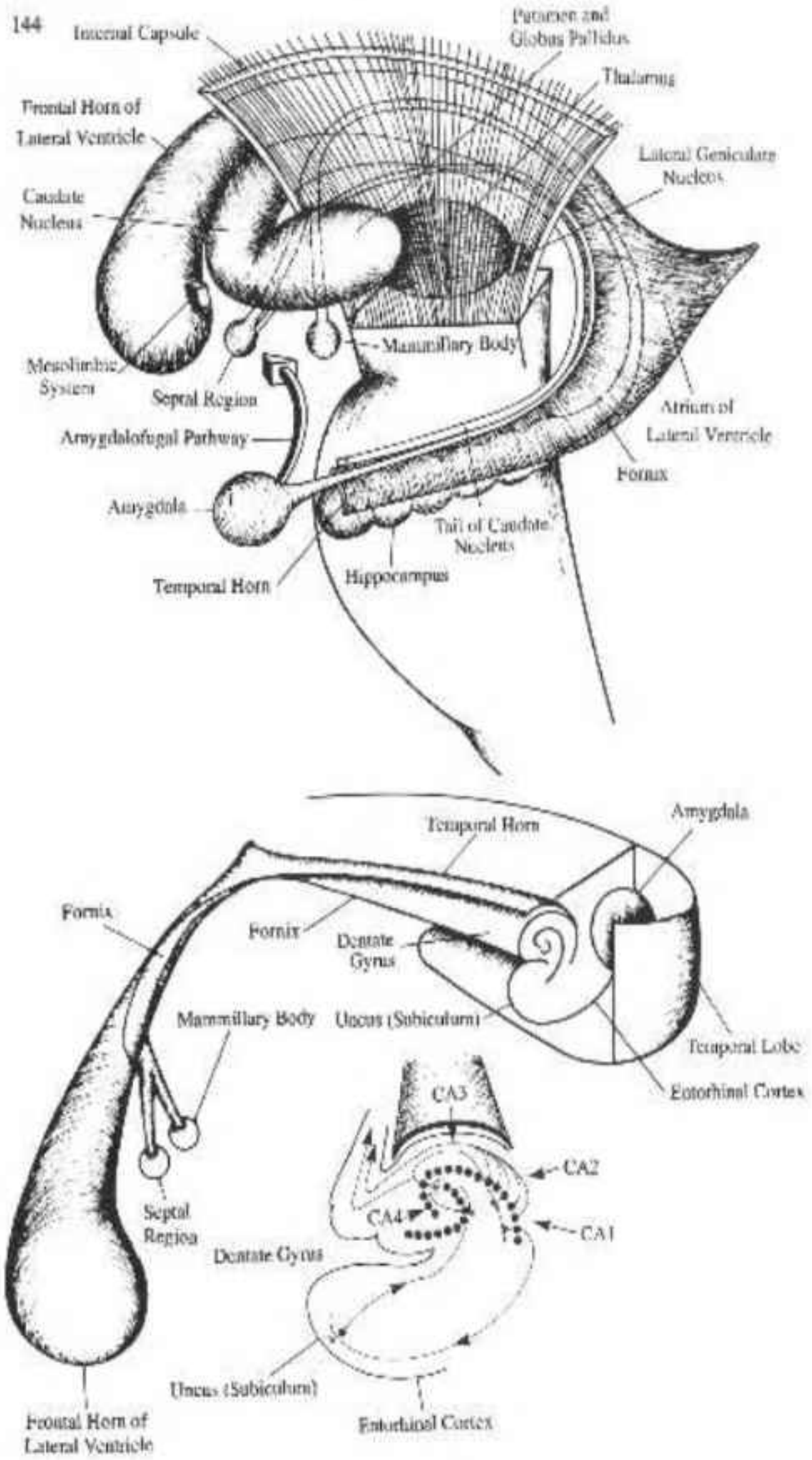
Mammillary Bodies: Each mammillary body projects a densely packed fiber tract, the mammillothalamic tract, upward to the anterior nucleus of thalamus, which then completes 'Papez' circuit' by returning to the ipsilateral temporal lobe via the cingulate gyrus.[25] The mammillary bodies contribute to the autonomic aspects of emotion by sending its other major outflow tract down the brain stem.

Postictal: Ictus means event; postictal means after the event, in this case, after the seizure.


Cingulate Gyrus
Fornix
Anterior Nucleus of Thalamus
Thalamus
Midbrain
Mammillary Body
Papez' Circuit
Mammillothalamic Tract
Amygdala
Hippocampus
Temporal Horn
Fornix
Hippocampus
Putamen and Globus Pallidus (Lenticular Nucleus)
Caudate Nucleus
Frontal Horn of Lateral Ventricle
Mammillary Body


Septal Region
Cribriform Plate
Olfactory Bulb
Olfactory Hair Cells
(projecting into nose)
Amygdalofugal
Pathway
Mamillary
Body
Stria Terminalis
Fornix
Hippocampus
Amygdala
Subiculum
(feeding into fornix)
Entorhinal Cortex (communicating with hippocampus)


Internal Capsule
Tail of Caudate
Nucleus
Temporal Horn
Hippocampus
Amygdala
Left Optic Tract


Internal Capsule
Putamen and Globus Pallidus
Thalamus
Frontal Horn of Lateral Ventricle
Lateral Geniculate Nucleus
Caudate Nucleus
Mammillary Body
Mesolimbic System
Septal Region
Amygdalofugal Pathway
Atrium of Lateral Ventricle
Fornix
Amygdala
Tail of Caudate Nucleus
Temporal Horn
Hippocampus
Temporal Horn
Amygdala
Fornix
Fornix
Dentate Gyrus
Mammillary Body
Uncus (Subiculum)
Temporal Lobe
Entorhinal Cortex
CA3
CA2
CA4
CA1
Septal Region
Dentate Gyrus
Uncus (Subiculum)
Entorhinal Cortex
Frontal Horn of Lateral Ventricle

How does a temporal lobe fit cause a forced memory? The anatomy of memory is only partly understood, but both clinical experience and experimental research emphasize that new memories are logged into the brain by one or the other temporal lobe[4]. What's *not* understood is which temporal lobe structure—hippocampus, amygdala, or temporal lobe cortex (or all three)—incorporates each new memory[4]. Also unclear is the exact structure being stimulated when a temporal lobe seizure evokes a forced memory[4,33]

Temporal Lobe: Removal of the left temporal lobe impairs our ability to lay down verbal memories, and removal of the right temporal lobe impairs our ability to lay down unnamed visual and unnamed auditory memories.[34] A bilateral temporal lobectomy will prevent us from learning virtually any new memory.[32]

New Memory: Some investigators believe that the hippocampus is *the* memory structure.[34] Horel offers the opposite view that the hippocampus has little or nothing to do with memory.[35] Still others have offered up the thalamus as a critical memory structure.[36]

Forced Memory: Let's speculate about memory for a minute, using vision as an example. Each visual memory begins as a collection of lights, darks, lines, and colors in the primary occipital cortex. These primary sensations must then be assembled into a more complex, three-dimensional image. The assembly process probably takes place in visual association cortex, conveniently adjacent to the primary occipital cortex.[37]

Before being stored as a memory, each newly assembled image must be recognized or, if it is truly novel, at least related to something familiar. This amazingly complex feat is probably done by rapidly comparing the initial perception with similar past experiences. Postulating a likely explanation for the image, we then seek additional clues from the object to confirm that initial assumption. But if those additional clues don't help, we quickly propose another familiar possibility, and again seek the necessary sensory clues, and so on. Each new possibility is checked against past experiences until we're satisfied that we've perceived something familiar. And until we *are* satisfied, strong emotions like caution, fear, anxiety, curiosity, and excitement keep us interested enough to explore the object further.[38]

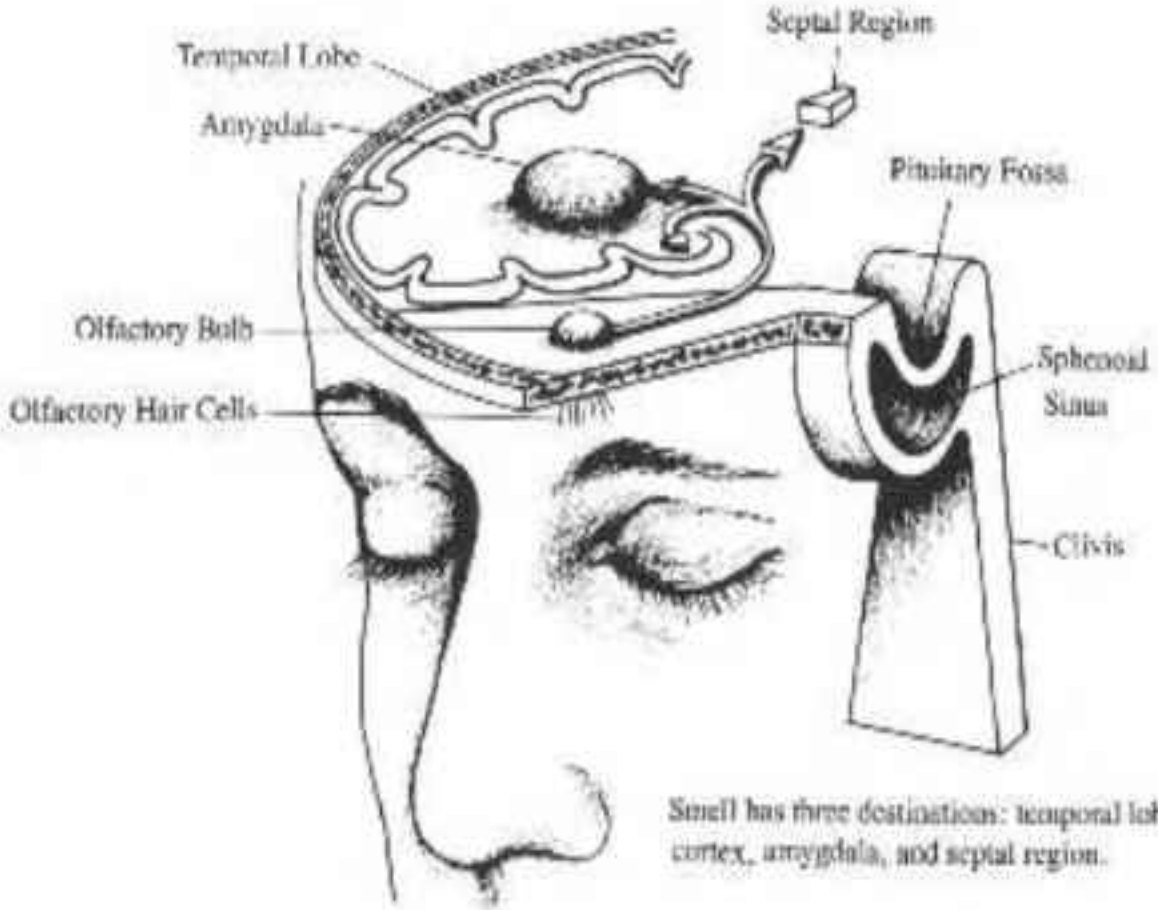
But how does each sensory association area make such rapid comparisons with past experiences? Do association areas keep old memories stored in adjacent cortex,[39] or do they retrieve old memories from distant areas of cortex? What happens if no match-up is ever made with an old memory? The patient will be able to describe what he sees but won't have any idea what he's looking at, a condition called visual agnosia.[40]

Once the brain decides to remember something, the new memory is shunted from each association cortex along strong direct connections to the temporal lobe for storage.[41] But where the temporal lobe stores that memory, and how we subsequently retrieve the memory, are still unknown. What does seem clear is that: 1) the temporal lobes are not necessary to retrieve old memories,[42] and 2) memories are stored throughout the entire cerebral cortex. That is, you cannot obliterate a particular memory by removing a focal area of cortex; the same memory seems to be stored throughout the cortex![43]

Interestingly enough, each association area projects to the entorhinal area of the temporal lobe,[44] an area that happens to be *the* major afferent source for the hippocampus, as well as an important afferent source for the amygdala and other areas of temporal lobe cortex.[45] Perhaps these tracts from each association cortex provoke (through temporal lobe—mesolimbic connections) the anxiety, caution, curiosity, fear, and excitement we experience when confronting something novel.[46] Or maybe they help mediate the sense of familiarity (deja vu?) after the perception is recognized.

It's understandable that the temporal lobes, busy incorporating new memories, should be so closely allied to emotion because as soon as a perception is recognized, the brain has to attach an emotional reaction to it.[47] Every experience, every perception is given an emotional handle—some bland, some highly charged—but everything evokes an emotion. The brain needs that emotion for motivation to remember the experience *and* to act upon it. Without that emotional attachment, the brain does neither; the best lessons in life are emotional ones*.

Smell, another common aura* of temporal lobe epilepsy, uses the temporal lobe to gain easy access to emotions and memory. Odors are detected by the olfactory bulb which sends a large fiber tract directly to the temporal lobe cortex and amygdala.[48]



Smell has three destinations: temporal lobe cortex, amygdala, and septal region.

Even without the temporal lobe, smell has immediate access to emotions by directly synapsing into the septal area of the mesolimbic system. This extremely close bond between smell and emotions is much more important to lower animals, most of whom sniff their way through the world. Remnants of this pathway still remain in humans, as anyone will attest to who has experienced involuntary emotional responses to

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Emotional Ones: Learning emotionally charged items is different from learning bland material against an emotionally charged background (like cramming for final exams). Even though modest stress helps learning, and depression hinders it, any college student will acknowledge that cramming under stress does not enhance long-term memory as well as learning emotionally laden material.

Aura: Any sensory symptom (but not a motor sign) prior to loss of consciousness is called the aura of a seizure. Aura is a misleading term because it implies a warning (aura means breeze, like the warning of an up-coming thunderstorm). An aura is not a warning of an impending seizure, it *is* the seizure, the beginning of the seizure. And knowing the physiology of an aura, there is no good reason to restrict the term to sensory symptoms without including motor signs as well.

fragrances, such as sexual arousal from perfume, tranquility from flowers, hunger from a steak, or disgust from sewage. It seems logical that there should also be odors producing fear and anger, but as yet the entire field of odors and emotions remains a potentially fruitful area of research.

Like smell and emotions, the connections linking smell to memory are vital to lower animals. But even in man, juxtaposition of smell and memory is evident to anyone who has chanced upon a fragrance which evoked an immediate, vivid memory.[45] The unidirection of this pathway is obvious from our inability to evoke a fragrance by simply thinking about it.

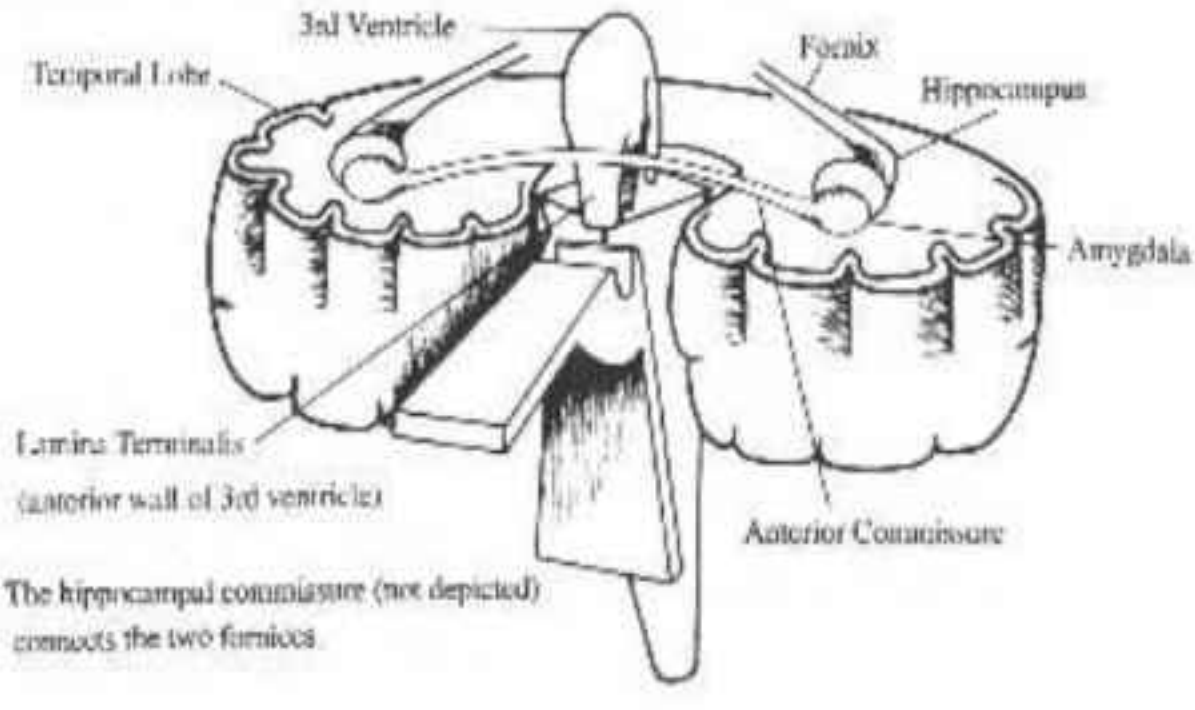
The last common manifestation of temporal lobe seizures is the automatism[46], a brief episode of automatic behavior during which the patient is unaware of his surroundings and is unable to communicate with others. The source of the automatism, the exact structure being stimulated during an automatism, is not known[4,56] Typi-

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Automatism: The fumbling, zombie-like state of an automatism gives temporal lobe epilepsy its other, preferred name: psychomotor epilepsy, a term which describes the phenomenon, not the site of origin. It turns out that some so-called temporal lobe automatisms actually stem from the frontal lobe.[50] Frontal lobe discharges may produce automatisms via projections (especially ones through the cingulate gyrus) to one or the other temporal lobe,[3] or perhaps via subcortical (basal ganglia?) structures.[51]

Not Known: Delgado-Escueta believes that automatisms beginning with a motionless state (Type I) result from temporal lobe discharges, while automatisms beginning with motor activity (Type II) result from discharges outside the temporal lobe.[52] Distinguishing type I from type II may be quite important, because Type II seizures appear less likely to improve following temporal lobectomy (surgical removal of the seizure focus by resecting the anterior part of the abnormal temporal lobe).[54]

As long as seizure activity remains confined to one hemisphere, the patient will retain conscious awareness and therefore be able to remember the sensory aura of smell, forced memory, or emotion. But as soon as the seizure spreads to the opposite hemisphere, the patient loses touch and will not remember what subsequently happens.[55] Perhaps in some patients automatisms begin when discharges from one temporal lobe spread to the other temporal lobe. The rest of the brain would not have to be involved because the temporal lobes are intimately connected to each other by two major pathways: the anterior and hippocampal commissures. (A commissure is a tract of white matter connecting two similar, contralateral brain or spinal cord structures.)



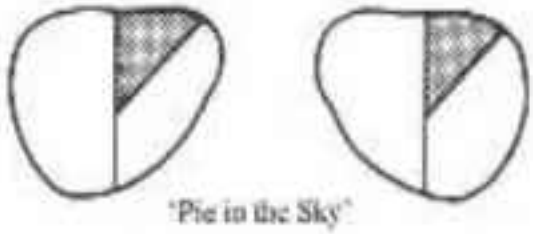
cally, the patient abruptly stops talking, changes facial expression, adopts a glassy stare, may begin to pick meaninglessly at his clothes, smack his lips, walk about, or carry on any minor purposeless activity. The behavior is almost never as complex as chasing another person or robbing a bank, but there have been patients who've wandered off for hours or even days *following* a temporal lobe seizure.[57]

Abrupt, stereotyped, recurrent attacks of an unusual smell, memory, emotion, or automatism are almost certainly temporal lobe seizures. Rarely, stereotyped sounds[58] herald a temporal lobe seizure—rarely, because sounds enter the posterior temporal lobes and the seizure focus is usually in the anterior or medial temporal region.[59] For this same reason, visual hallucinations (occipital-temporal focus) and Wernicke's aphasia only rarely initiate a temporal lobe seizure. Even rarer temporal lobe seizures include stereotyped attacks of vertigo, laughing, running, or macropsia or micropsia (objects look strangely bigger or smaller).[60]

The point about seizures being stereotyped is very important, because every emotion is obviously not a fit. To be a temporal lobe seizure, the experience should be the same one every time (or very similar). After all, the same abnormal neurons are initiating the seizure every time. In addition, true temporal lobe seizures should begin abruptly, terminate relatively abruptly, should not be remembered (if there was an automatism), and should be followed by postictal confusion or drowsiness.[61] If the spells meet these criteria, you can conclude that they are very likely coming from a temporal lobe, but not which temporal lobe. Both the right and left temporal lobes produce (with the exception of aphasia) the same kind of fit.

Visual Field Cut

The third sign of temporal lobe dysfunction, and weakest of the three, is a 'pie in the sky' field cut:



'Pie in the Sky'

Sounds: Music, like all sounds, enters our consciousness through the temporal lobes. With easy access to emotions and memory (via temporal lobe connections), it's no wonder that rock and roll, tender love songs, and patriotic music evoke such intense emotions and such emotionally laden memories. Music's hold on our emotions is far more gripping than either vision or touch, even more than pain.

It's difficult to remember pain (thank God, or else there'd only be one childbirth per family). From an anatomic standpoint this suggests that after traveling up the spinal cord and brainstem, pain does not head directly for the temporal lobes to establish long-term memory traces. Instead, pain synapses into the hypothalamus and mesolimbic system.[58] The hypothalamic connections account for the prominent autonomic and neuroendocrine responses to pain, and the connections into the mesolimbic system account for the anxiety, fear, anger, and the agony of pain. But the emotions elicited by pain—at times as intense as those elicited by music—do not evoke anywhere near the enormous spectrum of subtle feelings and autonomic responses evoked by music's extensive temporal lobe connections.

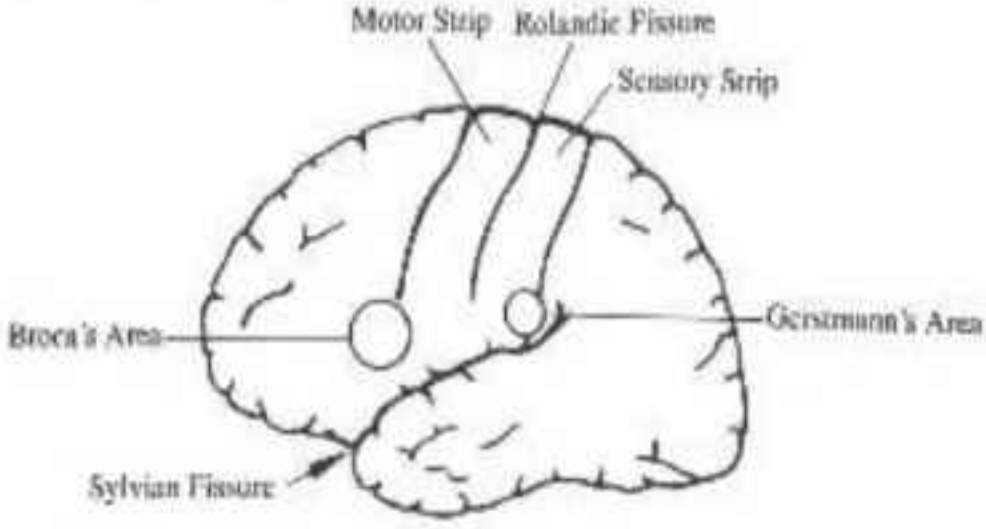
Return to the optic radiations (page 134). Notice that a loop, called Meyer's loop, dips into the temporal lobe.[62] These fibers originate from the contralateral inferior quadrant of each retina, corresponding to an upper, outer field cut—in medical terms, a homonymous superior quadrantanopia. The reason a superior quadrantanopia is the weakest of the three pathognomonic signs is that the same band of visual fibers streaking back to the occipital lobe may be ambushed anywhere behind the temporal lobe. Such lesions deep in the occipital lobe, however, generally produce a denser and more complete superior quandrantanopia than temporal lobe lesions.[63]

LEFT PARIETAL LOBE

That does it for the temporal lobe—Wernicke's aphasia, temporal lobe seizures, and pie in the sky field cut. Pathognomonic signs of left parietal lobe dysfunction include Gerstmann's syndrome, right-sided cortical sensory loss, and a right-sided sensory seizure.

Gerstmann's Syndrome

Just above Wernicke's area is an interesting area called Gerstmann's area. Lesions there produce finger agnosia, acalculia, right/left confusion, and agraphia. In English, the patient cannot identify the fingers on his hands, cannot add or subtract simple numbers, cannot tell left from right, and cannot write even though the hand is not paralyzed or incoordinated*.[64]



Color Dysnomia

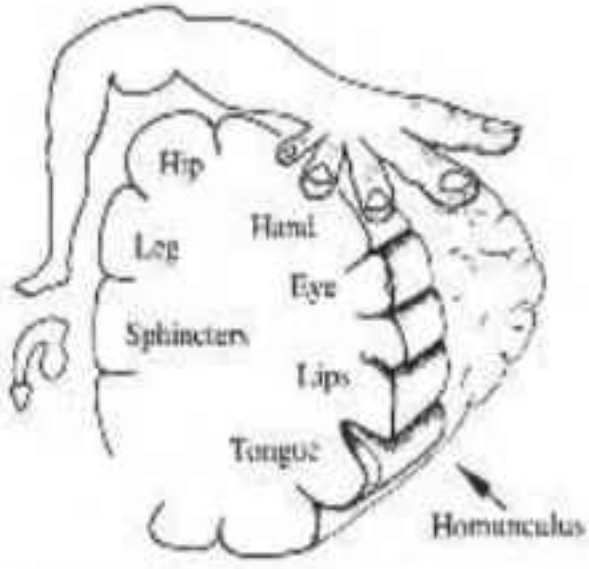
Color dysnomia (inability to name colors*) is akin to object dysnomia and is probably due to an interruption of fibers streaming from the occipital lobe (where they're seen) to Wernicke's area in the temporal lobe (or perhaps the dysnomia center). The lesion is usually in the border zone of the parietal, occipital, and temporal lobes.[65]

Not Paralyzed or Incoordinated: It's easy to remember Gerstmann's syndrome once you recognize that all four signs pertain to the hand: right/left hand, handwriting, finger identification, and counting on the fingers.

Inability to Name Colors: Color dysnomia is not the same as achromatopsia: inability to recognize or even match colors (as if all colors looked gray).[66]

Cortical Sensory Loss

Another sign of left parietal cortical dysfunction is cortical sensory loss, indicating a lesion in the sensory strip lying just posterior to the Rolandic fissure. In the 1930's Wilder Penfield, the renowned neurosurgeon from Montreal, and Herbert Jasper, the neurophysiologist of the team, electrically stimulated the sensory strip of an exposed brain with the patient awake and alert.[67] With the patient's cooperation they were able to map out a detailed anatomic representation within the sensory strip, a figure called the homunculus. (They also mapped a similar homunculus along the motor strip.) The genitals, the bladder, and the legs all hang in the interhemispheric fissure while the upper torso lounges backward over the hemisphere.[68]



A lesion of the sensory strip disturbs what's known as higher cortical function. A patient with cortical sensory loss is not able to identify numbers written on his skin (called agraphesthesia), the type of fabric rubbed across his skin, or the particular coin or the shape of a block placed in his hand (astereognosis). These deficits occur despite only a mild loss of light touch or pin sensation[a].[70] It's as if the building blocks of sensation were intact, but couldn't be assembled into a two-dimensional mental picture in the case of graphesthesia, or a three-dimensional picture in the case of astereognosis.

Sensory Seizures

A focal sensory seizure of the right side of the body also implicates the left parietal cortex. Just as tingling sensations were produced artificially by Jasper and Penfield, a sensory seizure consists of abrupt paresthesias[a] of the right hand, foot, or face depending on which part of the sensory strip was first excited.[71] If the seizure spreads up or down the sensory strip, the paresthesias spread as well.[72] This march of paresthesia is called a Jacksonian march, after Hughlings Jackson, the genius English neurologist who first correctly described the physiological basis of the march a full century ago.

Light Touch or Pin Sensation: Occasionally, cortical sensory loss severely disrupts proprioception, enough that the patient cannot even tell if you're holding his hand above his head or below his shoulder.[69]

Paresthesias: Numbness and tingling. Dysesthesias are unpleasant numbness and tingling in response to brushing or slapping the skin. Hypesthesia, a contraction of hypoesthesia (touch), simply means less than normal (but not unpleasant) sensation when the skin is touched.

A lot of people complain of tingling in a hand or foot, but how do you decide it's a sensory seizure*? As in temporal lobe seizures, you want to hear that the paresthesias are stereotyped, recurrent, abrupt in onset and termination, and most importantly, that they involve the face and hand (or hand and foot) simultaneously, preferably beginning in one particular spot and marching up the leg or arm to involve the face (or marching in the opposite direction). Another helpful clinical point is that since the lips, fingers, and foot have such a large cortical representation (see the homunculus), sensory seizures usually begin in these sites rather than an elbow, shoulder or thigh which have relatively little cortical representation.

LEFT FRONTAL LOBE

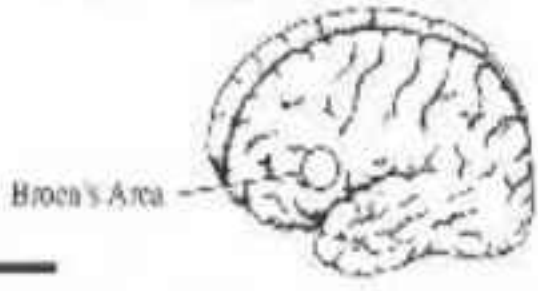
Motor Seizures

Now for the left frontal lobe. Step across the Rolandic fissure to the motor strip. Instructions from this vitally important gyrus will move almost any muscle in the body by sending instructions down the pyramidal tract into the brainstem or spinal cord. Like the sensory strip, the motor strip is organized into a homunculus whose shape nearly matches its partner's in the sensory strip. A focal seizure in the left motor strip causes focal jerking of the right arm, foot, leg, or face depending on where the seizure begins in the motor strip. If the spark of electricity marches up or down the motor strip, so does the focal jerking march in corresponding areas of the right side. Even if the march progresses into a major generalized convulsion, in which the patient falls unconscious shaking in all extremities, the fact that the seizure began with focal jerking of the right hand or face automatically places the origin of the seizure in the left motor strip.

An 'adversive' seizure also comes from the frontal lobe, from a strange little patch along the medial frontal lobe called the supplementary motor area.[73] During the seizure, the patient slowly turns his head away from the seizure focus as the hand contralateral to the seizure focus rises into mid-air.[74]

Broca's Aphasia

Not surprisingly, Mother Nature placed the motor center for speech—Broca's area*—adjacent to the tongue and lips in the motor homunculus.[75]



Sensory Seizure: Transient ischemic attacks, for example, may mimic sensory seizures by briefly interrupting the blood supply to ascending sensory fibers in the internal capsule (chapter 16) or to the parietal sensory strip. Arteriography (chapter 40) and electroencephalography (chapter 44) can usually distinguish sensory TIA's from sensory seizures.

Broca's Area: Paul Broca was the famous French neurologist who, in describing the area associated with this speech disturbance in 1863, pioneered the radical concept of cerebral localization. Prior to this time the brain was thought to be a homogeneous bowl of neurons, each area equally capable of carrying out all cerebral functions.[75]

Being on the motor side of the Rolandic fissure, Broca's aphasia is also known as a motor or expressive aphasia. Broca's aphasia is characterized by the absence of articles, prepositions, pronouns, participles, and conjunctions (grammatical errors) which likens the speech to a telegram: "Flower...green" instead of "The flower is green." In contrast to the fluent cadence of Wernicke's aphasia, Broca's speech is halting, slow, and nonfluent. Since Wernicke's area is intact, the patient can understand much* of what is said to him.

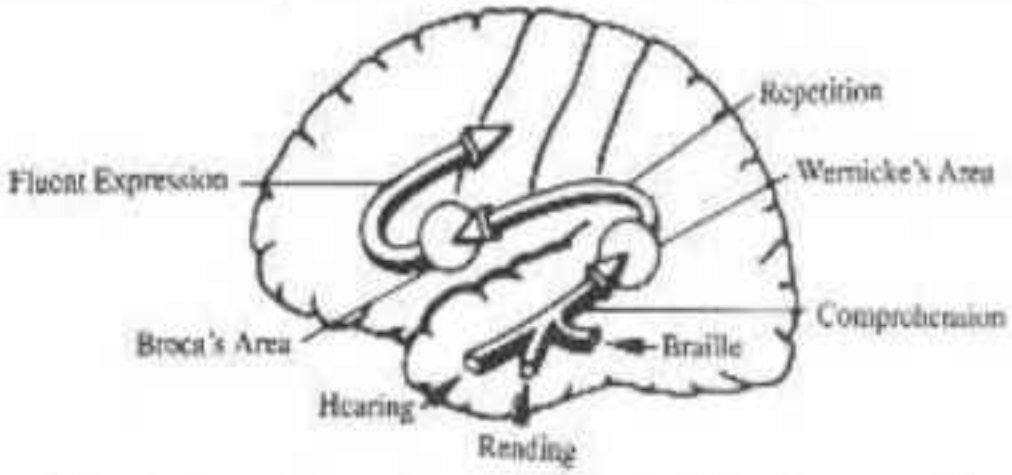
Sometimes the expressive difficulty is so severe that no words are expressed at all, a mute state. Recognizing the mute state as a severe aphasia is usually straightforward because the neighboring motor strip is almost always involved, too. In other words, Broca's aphasia, especially a severely mute Broca's, is typically associated with a right hemiparesis and inability to write. The association of speech and the right hand was recognized long ago by the biblical admonition "may your right hand lose its cunning and your tongue cleave to the roof of your mouth," a poetic description of a left frontal stroke. As you'd predict from the considerable distance separating Wernicke's area from the motor strip, Wernicke's aphasia is not accompanied by a right hemiparesis.[78]

Except for students of aphasia, there are only two major kinds of aphasia: Wernicke's and Broca's, or the combination of the two, global aphasia, which disrupts both comprehension *and* fluency. Less common is 'conduction aphasia' in which the patient makes spelling or grammatical mistakes while trying to repeat a phrase like 'no if's, and's, or but's*.' Even more unusual variants of aphasia* have helped elucidate

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Much: Patient's with Broca's aphasia omit the articles, pronouns, prepositions, conjunctions, and participles that establish the syntactical relationship of words to each other. Likewise, these patients have difficulty *understanding* these 'helper' words, but not enough to prevent them from understanding the main gist of a sentence.[77]

No Ifs Ands or Buts: One way to remember the features of each type of aphasia is as follows:



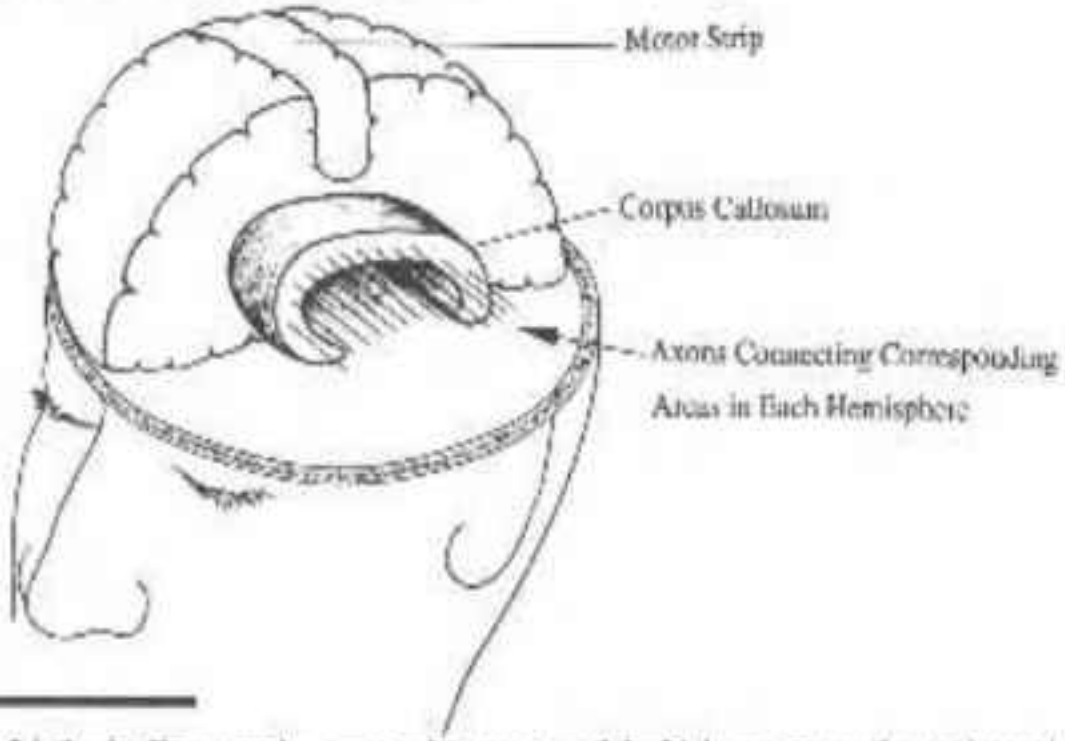
Each neuron in this chain performs a specific function—the temporal neuron, comprehension; the parietal neuron (the arcuate fasciculus), repetition, the frontal neuron, fluency. A lesion in Wernicke's area or Broca's area damages two neurons: the afferent and the efferent one. So,

A lesion of:	*Produces this deficit:*	*Type of Aphasia:*
Temporal Neuron	No comprehension but retained repetition and fluency	Transcortical Sensory
Wernicke's Area	No comprehension and repetition but retained fluency	Wernicke's
Parietal Neuron	No repetition but retained comprehension and fluency	Conduction
Broca's Area	No fluency and repetition but retained comprehension	Broca's
Frontal Neuron	No fluency but retained comprehension and repetition	Transcortical Motor

the physiology of language[6].

CORPUS CALLOSUM

Before moving to the right frontal lobe, there are several pathognomonic signs of the corpus callosum, the broad bundle of axons which tells the left hemisphere what the right hemisphere is doing, and vice versa.



Variants of Aphasia: For example, some patients are 'word deaf;' they cannot understand speech, but can still understand the significance of a telephone ringing, can still read, write, and even speak without difficulty.[29] Other patients may be unable to read, but fully capable of identifying the word if they hear it spelled.[30] And some alexic (unable to read) patients may be able to write what you tell them, but be unable to read what they just wrote![31] Similarly, some patients can read out loud, but be unable to understand what they just read.[32] Some patients can read words without being able to read the individual letters.[33]

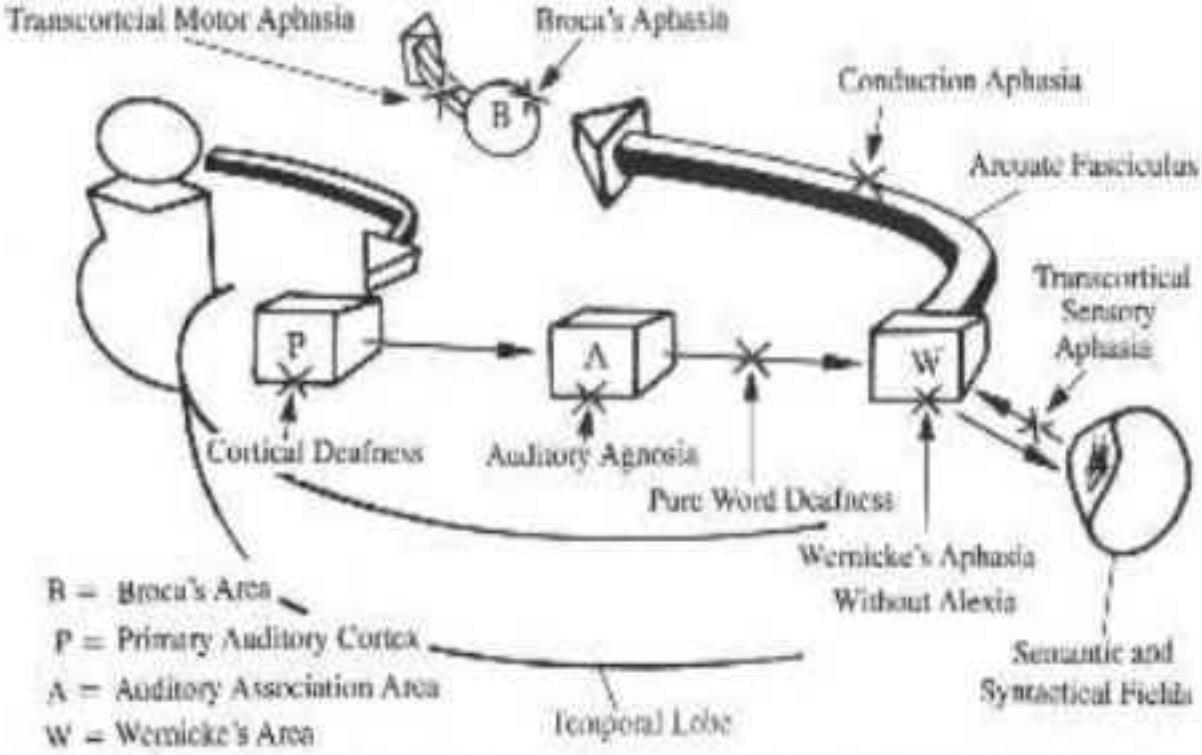
Physiology of Language: How the brain deciphers language is still very speculative. It seems that after reaching the medial geniculate nucleus in thalamus, all sounds enter consciousness through the primary auditory cortex (Heschl's gyrus) in *both* temporal lobes (sounds ascend both sides of the brainstem).[34] Bilateral lesions in Heschl's gyrus (presumably interrupting input from the medial geniculate bodies) could conceivably make a patient acutely deaf.[35] (Heilman disagrees; the lesions would have to extend beyond Heschl's gyrus into temporal association areas.[36])

The temporal association cortex then probably decides if the sounds heard by the primary auditory cortex are words and not, say, a mouse scratching behind the wallboard. Inability to recognize the nature of a sound is called auditory agnosia. Such patients would, for example, hear a doorbell ring, but not understand it as a bell.[37]

Having realized that we're listening to words, Wernicke's area must now pick out the fundamental sounds of words: the p's, b's, t's - the phonemic qualities. Without breaking up the stream of sounds into relevant bits and pieces, we can recognize that we're hearing words, but not which words. It's like listening to a rapidly spoken foreign language, a condition called pure word deafness.[38]

After identifying the phonemic qualities of language in Wernicke's area, we can now take individual words and decipher them. By comparing what we're listening to with meaningful words stored in our memory bank (wherever that is), we can determine both the *semantic* meaning of each individual word and the *syntactical* meaning based on each word's arrangement in the sentence. For example, in a sentence like 'the boy gives the girl a gift,' boy, girl, and gift have their own semantic meaning, but their arrangement provides additional syntactical sense.[39] (Cont. on next page. . .)

A lesion that denies the auditory association areas access to the semantic and syntactical 'fields' would prevent a patient from understanding the spoken word. But since the patient is still capable of discerning the components of speech, he can repeat a phrase. This condition of poor comprehension and retained ability to repeat phrases is called transcortical sensory aphasia.[30] Since the occipital cortex would still have access to the semantic and syntactical fields (through Wernicke's area), the patient would still be able to read and understand what he read.



Direct damage to the semantic and syntactical fields would prevent the patient from understanding spoken *and* written language, but he could repeat phrases since the Wernicke's area (the area that breaks 'streams into phonemes') is still all right.

A direct hit in Wernicke's area would prevent the patient from discerning or assembling the individual bits of words. The patient would be unable to understand or repeat the spoken word, and his speech would be filled with all the gibberish words typical of Wernicke's aphasia. Again, if the lesion were small enough not to involve the semantic and syntactical fields, the patient might still be able to read, even without being able to comprehend the spoken word or speak intelligibly.[31]

Lesions in the arcuate fasciculus, a dense bundle of fibers connecting Wernicke's area to Broca's, prevent patients from repeating phrases, especially phrases containing short syntactical words like 'no ifs, ands, or buts.' By not involving the semantic and syntactical fields, lesions of the arcuate fasciculus do not impair comprehension of the spoken word.[32]

A lesion in Broca's area prevents fluency and repetition, at least transiently. Permanent loss of fluency and repetition probably involves more widespread damage than Broca's area alone.[33]

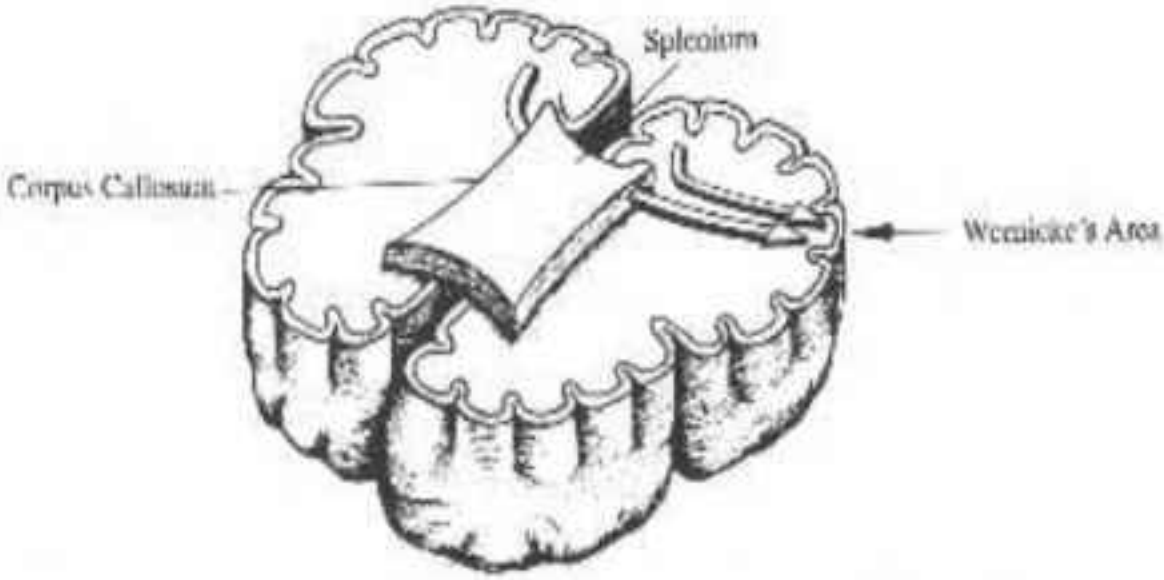
A lesion beyond Broca's area—perhaps in the supplementary motor area—blocks fluency without affecting repetition or comprehension, a condition called transcortical motor aphasia.[34]

Finally, some patients cannot speak fluently because they've damaged critical areas coordinating the lips, tongue, and pharynx. They cannot speak or repeat, but can still read and write grammatically correct English. This 'dysarthria' is a rare condition called aphemia.[35]

Reading begins as a series of simple lines and curves in the primary occipital cortex from which words are constructed in the occipital association cortex and then sent to the left temporal lobe for deciphering. Some authors speculate that the *right* hemisphere also recognizes words, not by analyzing letters, but by recognizing the shape of the word, or the visual image evoked by the word.[36] How in fact do we read? Do we translate written words into spoken words and then 'hear' what we read via the auditory association area?[37] Or, as our reading improves, do written words gain direct access to semantic and syntactical centers in the left temporo-parietal region without first going through the auditory association area?[38]

When you're told to move your left hand, the instruction is first processed through Wernicke's area for comprehension. The job of getting the understood instruction to the right frontal motor strip (which controls the left hand) is carried out by the corpus callosum. A lesion in the corpus callosum prevents this interhemispheric transfer of information, so the patient cannot follow instructions with his left hand, even though the hand is not paralyzed. In fact, the left hand may randomly do the very act it could not do when instructed to. What localizes the lesion causing this apraxia to the corpus callosum is the retained ability to perform the same instructions with the right hand, because there is no block, or disconnection, between Wernicke's area and the left motor strip.[99]

The other syndrome of the corpus callosum is alexia without agraphia, inability to read but retained ability to write; patients cannot read what they've just written! The lesion causing this strange condition extends from the left occipital lobe (producing a right homonymous hemianopia) into the splenium (the back end) of the corpus callosum. Printed words are seen by the right occipital lobe, but they cannot be relayed through the splenium to Wernicke's area to be translated into language.[100]



The lesion causing alexia without agraphia can be anywhere from the splenium to the left temporal lobe, as long as it damages the fiber tracts from both occipital lobes.

RIGHT FRONTAL LOBE

The right frontal lobe, despite its size, is a relatively silent lobe. The best pathognomonic sign is a focal motor seizure of the left side of the body. Aprosody, loss of speech intonation*, is also a right frontal lobe sign,[101] but one that may be difficult to discern without a perceptive ear. In a conversation these patients may seem unsympathetic (or dull), because they also have difficulty *understanding* the emotional intonations of speech.[102]

Intonation: The sing-song quality of speech, like the rise of disbelief, or the fall of a solemn pronouncement.

RIGHT PARIETAL LOBE

The right parietal lobe is an intriguing area. Naturally, left-sided cortical sensory loss and a left-sided sensory seizure, with or without a Jacksonian march, point to right parietal cortical dysfunction. But in addition, there are several very interesting apraxias produced by lesions of the right parietal lobe. These apraxias center around the job of the right parietal lobe to orient us in our surroundings and to discern the relationship between shapes and shadows, figures and forms.[103] For example, if you pull a bathrobe sleeve inside out, the patient with a right parietal lobe lesion may not figure out why he can't put his robe on, a situation called dressing apraxia. Another one is constructional apraxia in which the patient may be unable to draw simple figures like a square within a circle.[104]

Right parietal lobe lesions also cause a characteristic disturbance of space perception.[105] When taken a few feet from his hospital room and turned around, the patient may be unable to find his way back to the room without random hit and miss choices. Even stranger are right parietal patients who ignore the left half of their visual world.[106] When asked to fill in the numbers of a clock, for example, patients may ignore the left half of the clock.

I remember one charming woman referred in by the customers at her pizza parlor. Apparently this woman was serving up pizzas with goodies on only half of the pizza. On exam she had a left homonymous hemianopia. The hemianopia, however, was not enough to explain her performance, because most hemianopic patients get along just fine by turning their head to the left or right so that the hemianopic world is brought into the intact visual field. This woman had more than a simple homonymous hemianopia; she was blind to her left visual world in the fullest sense—she ignored it, and hence the horror on her customers' faces when the pizza arrived. Her CAT scan* documented the right parieto-occipital infarction.

In its extreme, right parietal patients with left-sided neglect may deny that their paralyzed left arm is paralyzed or that their left arm even belongs to them.[107] It's quite astonishing to pick up a patient's paralyzed left hand, put it in front of his face, and listen to the patient say it's *your* hand.

One note of caution when testing for right parietal lobe lesions: be sure that dressing apraxia, constructional apraxia, spatial disorientation, and left-sided neglect are not part of a more profound confusional state (chapter 15).

RIGHT TEMPORAL LOBE

Lesions of the right temporal lobe produce the same abnormal signs as lesions of the left temporal lobe (except for aphasia): contralateral pie in the sky field cut and temporal lobe seizures.

RIGHT OCCIPITAL LOBE

We finally end up in the right occipital lobe where the only pathognomonic signs are seizures or palinopsia in the left homonymous visual field (palinopsia is far more common after right hemispheric lesions than after left hemispheric ones).

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*CAT Scan: Computerized Axial Tomography – a revolutionary brain scan which, by computer analysis, produces xray slabs of the brain (or body), all within minutes and without significant danger or discomfort.

BILATERAL CORTICAL SIGNS

MOST FUNCTIONS OF THE CEREBRAL CORTEX—ones having to do with consciousness, attention, and thinking—require the interchange of both hemispheres. Signs like lethargy, stupor, coma, disorientation, confusion, amnesia, dementia, impaired judgement, delirium, and all the psychiatric afflictions like paranoia, hallucinations, and flight of ideas do not, with rare exception*, result from a simple focal cortical lesion. These signs are due to diffuse, or at least multifocal, bihemispheric dysfunction. Bihemispheric cortical signs fall into two broad categories—level of consciousness and clarity of thought, or, if you will, the quantity of thought and the quality of thought.

LEVEL OF CONSCIOUSNESS

Level of consciousness is commonly divided into alert, lethargic, stuporous, and comatose states. Being adjectives, these words mean different things to different people, so objective criteria are used to label the state of consciousness. In describing the level of consciousness, a number of things must be kept in mind. First, you want to elicit the *highest* level of consciousness, because the highest level is more meaningful and reliable than the average level of consciousness. Besides, it's embarassing to label someone comatose when stimulation reveals that he was only sleeping.

Second, and this is something that needs emphasis and re-emphasis, the label you attach to the patient is far less important than a description of the stimulus you used and the patient's response to that stimulus.[2]

Third, the level of consciousness is the single most important part of the neurologic exam. After all, vision, speech, gait, or for that matter, the heart, lungs, kidneys, none of these are worth a hoot if the patient is not awake enough to use them. Your entire career in medicine is devoted to the preservation and protection of consciousness first, and then, but only then, the quality of life.

Before you can take appropriate steps to protect consciousness, you have to know how close the patient is, and just as importantly, how fast he is approaching a state of irretrievable coma. This last point is something you use in medicine all the time. It's one of the first questions you unconsciously ask yourself every time you approach a patient—"how much time do I have before this patient is dead?" If the level of consciousness is falling, if short runs of ventricular tachycardia appear on the monitor during an acute myocardial infarction, if the blood pressure is falling, etc., the answer is "not much," and you better move quickly with treatment.

With Rare Exception: Exceptions occur with right parietal lesions which may occasionally make a patient acutely disoriented and confused.[1]

Understanding the critical importance of assessing the level of consciousness, let's look at the flow chart.



NOTE: The terms stupor and coma are not used.

If you approach the patient and he makes (and maintains) eye contact, the patient is alert whether or not he follows commands or speaks. If the patient appears unconscious, first call his name, then gently shake him, and if necessary firmly pinch the belly (not the overlying skin) of the sternocleidomastoid muscle*. If he makes eye

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Sternocleidomastoid Muscle: The prominent muscle running along either side of the trachea.

contact to any one of the above maneuvers, but drifts back into drowsiness, then his highest level of consciousness is 'eye contact.' Remember that we're interested in the highest level of consciousness and more importantly what it took to get him there. So write down that it took painful pinching of the sternocleidomastoid to obtain eye contact, but the patient drifted off into a sleepy state when pinching was stopped. If someone else wants to call that lethargy or stupor, fine. But if two hours later painful pinching only produces undirected thrashing about, you know you've got trouble because the level of conciousness is falling, and unless appropriate steps are taken, may continue to fall. If the patient makes eye contact, but won't follow commands, suspect Wernicke's aphasia or deafness.

Suppose the patient opens his eyes to gentle shaking or sternocleidomastoid pinching but doesn't make eye contact. Determine then if he can converse with you* or follow commands. It's usually helpful to stimulate him a little by moderately slapping one cheek or gently pinching the sternocleidomastoid muscle. Be sure to get next to his ear and yell the commands to overcome partial deafness.

If he still won't follow commands, the next thing you need to know is whether he responds to pain appropriately. Squeeze the belly of the sternocleidomastoid muscle. Does he: 1) try to remove your hand, 2) simply thrash about, 3) demonstrate decorticate posturing, or 4) decerebrate posturing. As a general rule, if the patient can localize painful stimuli, then the pain must have reached the contralateral parietal cortex. If he only thrashes to pain, then the pain only got as far as thalamus where pain is grossly recognized but not localized.

Decorticate posturing is a reflex consisting of flexion of the arms across the chest with extension and stiffening of the legs. Decerebrate posturing is extension, internal rotation, and adduction of both arms with the same leg extension as in decorticate posturing.



DECEREBRATE
(Arm Extended)



DECORTICATE
(Arm Flexed)

The simplest way to view the physiology of decerebrate and decorticate postures is to imagine skimming off the cerebral cortex (decorticate) or removing the entire hemisphere (decerebrate). To determine if the patient's posturing is truly reflex and not semiappropriate, pinch the medial side of the arm. If the arm adducts into a decorticate or decerebrate posture, the movement is reflex because the appropriate

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*Converse With You: Not just talk incoherently, but respond to your questions and commands with appropriate answers.

movement would have been to abduct away from the stimulus. For this reason avoid knuckling the sternum, because decorticate posturing may be misinterpreted as an appropriate attempt to remove the painful stimulus. For the same reason, don't pinch the nipple; besides, pinching the nipple is offensive. Remember, take the time to write down what you did, and what the patient did in response.

If the patient does follow your commands but without making eye contact, get on the other side of the bed because you may be in his hemianopic field. If he still doesn't make eye contact, the patient may be blind, or inattentive, or psychiatrically disturbed. If nothing you do can make him follow commands or make eye contact despite his glancing about the room, the patient may be awake but not alert. Without getting too philosophical, there *is* a difference. Awake means conscious; alert means aware.[3] Awake but not alert is also known as the syndrome of 'the lights are on but nobody's home.' Such states, called apallic states*, usually occur after serious head trauma, hypoxia, or hypoglycemia, and imply severe, diffuse cortical damage that spares the awakening center in the midbrain—the reticular activating system (chapter 22).

CONFUSION

Impaired quality of thinking is called confusion, a broad term used to cover all thinking that the patient would know is incorrect if it weren't for his disease. A patient who can't remember, can't reason, can't calculate, believes he is on fire, hears persecutory voices, believes he should invest in Iranian real estate (and does), sees nothing wrong with child abuse, genocide, indecent exposure or anything else you don't like—is confused.

Be sure you don't mistake Wernicke's aphasia for confusion. Just because someone doesn't make sense doesn't make him confused. His speech may be confused but not necessarily his thinking. Similarly, if you can't make a patient understand what you want, you can't tell if he's confused. Be sure all the patient's words are English before labelling him confused.

Being the most sophisticated accomplishment of Mother Nature, thinking is vulnerable to a slew of disturbances. Simply describing and defining the many nuances of faulty thinking has occupied as much time and effort as understanding their physiology and discovering a treatment. What's the difference between delirium, dementia, disorientation, encephalopathy, delusion, illusion, amnesia, psychosis, and loss of insight, reasoning, or judgment? Before we begin, forget the term 'organic brain syndrome'*; it carries too little meaning. Be specific: is the patient demented, delirious, disoriented, delusional, or amnesic; or has he lost insight, reasoning, or judgment?

Apallic State: Synonyms: coma vigil, persistent vegetative state, akinetic mutism.[4] Some cases of akinetic mutism have been due to thalamic infarctions or potentially curable third ventricular masses.[5]

Organic Brain Syndrome: The new DSM III is excellent at clarifying many different types of cerebral illnesses, but a vague term like organic brain syndrome only begs the question: '*Which* organic brain syndrome?' It's much more meaningful to use the specific diagnosis or at least the clinical findings that led to the diagnosis of organic brain syndrome.

DSM III stands for Diagnostic and Statistical Manual, a compilation and description of all psychiatric disturbances. Without objective laboratory tests to diagnose psychiatric diseases, psychiatrists have compiled descriptive clinical guidelines into a Diagnostic and Statistical Manual. DSM III is the revised, 1980 edition.[6]

Orientation

Let's begin with the simplest term, disorientation. To be oriented you must understand your relation to time, place, and person. I typically ask the patient what time it is, what day of the week, and the date. For place, I ask what floor of the building he is on, the name of the building, and the city we're in. For person, I ask what I do for a living. Orientation to person does not mean he knows his name. A patient who has forgotten his own name isn't disoriented—he's dead and just hasn't fallen over. Orientation to person means the person understands who he is in relation to other people just as he understands his relation to his physical surroundings (place) and to his passage through life (time).

Attention Span

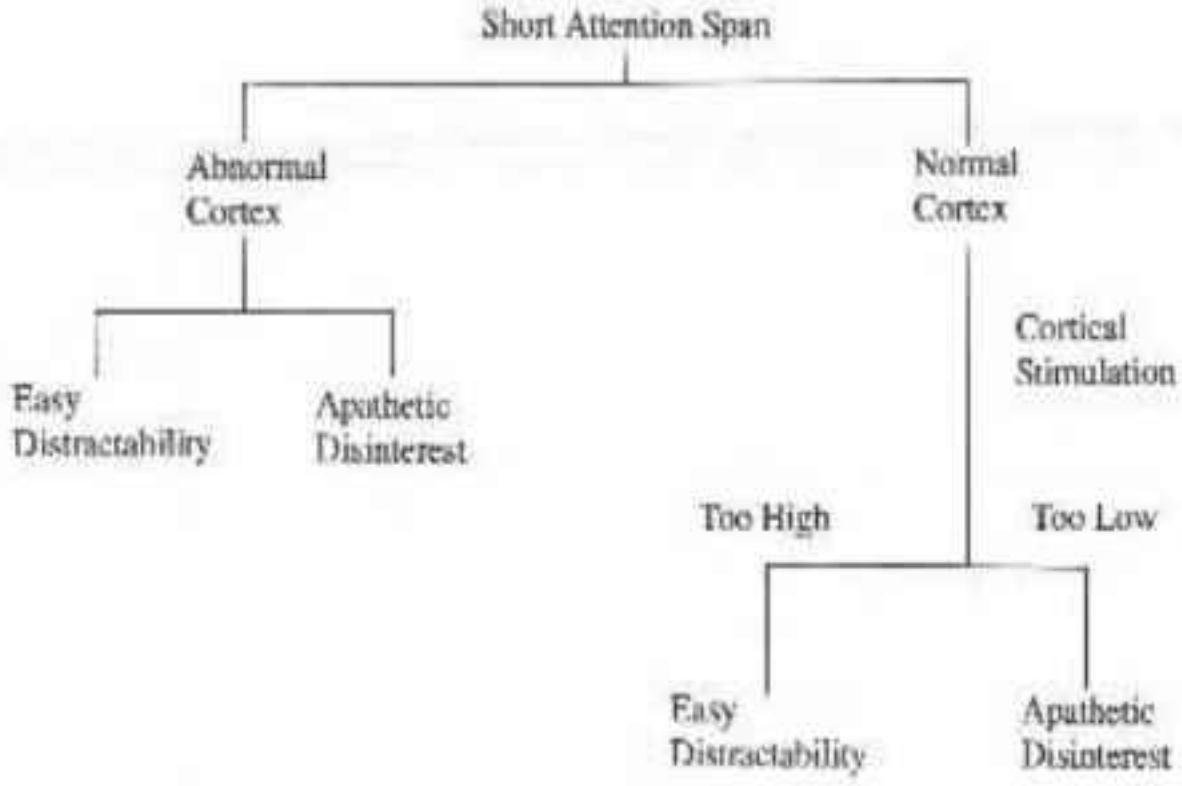
In order to think, the brain must perform four critical tasks: focus its attention, assemble incoming sensations into a meaningful picture, perform logical reasoning, and remember facts. Exactly how we focus our attention is still unknown, but since attention is so fundamental to survival, it seems doubtful that Mother Nature would have waited to invent the cortex before devising a way for animals to concentrate on what they're doing. For this reason the thalamus must be critical for concentration.[7] After all, concentration requires suppressing all distracting sensory stimuli, and what organ is better suited to do this than the thalamus? Except for smell, all sensory stimuli—vision, hearing, touch, pain, temperature, proprioception, and vibration—are screened by the thalamus. The thalamus has the prerogative of sending those sensations on to cortex and consciousness, or of disposing of them without disturbing cortical attention. To serve this role as chief of staff, the thalamus is appropriately situated in the center of the brain, balanced on the ledge of the midbrain at the crossroads of occipital-bound visual fibers and ascending sensory fibers from the spinal cord and brainstem.

In higher animals, the thalamus is undoubtedly under cortical control; the thalamus knows which sensations to pass on to cortex because the cortex has told it which sensations are too important to ignore[8]. Sometimes cortical instructions can be quite strict, demanding absolute concentration, like a wounded soldier suppressing the pain of a bullet until he is safe[9].

A short attention span is a common and very important sign of cortical dysfunction. The attention span may be short for one of two reasons: easy distractability or apathetic disinterest. Easy distractibility may, in turn, be due to a widespread lesion of the cortex, like senility, or to bombardment of a hopped up cortex as happens in drug withdrawal. Apathetic disinterest may also reflect intrinsic cortical damage, or a normal cortex suffering from inadequate charge, like depression or hypothyroidism. Looked at another way:

Too Important To Ignore: A very complex issue is: what cortical area directs our attention? And what information does that cortical area use to make its decision?[5]

Safe: Another explanation for the absence of pain during stress is that the pituitary releases both ACTH and a large polypeptide, beta-lipotropin. Sections of beta-lipotropin, called endorphins, are known to inhibit pain. Interestingly enough, ACTH and beta-lipotropin are both found in the same pituitary cells.[5] The adrenal glands also contribute to stress analgesia by secreting endorphins.[10]



If you find yourself getting angry at a patient because he won't pay attention or won't cooperate, stop what you're doing and look at his attention span. If the patient can't focus his attention, is it because he's easily distracted or apathetic? And is that because of something wrong with his cortical engine, or with the accelerator? Look for the absence of confusion to separate out those patients whose normal cortex is being over or understimulated.

Memory

Besides concentrating, the brain must remember. Loss of past memories is called retrograde amnesia; the patient cannot remember past events, usually the events of a specific time period. But that is all. The patient can still construct the world around him using memories learned prior to the amnestic period. He knows what a blanket is for, how to use a TV or radio, how to use money, take a shower, and flush a toilet. Retrograde amnesia often occurs after head trauma when the patient may not recall the accident itself or the events hours to days before the accident.[11]

Anterograde amnesia, in contrast, is an inability to lay down new memories. When told where he is, the patient won't recall when asked just a few minutes later. In both anterograde and retrograde amnesia the patient may or may not be aware of his memory impairment. If, however, the patient begins to make up stories to cover his memory loss, that is, to restructure his past and present world to compensate for his memory loss, he is confabulating.[12] This misrepresentation of reality is called Korsakoff's psychosis[13]—confabulation with retrograde and striking anterograde amnesia—after Sergei Korsakoff, one of the founders of Russian neurology, who described this condition in the 1880's.

Some of the strongest evidence that the temporal lobe is intimately connected with memory rests on a now famous case operated upon by Dr. Wilder Penfield in the 1950's. This unfortunate patient underwent a unilateral temporal lobectomy for removal of an uncontrollable seizure focus. Unbeknownst to Dr. Penfield, the patient was born with a useless, vestigial hippocampus (and surrounding tissue) on the

opposite side. From that operation until his death years later, the patient was virtually unable to learn new facts, though he retained nearly everything he knew prior to surgery*.[18]

A similar experiment of Nature continues to occur today—called transient global amnesia.[19] Generally older folks, these patients are suddenly disoriented about who they're with, where they are, why they're there, and what date it is. Even when told the answers, they repeatedly ask the same questions since they are unable to remember your answers for more than about fifteen seconds. No one knows the exact cause of this striking clinical picture because these patients recover after several days, but a good bet is that both hippocampi are temporarily on the fritz either because of ischemia* or focal seizure activity in both temporal lobes.[20]

Just as recent memory loss predominates in the acute situation of transient global amnesia, so it does when the patient *gradually* loses his ability to lay down new memories. The patient may describe his World War I experiences in painful detail, but can't tell you what he had for dinner last night. Far and away the most common illness causing a slowly progressive recent memory loss and inability to lay down new memories (i.e., to learn) is Alzheimer's disease, named after Alois Alzheimer, another of the great German neurologists and neuropathologists at the turn of the century.

The brains of patients with Alzheimer's disease reveal specific microscopic changes most severe, not surprisingly, in the hippocampi and neighboring temporal cortex.[21] Though we accept recent memory loss as a natural concomitant of old age, virtually all demenating grandparents show the same microscopic changes of Alzheimer's disease, changes which are absent in old people with normal intellect. The dementia of old age is not due to 'hardening of the arteries' (atherosclerosis) or lack of oxygen, but instead to the physiologic consequences of the microscopic lesions described by Alzheimer. More importantly, these same Alzheimer changes are also seen in young people (less than 65 years) who begin to lose their memory to a descriptive illness called presenile dementia, which is nothing more than early Alzheimer's disease.

What, then, is the difference between amnesia and dementia? If a person cannot recall past events and cannot retain new ones (retrograde and anterograde amnesia), isn't he demented? Not exactly. Dementia implies dysfunction of a person's entire intellect, and memory is only one part of intellect. Memory is nice, but not necessary; insight, reasoning, and judgment play a more important role than memory in keeping us out of chronic care facilities. Who, what, where, and when questions may tap memory, but how and why questions get you into the patient's intellectual network. Who were the Democratic presidential candidates for 1984? assesses memory, but why Mondale should have been elected requires reasoning, judgment and rationalization—abilities lost in dementia but not amnesia.

Prior to Surgery: One of the major arguments against the temporal lobe playing a role in memory is that almost all cases of Korsakoff's psychosis share a common denominator—bilateral lesions in the dorsal medial nucleus of thalamus.[16] Other examples of thalamic lesions (besides alcohol) causing amnesia have also been described.[17] Thalamic lesions causing amnesia are far more likely to result in confabulation than temporal lobe lesions.[18] See reference 17 for the differences between thalamic and temporal lobe amnesia.

Ischemia: For an explanation of how a single artery, the basilar artery, can account for bitemporal dysfunction, see chapter 31.

Reasoning and Judgment

The difference between reasoning and judgment is subtle. Reasoning is the ability to arrive at a conclusion when all the facts are known, by linking (i.e., reasoning) disparate facts into a composite solution. Judgment, on the other hand, is the ability to arrive at a conclusion when all of the facts are not known*. It means taking fact A and fact B, inserting an indefinite probability factor based on your cultural background, past experiences, and current emotional feelings, and then reasoning this mixture of known and unknown facts into a composite solution. You *reason* out a problem when there are one or more clearly correct answers. You *judge* the answer to a problem when there is no correct answer, only an answer that's correct for you. For example, in planning a trip, you may correctly reason that it will take six hours to travel from point A to point B traveling forty miles per hour. But judgment tells you to plan eight hours because you may run into some unforeseen complication.

Another aspect of judgment not fully shared by reasoning is deciding when to act. Your ability to judge the unknown factor—in this case, the *consequences* of your actions—guides your decision to hesitate or act. Social graces, financial decisions, driving a car, home care—virtually any action which promotes a person's well-being—requires good reasoning, but deciding *when* to act requires good judgment. The fellow who sees his boss' wife as coarse, overbearing, obtrusive, and demanding may reason correctly that she's an obnoxious pain, but more importantly, good judgment tells him to keep his mouth shut.

The reason to distinguish reasoning from judgment is that reasoning seems to be a diffuse cortical function—all areas of cortex participate—while judgment seems to be a more specific frontal lobe function. People without normal frontal lobes (both frontal lobes must be involved), besides being confused, lose the ability to judge, or care about, the consequences of their actions—about their fate. Their behavior falls into one of two general categories: they're either apathetic or impulsive*.[22] The impulsiveness may take the form of poor business decisions, verbal abuse, inappropriate humor, or any other impulsive behavior unleashed by poor judgment.

It is often difficult to test judgment and reasoning in a formal mental status examination. Questions which assess intelligence often upset a patient and injure your supportive relationship with him. He stops seeing you as someone trying to help, but rather as an inquisitor. To avoid this, try to assess the patient's intellect without corraling how and why questions into a formal mental status exam. Instead, during the history-taking, engage the patient in a conversation. Inquire into the patient's work and home life. Pretend you're sitting next to him on an airplane, and try to find something the patient is interested in—a hobby, a news event, sports. To test his memory, ask him non-threatening who, what, where, and when questions you feel he should know (and to which you know the answers!). Then slip in some how and why questions to test his reasoning and judgment. Ask him what's been the biggest change in America since he was a young boy. What things have stayed the same? What does he see as the biggest problem facing America today? You may disagree, you may

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Not Known: Being able to decide questions without all the facts is why the Judge is called the Judge.

Apathetic or Impulsive: Apathy and impulsiveness without confusion are usually not due to bifrontal dysfunction. More often than not, isolated signs of apathy or impulsiveness stem from emotional upset, stress, or disturbances of motivation and personality.

learn something, but you'll almost always enjoy the response. Ask him what his plans are once he leaves the hospital. His answer, which depends on insight, may surprise you by its lack of judgment.

Other tipoffs to loss of judgment are impulsive or discourteous behavior during the interview. Also, dementing patients, losing their insight, often think everything is just hunkey-dorey ('you worry about the patient who doesn't'), but many patients with early dementia, realizing their faculties are slipping, are understandably irritable* and depressed. Dementing patients often look apathetic and dull, failing to initiate conversations, make eye contact, or even make their wants known.

Forgetfulness for recent events alone is not dementia (I hope not) unless accompanied by disorientation, faltering calculations, impaired reasoning, impaired judgment, and lack of insight. But when forgetfulness for recent events merges into forgetfulness for immediate events (i.e., inability to learn), you can bet that other signs of dementia won't be far off.

Mental Status Exam

By the time I get through the history and arrive at the mental status exam, I pretty well know the patient's intellect. Attention span, eye contact, quickness of responses*, insight, sense of humor,[23] memory for dates, events, doctors' names, laboratory tests, treatments, how and why questions about his illness or his job, and current news events—all contribute to my assessment. Unfortunately, my impression of the patient's memory, judgment, and reasoning, is just that—an impression, and fair recall for one doctor is poor recall for another doctor. Understandably, we generally frown on a Barry Goldwater approach to medicine ('I know in my heart the patient's memory is okay'). The upshot is that more or less standard bedside mental status tests are used, so that everyone can look at your patient's responses and judge them against their own experience with intellectually normal patients.

The memory part of the mental status exam is divided into anterograde, immediate, recent, and remote memory, and then general information. Immediate memory means asking the patient to repeat a telephone number forward and then four or five numbers backwards. Anterograde means giving the patient three things to remember, engaging him in other tasks, and asking for the three items several minutes later. Recent memory is assessed by asking the patient when he came to the hospital, what tests he has had, recent news events, etc. Remote memory I do not often test because it is the last thing to go in dementia. The final area of memory is general information—items which may have been learned years ago, but which are periodically refreshed. This is generally assessed by having the patient list the Presidents backwards and describing how each came into office.

Irritable: For this reason, don't get offended by brusque, rude remarks. You may be overlooking an important clue to the patient's illness.

Quickness of Responses: It's easy to overlook sluggish responses if the answers come out correctly, but pay attention to dullness. Does your question seem to rattle around the patient's brain before being processed into a response? In my experience, dullness without confusion often signifies compression of the brain (meningioma, subdural hematoma, hydrocephalus, etc.) rather than destruction or degeneration of brain parenchyma.

The hardest part about making a diagnosis of early dementia is not assessing a patient's intellect, but convincing yourself that his present intellect represents a decline from six months ago. You either have to judge that the patient's intellect is worse than expected, or seek historical help from friends and relatives. A perceptive wife is often worth a roomful of neuropsychologists; ask her if her husband is the same person she married.

Confusional States

The term dementia refers to chronic confusion, typically longer than three or four months. Less than about four months the patient is *becoming* demented, or else suffering an acute or subacute confusional state. Dementia does not imply irreversibility. Surgical removal of a longstanding frontal lobe meningioma, for example, may reverse a patient's failing intellect.

Many of the labels for confusional states revolve around the presence of agitation. For example, an agitated confused patient is called delirious or 'encephalopathic.' If the etiologic agent is a known exogenous toxin or drug, the diagnosis is further refined to toxic encephalopathy or toxic psychosis. If the etiologic agent is due to internal organ failure, like lung, heart, liver, or renal failure, the confusional state is then called metabolic* encephalopathy.

Delirium is an acute confusional state whose hallmarks are a short attention span, agitation, and fluctuating level of awareness.[34] Driven by agitation, the patient's eyes and thoughts scurry about the room, distracted by everything around him and harassed by internal stimuli darting into his mind. Unable to rivet his attention on your questions, he is disoriented, amnestic (both retrograde and anterograde), irrational, and hallucinatory. Wildly misinterpreting sensory information, he may, for example, carry on a telephone conversation if he hears the TV, or misinterpret paresthesias as ants crawling on his skin. The delirious patient is wide-eyed and tremulous, easily startled, incoherent, barely in control of his sympathetic nervous system* speeding along in fifth gear overdrive.

Metabolic: Due to an imbalance of a chemical normally found in the body (i.e., not an exogenous toxin).

Sympathetic Nervous System: Together the sympathetic and parasympathetic nervous systems comprise the 'autonomic nervous system,' an entire nervous system anatomically separate from the voluntary one. Autonomic nerves devote themselves to silent, involuntary bodily concerns: temperature regulation (shivering, sweating), heart rate, blood pressure, salivation, pupillary adjustment, gut movement, and erections. Stimulation of the sympathetic half of the autonomic nervous system prepares you for stress. Parasympathetic nerves take over during pastoral activities like grazing in the kitchen, relaxing in front of the tube, reading a book, and the like.

PSYCHIATRIC DISTURBANCES

Psychosis

Psychosis is a disturbance of thought and behavior, severe enough to prevent a patient from functioning in society. Psychotic thinking is characterized by delusions, hallucinations, and loosening of associations.

Delusions commonly cluster into delusions of persecution, delusions of reference (that, for example, the TV is talking about him), and delusions of control (thoughts and emotions are being inserted, broadcast, or removed from his body). Any preposterous idea, however, may qualify as a delusion, as long as the patient is the only one who believes it.

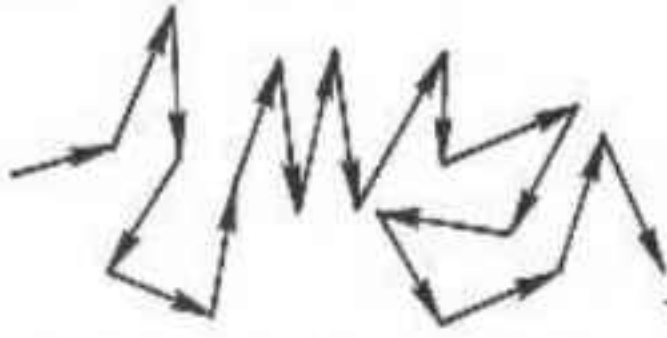
Hallucinations are sensory perceptions—auditory, visual, tactile (touch), or olfactory—felt by the patient, but he's the only one in the world who believes he felt them. Why delusions and hallucinations occur is, of course, unknown, but they are quite real to patients, so real that no amount of logic can sway a psychotic from what he knows to be true. He feels and senses his 'reality' with as much intensity as you or I feel the wind blowing in our faces.

Loosening of associations, or worse, flight of ideas*, may be seen in either mania or schizophrenia.[25] What do you suppose is happening inside this patient's mind when her conversation loses normal associations and logical, sequential thought?

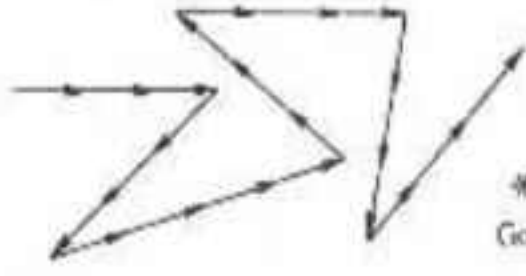
Flight of Ideas: Pictorially, flight of ideas—the loss of logical connections between thoughts—may be depicted as:



Circumstantial thought—excessively detailed inclusion of irrelevant details which obscure the main point (grandma does this a lot)—looks like this:



The following would be tangential thought. Instead of completing an idea, the patient takes off on another subject brought to mind by something he just said:



"I'm a doctor, you know. I don't have a diploma, but I'm a doctor. I'm glad to be a mental patient, because it taught me how to be humble. I use Cover Girl creamy natural makeup. Oral Roberts has been here to visit me. My sister's name is Joyce Frumkin, and I like her. My father is five feet two inches, my mother is five feet three inches. They're like Napoleon and Josephine, and they're shrinking. Joyce is five-two. I'm only five foot four and I'm the tallest one in my family. This place is where Mad magazine is published. The Nixons make Noxon metal polish. When I was a little girl, I used to sit and tell stories to myself. When I was older, I turned off the sound on the TV set and made up dialogue to go with the shows I watched. The people in Creedmoor are Hobbits. I dictated the Hobbit stories to Tolkien, and he took them all down. I'm the Hobbit. Ask John Denver. He told me I was. I'm the only person who ever got Ringo Starr angry. All the trouble started when my father decided to move from Brooklyn to Queens when I was seven. I went to the eleventh grade twice—once at Music and Art, a public school for gifted musicians and artists, and once at a private school. Jesus told me he was born nineteen hundred and seventy-three years ago. He's my best friend. I call him J. C. I was unhappy at school because I was bad in gym. I was unhappy at school because I was only friendly with the underdogs. I had a car accident when I was fifteen. After that, my mother said, my eyes were never the same. My mother's the real dictator. My grandmother left me all her money. I was named for my grandfather Saul, who died five years before I was born. He was born on Easter Sunday. I'm a week pregnant. I have schizophrenia—cancer of the nerves. My body is overcrowded with nerves. This is going to win me the Nobel Prize for Medicine. I don't consider myself schizophrenic anymore. There's no such thing as schizophrenia, there's only mental telepathy. I once had a friend named Camilla Costello. She was Abbott and Costello's daughter. She said to me, 'You know, Sylvia, I have a lot of friends, but you're my best friend.' I'm working here. I'm an interne at Creedmoor. I'm in the Pentecostal Church, but I'm thinking of changing my religion. I have a dog at home. I love instant oatmeal. When you have Jesus, you don't need a diet. Mick Jagger wants to marry me. I want to get out the revolving door. With Jesus Christ, anything is possible. I used to hit my mother. It was the hyperactivity from all the cookies I ate. I'm the personification of Casper the Friendly Ghost. I used to go outside asking the other kids to be my friend when I was little. California's the most beautiful state in the Union. I've been there once, by television. My name is Jack Warden, and I'm an actress."[26]

Talking to psychotic patients for the first time is a strange experience indeed. Sometimes it's humor, sometimes fear, but always a sense of bewilderment at the breakdown of a mind. How do you approach someone who is convinced that snakes are slithering through his intestines, or that acquaintances are plotting against him and a preemptive murder is his only defense? I remember one patient referred in because he was nervous—he felt his fellow workers were "hassling me." I said to myself, big deal, until he said "I am going to have to kill them." At that point I knew he was crazy. After the psychiatrist saw him, I asked the psychiatrist how he knew the patient was psychotic. He replied that he knew the patient was crazy because "I kept looking at the door to make sure I could get out of the room if I needed to." It was an interesting answer, showing that psychiatrists monitor their own feelings as well as the patient's, but the answer provided no guidelines to follow, no logical method to dissect disturbances of thinking.

In assessing a thought disturbance, psychiatrists first decide if the thinking problem is cognitive (orientation, memory, calculations, insight) or psychotic (delusional, hallucinatory). If psychotic, the next question is whether his psychotic thinking has an organic cause (structural, chemical, or drug-induced) or a functional one (no known

cause, i.e., crazy). In other words, psychotic thinking is not synonymous with functional psychosis. Psychotic thinking is only a sign of disordered thinking which may be due to organic etiologies. A person can only be labelled psychotic after organic causes of psychotic thinking have been ruled out*.[27]

The linchpin in the search for functional psychosis is the patient's memory. If you can demonstrate faulty memory or disorientation, organic instigators lurk somewhere offstage*.[29] Your assessment of the patient's memory should crystallize as you determine how the patient arrived at his ideas. Trace the patient's reasoning back to its source. Why did he say this and what makes him say that? To be functionally psychotic the patient should be able to recall with a clear sensorium the circumstances which led him to his current (faulty) thinking. The clear sensorium is very important—a patient whose attention span is too short (delirious) or who is too depressed to carry on a mutual conversation cannot be called functionally psychotic.

If, by your exam, the patient has taken correct memories and proper observations, and then distorted them into a bizarre construct, he is functionally psychotic. He should be able to tell you when he began to feel this way, where he was, what he was doing, and why he arrived at his present reasoning. If, however, the past is confused for the patient, if the basic building blocks of memories are incorrect, then the subsequent bizarre construct suggests an organic etiology.

For example: suppose a patient thinks his hospital room is a jail cell. Is that a psychotic delusion or a confusional state? Trace his reasoning back to its source. Was his reasoning based on an incorrect memory or observation (organic) or misassembled from correct memories (functional)? If he thinks the room is a cell because he cannot account for the last three weeks when he was freed from jail, he is organically confused. What if he thinks the room is a cell because he thinks people in white uniforms are policemen? Now is he psychotic? Keep following his ideas. What makes him say that people in white are policemen? If voices told him, he is functionally psychotic. If he thinks policemen's uniforms are normally white, he is confused and the subsequent delusion (jail cell) stems from an original incorrect memory. If he can't tell you when he began to think his hospital room was a jail cell, why he is in a jail cell, how long he has been there, and what events have taken place in his jail cell, then his confusion is organic. His subsequent treatment is based not on the nature of the confusion, but on the cause of the confusion which will hopefully yield to your investigation.

In short, when someone's thoughts appear confused, trace back the patient's reasoning at the same time keeping tabs on his memory of past events, his present orientation, and his ability to focus his attention enough to maintain a conversation with you.

Ruled Out: For this reason, when patients present with acutely psychotic thinking I tend to blur the distinction between cognitive and psychotic thought disorders. Instead, I simply say the patient is confused and get right into the organic/psychotic etiology question. After all, the acute treatment is usually based on the etiology of the faulty thinking, not the faulty thinking itself—unless the patient is so uncontrollable that he needs temporary sedation. For example, amphetamine can impair memory (cognitive thinking) or precipitate delusions (psychotic thinking), but unless the patient is speeding his little heart out, screaming, taking off his clothes, or otherwise a danger to himself or others—in which case he needs sedation—the definitive treatment is withdrawal of the amphetamines.

Offstage: Though memory is supposed to be intact in functional psychoses, it probably isn't perfect.[29]

Schizophrenics* may display two other important features besides delusions and loosening of associations: withdrawn behavior and blunted affect. Preoccupied with their own private, delusional world, they shelter themselves from social contacts. Also, the content of their conversation fails to match the emotions projected between the lines. They may laugh when discussing something sad or be blank when discussing something emotionally moving.

Depression

Like other psychiatric signs, disturbances of mood and affect reflect bihemispheric dysfunction*. Mood refers to the background spirits from which affect stands out in relief. Affect is the immediate feeling in response to a specific stimulus—"How do you feel about. . . ." "How've your spirits been?" reaches for the patient's mood. Depression and mania are the two most important disturbances of affect and mood.

Depressives are listless, without spark and spontaneity; they speak in a soft monotone, do not make eye contact, and will often admit to depression if asked about their feelings. Once in a while, the psychomotor retardation that accompanies severe depression can be severe enough to be mistaken for dementia.[31] Ask directly about poor appetite, insomnia, early awakening, crying, being withdrawn, feelings of inadequacy, worthlessness, or guilt. Does he have any interest in a satisfying hobby?

Mania

Manic patients are simply a joy to interview. One manic fellow came to clinic wearing a T-shirt emblazoned with: "I'm Hell when I'm well, and I ain't never been sick." They're effusive, optimistic, buoyantly self-confident, enthusiastic, talkative to the point of irritation, and unable to sit still. But their whole manner is hollow. They're skating, not plowing. Manic patients dash helter-skelter from one idea or task to another without foresight or planning. Their thoughts and actions are grossly impractical and unproductive. Nevertheless, their enthusiasm, self-confidence, and exhilaration are comical if not infectious.

Psychiatric History-Taking

Eliciting a history from psychiatric patients differs considerably from neurologic and medical history-taking. While psychiatric history-taking may be a hearty challenge to some doctors, it is a frustrating irritation to others. The patient may, for example, want to hide certain symptoms if he feels you're going to use his answers against him. In fact, his paranoid suspicions may resist *whatever* direction your questions want to lead. A psychiatric patient may frequently have no insight into his problem, or be so depressed that he cannot even relate a history. Also, in internal medicine the facts of the case assume primary importance; in psychiatry, and to some extent neurology, the *manner* in which the facts are related is as important as the facts themselves. Psychiatric interviewing usually requires broken field pursuit of the patient's thoughts. You simply cannot expect a straightforward recitation of symptoms from emotionally disturbed patients.

Psychiatric disturbances of thought and feeling become truly serious when they interfere with a patient's behavior to such an extent that he has trouble holding a job or

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Schizophrenia: Schizo(split) phren(al mind).

Bihemispheric Dysfunction: Significant depression can also accompany left hemispheric strokes.[32]

establishing and maintaining relationships. This, then, is the thrust of your history-taking—trying to decide when craziness really counts. Exactly how does the emotional problem disrupt your patient's job and home life? Is it because of hallucinations, delusions, paranoid ideation, depression, hypochondriasis, or frequent run-ins with the law? To get at this information, keep in mind that you must not only gain the patient's confidence with straightforward, non-threatening questions, but must also pay particular attention to the patient's choice of words. Your questions will frequently be requests for clarification and amplification of a phrase or tone of voice, or even a facial expression.

With these thoughts in mind, a typical psychiatric history might include the following questions:

"Hello. I'm Dr. So and So. Are you Mr. Wilson?"
"Where are you from?"
"How old are you?"
"What do you do for a living?"
"Are you married? First time?"
"Do you have children?"
"Who lives with you at home?"
"Do you smoke?"
"Do you drink?"
"Do you take any medications?"
"Do you take any unprescribed medications or drugs?"

These introductory questions tell you how the patient is functioning in society and, being relatively non-threatening, help gain the patient's confidence.

"Tell me about the problem you've been having."

As you listen now to the bulk of the psychiatric history, follow up the patient's responses with clarification and amplification questions while focusing on hospitalizations, treatments, and whether the problem has interfered with the patient's job and home life. Has the problem disrupted his life because of distorted perceptions or severe mood aberrations?

If the following points haven't yet been raised, ask them now in a neutral, non-threatening manner, as if you expected each answer to be "yes."

(Mood)
"Do you ever have periods of unbounded energy?"
"Do you ever get low?"
"Have you ever thought about ending your life?"
"Has anyone in your family ever taken their life?"
"Is there anyone in your family with a nerve problem?"
"How is your eating? Sleeping? Any weight loss?" (vegetative symptoms)

(Delusions)
"Have voices been talking to you or about you? Does the TV have special meaning for you?"
"Are you seeing things?"
"Are you religious? Have you had any very religious experiences?"
"Do people plot against you? Are you afraid to be around people?"

(*Neurotic Hypochondriasis*)
"How is your physical health?"

(*Psychopathic Personality*)
"Have you ever been arrested?"

(*Organic*)
"Have you had any trouble with your memory?" At this point, do a neurologic mental status exam of speech, Gerstmann's area, right parietal lobe function, memory (anterograde, immediate, recent, general knowledge), judgment and insight.

NON-FOCAL SEIZURES

Turning away from psychiatry, another important pathognomonic sign of cortical dysfunction is a non-focal seizure, a seizure which, judged by your history or direct observation, begins without a focal cortical onset*. Such a 'generalized' seizure might begin with a cry or sudden collapse to the floor, or simply a fluttering of the eyelids, none of which can be attributed to a specific area of cortex.

Though not *clinically* focal, non-focal seizures are probably *electrically* focal in onset, often demonstrable by electroencephalography. Instead of discharging into neighboring areas of cortex to produce focal symptoms, the cortical epileptic site probably projects the discharge rapidly across the corpus callosum to produce a nearly synchronous electrical discharge in both hemispheres.[15] Even though generalized seizures do not direct your attention to a specific area of cortex, they are still a terribly important sign of cortical dysfunction*. Petit mal seizures may be the only exception to the rule that *all* seizures begin in the cortex; petit mal seizures may actually originate in a deep gray matter structure like the thalamus*.

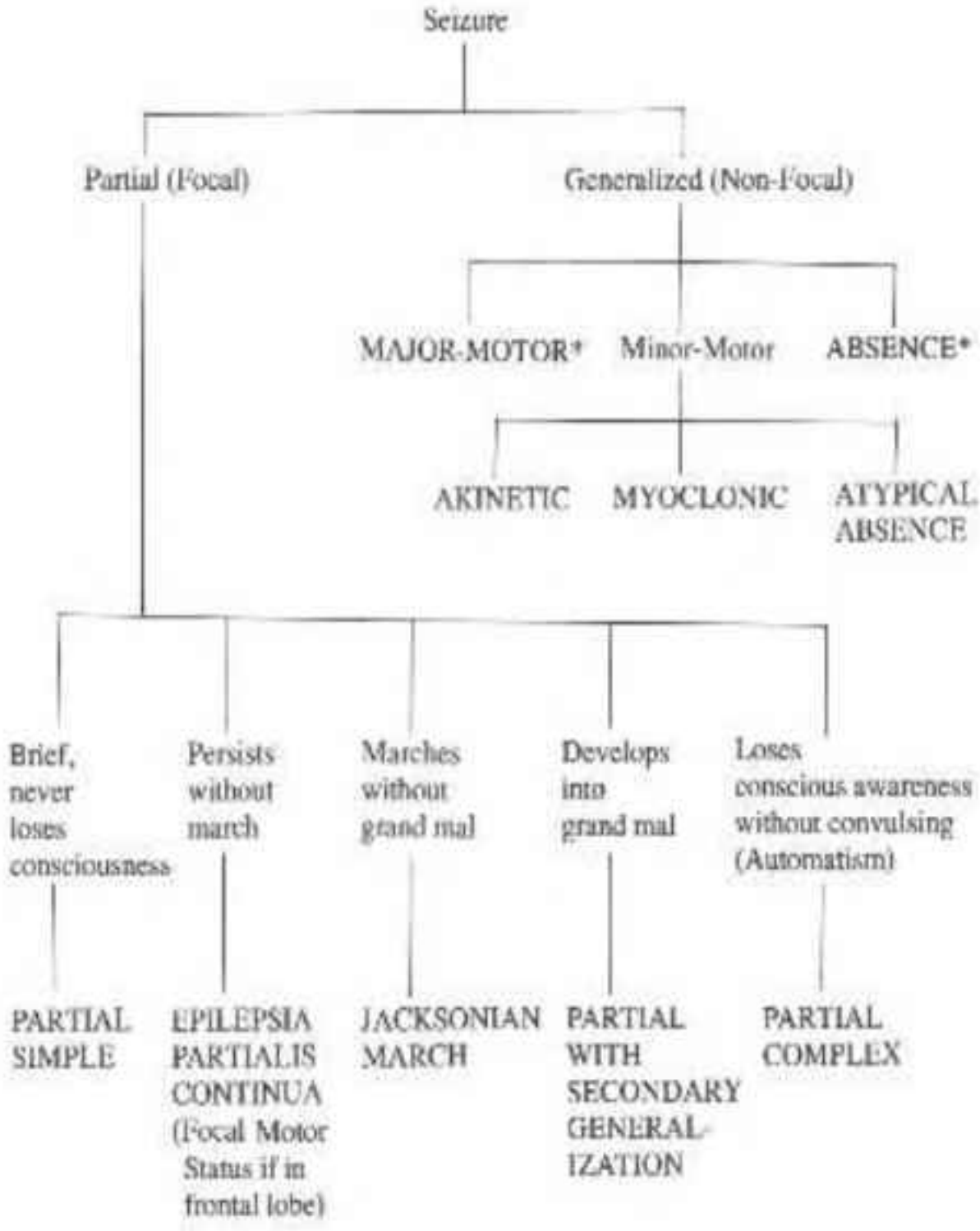
A focal, or 'partial,' seizure may originate from any cortical area. Your job is to listen to the patient's or family's description of the seizure and determine from which focal area of cortex the seizure began. The entire classification of seizures is a little confusing because seizures are classified by their clinical, not their physiological, behavior.[16] Say, for example, the patient has a right frontal abscess. You *know* his seizures begin focally from around the abscess, but unless you uncover focal symptoms (a sense of fear, left hand paresthesias) or signs (twitching of the left thumb) at the onset of the seizure, you have to label the seizure a non-focal one, at least clinically non-focal.

Without a Focal Cortical Onset: In the old days focal seizures meant a long and painful search for focal cortical pathology, like a tumor or arteriovenous malformation.[12] But since non-focal seizures may also be caused by focal pathology, even non-focal seizures should prompt a search for focal pathology (not everyone agrees[13]). Cat scans should especially be done if the seizures are of recent onset, the neurologic exam is abnormal, or the EEG shows focal slowing.[14]

Also worrisome are seizures that worsen clinically, either involving more and more of the body, or requiring more and more anticonvulsants to control. Such seizures suggest an evolving structural lesion like a tumor or arteriovenous malformation.

Cortical Dysfunction: Though seizures are a gray matter event, lipomas of the corpus callosum—a white matter lesion—may also cause seizures, presumably by undercutting and isolating islands of highly excitable cortex.[15]

Thalamus: Some epileptologists feel the cortex is still the structure at fault in petit mal seizures; a normal cortex wouldn't allow itself to be discharged.[17]



A partial seizure that remains partial without clouding of consciousness is called a partial *simple* seizure. (Simple means there was no clouding of consciousness; complex means there was.) If a seizure begins focally, but evolves into a generalized convulsion, it's called a focal seizure with secondary generalization. If a seizure produces continual jerking of one set of muscles without evolving into a convulsion, it's called epilepsia partialis continua or focal motor status*. If the seizure begins focally in the temporal lobe (as a foul odor, emotion, or forced memory), but develops into an automatism with clouded consciousness, it's called a partial complex seizure.

Major-Motor Seizures: Also called Tonic/Clonic, Grand Mal, or Convulsive Seizures.

Absence Seizures: Absence seizures are true Petit Mal seizures.

Status: A continuous state of seizure activity.

Generalized seizures begin with either loss of consciousness or, on occasion, bilaterally symmetrical motor signs, bypassing the focal signs and symptoms of a focal (partial) seizure*. A generalized seizure may be: 1) an abrupt tonic-clonic*, major motor convulsion, 2) a brief spell of eye-fluttering absence (loss of consciousness without falling), 3) a sudden loss of all body tone plummeting the patient to the floor (akinetic drop attack), or 4) a sudden, lightning-fast myoclonic jerk of a limb or, more commonly, the trunk.

As depicted in the seizure chart, there are two kinds of absence seizures: petit mal ('typical') and minor motor ("atypical"). The distinction between them is both a clinical and an electroencephalographic one. Petit mal seizures begin in childhood and consist of a brief spell of loss of consciousness—the child suddenly stops talking and flutters his eyelids, but he immediately picks up where he left off without postictal confusion or sleepiness. You should be able to elicit a petit mal seizure by having the child deeply hyperventilate for three or four minutes. An attached EEG will demonstrate abrupt, high amplitude, synchronous, bifronto-central, three per second spike and wave discharges. In about 80–90% of otherwise normal children, petit mal seizures disappear by age twenty. The remaining 10–20% continue to have petit mal seizures or develop grand mal seizures.[47]

An atypical absence attack can mimic a petit mal attack, except that atypical absences occur primarily in retarded children. Unlike true petit mal, atypical absences are not exquisitely sensitive to hyperventilation, nor do they demonstrate the three per second spike and wave discharges of true petit mal seizures. The EEG may reveal, for example, two per second spike and wave or perhaps a run of bihemispheric polyspike activity.[48]

Focal (Partial) Seizure: Dilantin (phenytoin), phenobarbital, and Tegretol (carbamazepine) are all first-line drugs for local and generalized major-motor seizures.[39] No one drug is more effective than another; the choice should depend on toxicity and compliance (adherence to treatment). Valproate is also useful in generalized seizures but, so far, only a second-line drug for focal seizures.[40]

Dilantin is particularly useful because it can be given once a day which improves patient compliance.[41] Phenobarbital can also be given once a day, but as single drug therapy, phenobarb tends to make patients drowsy and dull.[42] Tegretol and Valproate are excellent drugs for patients reliable enough to take medications two to four times a day.

It's probably best to begin with one anticonvulsant and slowly increase the dose until one of two things happens: either the seizures become controlled or side effects intervene.[43] Increasing the Dilantin dosage too quickly may suddenly saturate the liver's ability to metabolize Dilantin, resulting in a rapid rise in the serum Dilantin level and subsequent intoxication.[44] Because of its long half-life, Dilantin can be gradually increased by having the patient take an extra capsule every other day (the odd number of capsules on the odd days of the month, even number of capsules on the even days).

Drug levels are helpful, particularly if the seizures cannot be controlled or slip out of control. One mnemonic to remember the blood levels by is that the childhood DPT immunizations (diphtheria, pertussis, tetanus) also stand for Dilantin, Phenoburb, and Tegretol, and their respective blood levels range from (you'll have to provide the decimal point depending on whether your lab reports in ug/ml or mg%): 10–20, 20–40, and 40–80. Try to get Tegretol as close to 8 mcg/ml as possible, and even up to 12 mcg/ml when prescribing Tegretol alone.[45] Valproate levels fit into the mnemonic at 50–100 mcg/ml.[46]

Tonic-Clonic: Tonic means stiffening. Clonic refers to the jerking. Tonic-clonic seizures (convulsions) are alternating phases of jerking and stiffening of the trunk and limbs.

Absence spells also occur in adulthood, but some neurologists' temples bulge if you call anything but true petit mal an absence seizure. Strictly speaking, an absence seizure means petit mal, but clinically similar attacks occur with either brief temporal lobe seizures, too brief to blossom into a ripe automatism, or brief bursts of bifrontal seizure activity.[49] In general, petit mal absences differ from temporal lobe seizures in the following ways: no aura, more easily elicited by hyperventilation, briefer in duration, less complex automatisms, no postictal confusion or sleepiness, and most importantly, bifrontal three per second spike and wave discharges during the petit mal spell.[50]

BILATERAL OCCIPITAL LOBE SYNDROMES

Focal cortical pathology in *both* occipital lobes produces a highly characteristic syndrome of 'cortical blindness:'[51] the patient is obviously blind, but denies it.* The pupils remain reactive to light because neurons mediating the pupillary light reflex (chapter 20) depart the optic tracts before any visual fibers reach the occipital lobes.

Prosopagnosia is a rare syndrome of the occipital association areas. The patient is unable to recognize a once familiar face (like a family member's), but can instantly identify the person by the sound of his voice.[52]

CORTICAL RELEASE SIGNS

Cortical release signs, also pathognomonic of bihemispheric (specifically, bifrontal) dysfunction, resemble cute things that infants do, but which are lost as the maturing cortex suppresses them. When a patient's cortex begins to skid, these primitive signs are no longer inhibited. For example, if you place something in an infant's lips, he immediately puckers and sucks: same for the demented adult when his lips are stroked or tapped. You can pick up an infant off a bed simply by putting your fingers in his palms and pulling. This involuntary grasp* of the infant mimics the involuntary grasp of an adult whose cortex is deteriorating.[53] There are a number of other cortical release signs, but the suck and grasp reflexes are the most reliable predictors of bifrontal impairment.[54]

Denies It: Though no one knows the true site of Anton's syndrome, the lesion is speculated to extend from primary occipital cortex (area 17) into visual association areas (area 18 and 19) where images are probably assembled into meaningful three-dimensional shapes.[52]

Lesions downstream from the visual association area that deny us access to previous memories (and their emotional connections) prevent us from recognizing an object - knowing how it works, whether it's dangerous, comforting, useful, or amusing. This condition is called visual agnosia.[52]

Grasp: Occasional stroke patients demonstrate a variant of the grasp reflex called cortical thumbing, a normal infant hand posture which is lost at about three to four months as the cortex suppresses the grasp reflex. Also, a grasp reflex may be unilateral, reflecting a focal disturbance of the contralateral frontal lobe.

MARCHE A PETIT PAS*

As your grandparents become more feeble, they begin to patter about with short, almost shuffling steps, vulnerable to anything that might push them off balance. Bilateral frontal lobe dysfunction is probably the primary cause of this characteristic gait deterioration, but almost certainly other cortical areas contribute, too.

MYOCLONUS

Apart from these primitive reflexes, the cerebral cortex also inhibits strange involuntary jerks known as myoclonus. A myoclonic jerk is lightning-fast, faster than any contraction you can do voluntarily. We have all experienced myoclonus on our descent into sleep—a sudden bodily jerk, the same generalized myoclonic jerk we experience when suddenly startled.[57] The exact myoclonic generator is still problematic, complicated in part by the fact that there are several different types of myoclonus: cortical, reticular, segmental, and palatal.

Cortical ('focal') myoclonus originates in the cortex as a sudden cortical discharge which jerks one part of the body, looking suspiciously like an aborted focal seizure*. Cortical myoclonus may erupt spontaneously ('spontaneous cortical myoclonus'), or in response to some sensory stimulus like touching the skin, stretching a muscle, or rapidly moving a limb ('cortical reflex myoclonus').[58] In either case, only a single limb or one side of the body jerks.

In reticular ('generalized') myoclonus, the jerks are more widespread, affecting the whole body, the trunk, and the limbs bilaterally—either synchronously or asynchronously. In the asynchronous variety, the myoclonus is random, affecting an arm, then a leg, then the face or trunk, a pattern appropriately called multifocal myoclonus and seen most commonly in renal failure and hypoxia.[59] Reticular myoclonus is generated by the brainstem reticular formation, a thick feltwork of phylogenetically ancient neurons occupying the core of the brainstem.[60]

Like cortical myoclonus, reticular myoclonus may occur spontaneously ('spontaneous reticular myoclonus'), or else in response to a sensory stimulus like a sudden sharp sound, touching the skin, stretching a muscle, or moving a limb.[61] (Note that in reticular myoclonus, a *focal* sensory stimulus elicits a *generalized* myoclonus jerk.)

		Precipitating Stimulus Necessary?	
		No	Yes
Site of Origin	Cortex	Spontaneous Cortical Myoclonus	Reflex Cortical Myoclonus
	Reticular Formation	Spontaneous Reticular Myoclonus	Reflex Reticular Myoclonus

Marche a Petit Pas: French for 'March of Small Steps.'

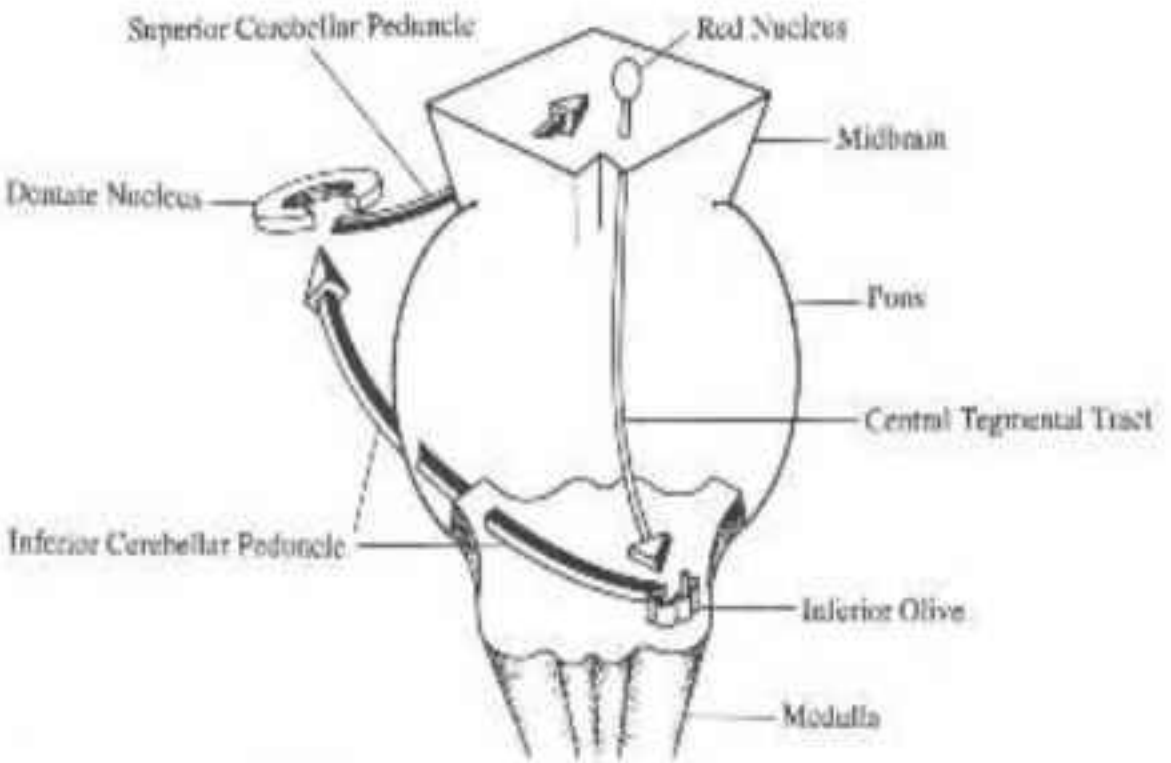
Aborted Focal Seizure: The term 'myoclonic seizures' is a bit vague. Myoclonic seizures may take one of several different forms: single myoclonic jerks of the trunk, or else focal or generalized seizures that are either preceded by a single myoclonic jerk or simply associated with myoclonic jerks that occur independently of the seizures.

Of the scores of causes of generalized myoclonus, most if not all share a single common denominator: they affect the cerebral cortex diffusely, as if the brainstem myoclonic generator were kept in check by a normal cerebral cortex. Even cortical myoclonus usually results from a widespread cortical insult (?reflecting insufficient inhibition within the cerebral cortex). Unfortunately, it's difficult to predict which site—cortex or brainstem reticular formation—a myoclonic disease will use to initiate myoclonic jerks. Hypoxia, for example, may cause both cortical and reticular myoclonus.[62]

Reflex myoclonus—cortical *or* reticular—can be very disabling.* When the patient reaches for something, his arms may jerk uncontrollably with 'intention myoclonus'*. With his arms held outstretched, the patient looks like a jerking marionette. What's so unfortunate about patients with reflex myoclonus is that they are at the mercy of any sudden stimulus: a door slam, a shout, a back slap, a bright light, etc.

Besides generalized, focal, and multifocal myoclonus there is another type called segmental myoclonus, so named because the myoclonic jerks remain confined either to the brainstem (face and neck) or spinal cord (affecting one extremity only).[64]

Finally, there's palatal* myoclonus, a misnomer that refers to a slow rhythmic tremor or jerking of the palate. Palatal myoclonus results from a lesion in the posterior fossa (chapter 18) somewhere between the red nucleus in the midbrain, inferior olive in the medulla, and contralateral dentate nucleus in the cerebellum (Mollaret's triangle).[65]



Disabling: *The* most disabling variety of myoclonus afflicts the Jumping Frenchmen of Maine, a group of families who startle with such intensity that when surprised by a sudden command they react by repeating the command and then *doing it!* This includes ripping off their shirt, striking the person next to them, or staring their ass with their finger.[63]

Intention Myoclonus: Intention means brought on or worsened by reaching for something. Intention myoclonus looks like a coarse, almost violent intention tremor.

Palatal: The hard palate forms the roof of the mouth. Behind the hard palate is the soft palate which closes off the nasopharynx from the mouth during swallowing and speaking.

ASTERIXIS

Asterixis, another bihemispheric cortical sign, is seen typically in liver failure but also occasionally in renal or pulmonary failure. Asterixis is demonstrated by having the patient hold his arms outstretched in front of him with the hands held back ("like a policeman stopping traffic"). The hands will suddenly flap downward and return to their previous hyperextended position. The flap is due to sudden, transient weakness of the wrist and finger extensors. The exact physiology is unknown.[66]

PERSEVERATION

Perseveration is another common sign of diffuse cortical dysfunction. As the name implies, the patient remains stuck on a subject, oblivious to the fact that you've gone on to something else. When asked a question or given a command, he repeats a previous answer or performs a previous command.[67]

In summary, the common clinical signs of diffuse or bihemispheric cortical dysfunction include: diminished level of consciousness, confusion (disorientation, loss of memory, reasoning, and judgment, insight, and psychotic perceptions), mood disturbances, nonfocal seizures, cortical blindness, cortical release signs, myoclonus, asterixis, and perseveration.

PYRAMIDAL TRACT

IT TOOK US A LONG TIME TO REVIEW THE PATHOGNOMONIC SIGNS OF CORTICAL DYSFUNCTION, but then again, it took a long time for Mother Nature to design the cortex. The next subsystem is the pyramidal tract*, also a relatively recent acquisition by the brain. The importance of recognizing pyramidal tract signs cannot be overstated, because the vast majority of central nervous system motor problems involve the pyramidal tracts.

When a person decides to move a muscle, any muscle, he needs to enlist the help of two neurons, an upper motor neuron and a lower motor neuron*. The upper motor neuron descends from the motor strip through the internal capsule and crosses to the opposite side of the brainstem if the muscle is one innervated by a cranial nerve, or on through the brainstem to the opposite side of the spinal cord if the muscle is below the chin. The left cerebral hemisphere, then, controls the right side of the face and body; the right hemisphere, the left face and body. The second neuron, the lower motor neuron, takes over from the upper motor neuron and carries instructions horizontally from the brainstem or spinal cord via a cranial or peripheral nerve to the outlying muscles.

Though most areas of the cortex contribute to the pyramidal tract via the corona radiata*, from a functional, clinical standpoint the pyramidal tract begins in the motor strip. Unfortunately, the pyramidal tract changes names as it courses downward through the brain into the spinal cord. High up in the hemispheres it's called the corona radiata. In the deep part of the hemisphere, the pyramidal tract becomes the internal capsule; in midbrain, the cerebral peduncle*; in the medulla, the pyramidal tract; and in the spinal cord, the corticospinal tract. Fibers which drop off in the pons or medulla to stimulate the lower motor neurons there are called, respectively, corticopontine and corticobulbar* fibers.

Pyramidal Tract: So named because of its triangular, cross-sectional shape in the medulla, the lowest section of the brainstem. Above the medulla is the pons, and above that, the midbrain.

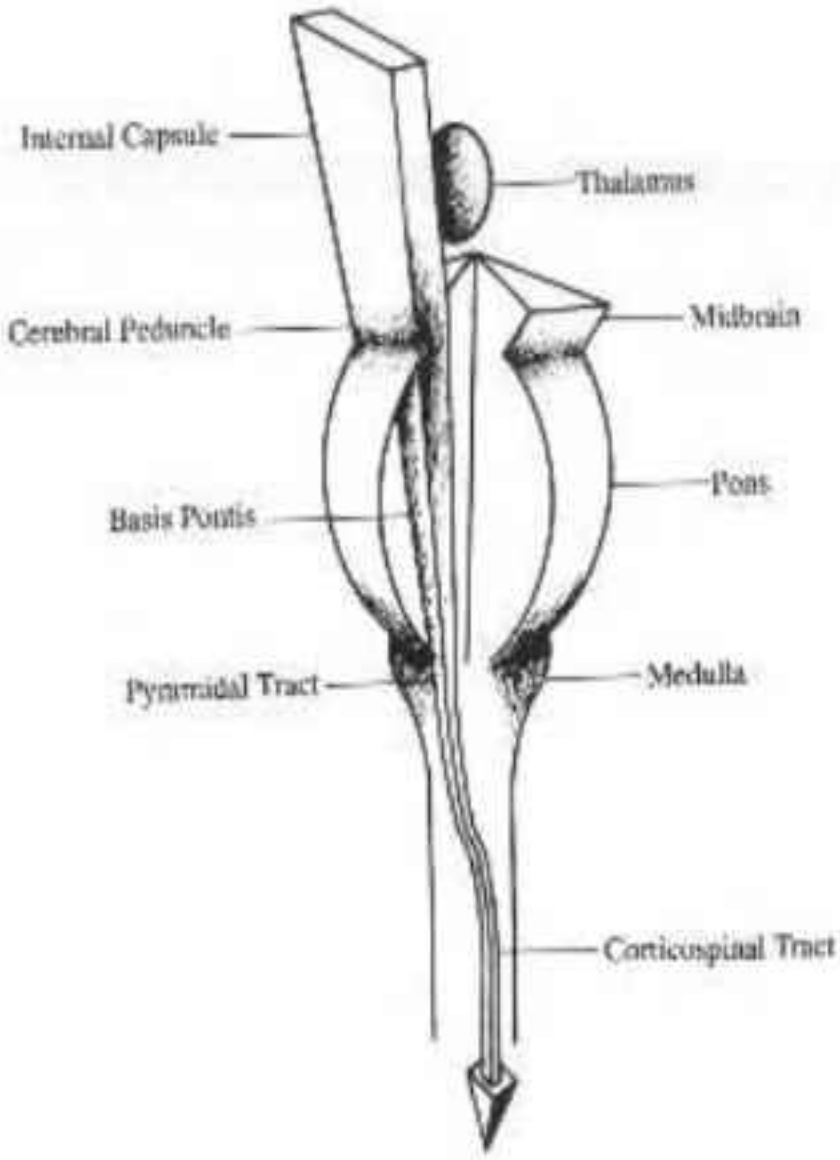
Lower Motor Neuron: The cell bodies for lower motor neurons exiting the brainstem are clustered into various brainstem nuclei, while the cell bodies for spinal cord lower motor neurons lie in the cord's ventral horns.

Lower motor neurons control ipsilateral muscle groups with two exceptions, both in the brainstem: the superior oblique eye muscle controlled by the contralateral fourth (trochlear) nerve nucleus, and the superior rectus eye muscle controlled by the contralateral third (oculomotor) nerve nucleus. The trochlear nerve wraps around the back of the brainstem to the opposite side, while the oculomotor nucleus directs its superior rectus axons through the midbrain to the contralateral oculomotor nerve.

Corona Radiata: The crown of axons between the internal capsule and cerebral cortex. Some of the axons in the corona radiata are funneling downward into the internal capsule from widespread areas of the cerebral cortex, and other (sensory) axons are radiating upward through the internal capsule on their way to the cortex.

Peduncle: Means stem.

Corticobulbar: Bulbar refers to the shape of the medulla which, to the early anatomists, resembled upside down tulip bulbs.



Although changing the name of the pyramidal tract helps localize the section of pyramidal tract being discussed, functionally, a lesion anywhere along the pyramidal tract produces roughly the same 'long tract' signs. Unfortunately, this makes it difficult to pinpoint a pyramidal tract lesion without the aid of intersecting horizontal signs indicating the level of the pyramidal tract lesion.

The signs of pyramidal tract dysfunction are spasticity, weakness (preferably hemiparesis, but monoparesis*, paraparesis*, or quadriparesis* will also do), awkward slowing of precise and skillful movements (particularly rapid alternating movements), hyperreflexia, and a Babinski* sign.[7] Finding all five of these signs would be ideal, but most of the time only one or two of them will be present. In such cases, it may not be so easy to decide if your patient has a pyramidal tract lesion. Let's take one sign at a time.

Monoparesis: Weakness of one limb—an arm or a leg.

Paraparesis: Weakness of both legs.

Quadriparesis: Weakness of all four limbs.

Babinski: A student of Charcot, Joseph Babinski (born in Poland) became a leading French neurologist by the late nineteenth century and remained so for nearly forty years. In addition to describing the famous toe sign in 1896, he led French neurosurgeons to their first resectable (surgically removable) spinal cord tumor in 1922, something Sir William Gowers had done for the famous English neurosurgeon, Sir Victor Horsley, in 1888.

SPASTICITY

Spasticity is one type of increased tone; the other major type is rigidity produced by basal ganglia dysfunction (chapter 17). Tone is the resistance of a relaxed limb to flexion and extension. Don't confuse tone—how loose a joint is—with muscle firmness which is muscle consistency or tension. Tone is assessed by stabilizing the arm at the elbow, and *snapping** the forearm forward into extension. If you feel an initial free interval, interrupted by an abrupt 'catch' about midway into extension, and from then on, increased resistance (like extending the limb through oil), you've got yourself a spastic arm. The initial free interval is crucial to elicit, because rigidity (which implies basal ganglia disease) has no such free interval. The clasp knife phenomenon routinely mentioned in spasticity refers to the Boy Scout observation that as you fully extend the blade of a pocketknife, resistance suddenly gives way.[6] Clasp knife isn't terribly useful; it's easier to feel for a spastic catch than for relaxation of resistance as you continue extending the muscle.

Another place to look for spasticity is at the wrist. Hold the patient's hand as if you were going to shake hands, but move your fingers into his palm. Now rapidly rapidly rotate the hand from a pronated to a supinated position (not vice versa). Use your thumb on the back of his hand to help snap the hand into supination. Again, feel for that free interval and sudden catch. Try lifting both of the patient's wrists above his head and shaking the hands vigorously. The less floppy hand has increased tone, either spasticity or rigidity.



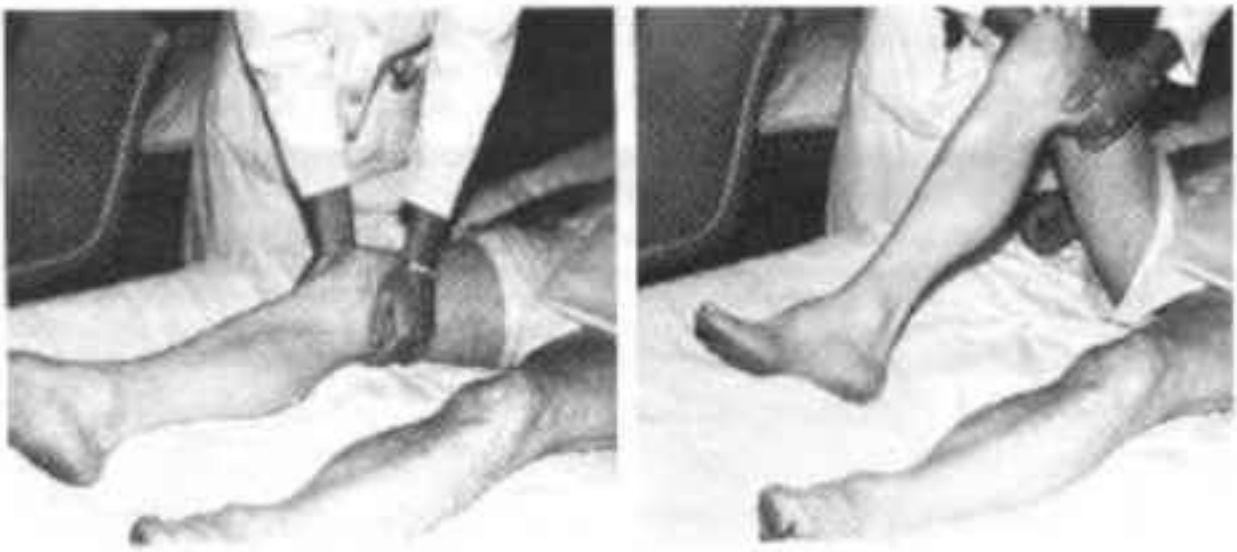
Testing for spasticity by rapidly supinating the hand.

← Support the elbow.

In the legs, spasticity is elicited by placing the patient flat in bed with his arms at his side, even removing the pillow from behind his head. Put both your hands behind the knee in the popliteal fossa and snap the knee up toward the ceiling. Don't pussyfoot—if a tennis ball were on the knee, it should hit the ceiling (well, almost). In a normal leg the heel slides along the bed, but in a spastic leg the heel kicks off the bed with a spastic catch. Be sure the patient is fully relaxed; a tense leg will appear spastic. To help relax the leg, roll it from side to side and then suddenly snap the knee upward. If you're still unsure, place your left hand behind his knee and grab his ankle with your right hand. Work the knee back and forth a little to help relax the leg, and then snap the knee upward while feeling for a spastic catch.

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*Snapping: Unlike rigidity, spasticity is velocity-dependent—you often have to snap the arm into extension to feel the spastic catch.[7]



In a normal leg, the heel should slide along the bed.

Sometimes, instead of making the limb spastic, pyramidal tract lesions do just the opposite—make the limb flaccid*. In general, this happens in 'pure' pyramidal tract lesions, before the pyramidal tract has received tributaries from the prefrontal cortex*, red nucleus* (in midbrain), and perhaps other brainstem structures.[5] So pyramidal tract lesions in the motor strip often produce much less spasticity than lesions below the motor strip*. *Acute* lesions anywhere along the pyramidal tract may also produce a flaccid hemiparesis, at least initially, with spasticity developing later.

At first glance, flaccidity can lead you astray because a flaccid, weak limb is a sign of lower motor neuron weakness (chapter 23). Fortunately, though, this dilemma is rare because other features of a pyramidal tract lesion are usually present—like hemiparesis, slowing of rapid alternating movements, hyperreflexia, and a Babinski sign.

WEAKNESS

Weakness is the second component of pyramidal tract lesions. Pyramidal tract lesions typically produce simultaneous weakness of an arm and leg (hemiparesis), or face and arm, or all three together. Depending on the size of the lesion and its specific location, however, pyramidal tract lesions can produce monoparesis, paraparesis, or quadriparesis. The terms hemiparesis, monoparesis, paraparesis, and quadriparesis simply describe weakness and do not by themselves implicate the pyramidal tracts. In fact, there is no distribution of weakness truly pathognomonic of a pyramidal tract lesion, because illnesses of the lower motor neuron or muscle may mimic the very same pattern of weakness.

Flaccid: Floppy, limp.

Prefrontal Cortex: The cortex in front of the motor strip.

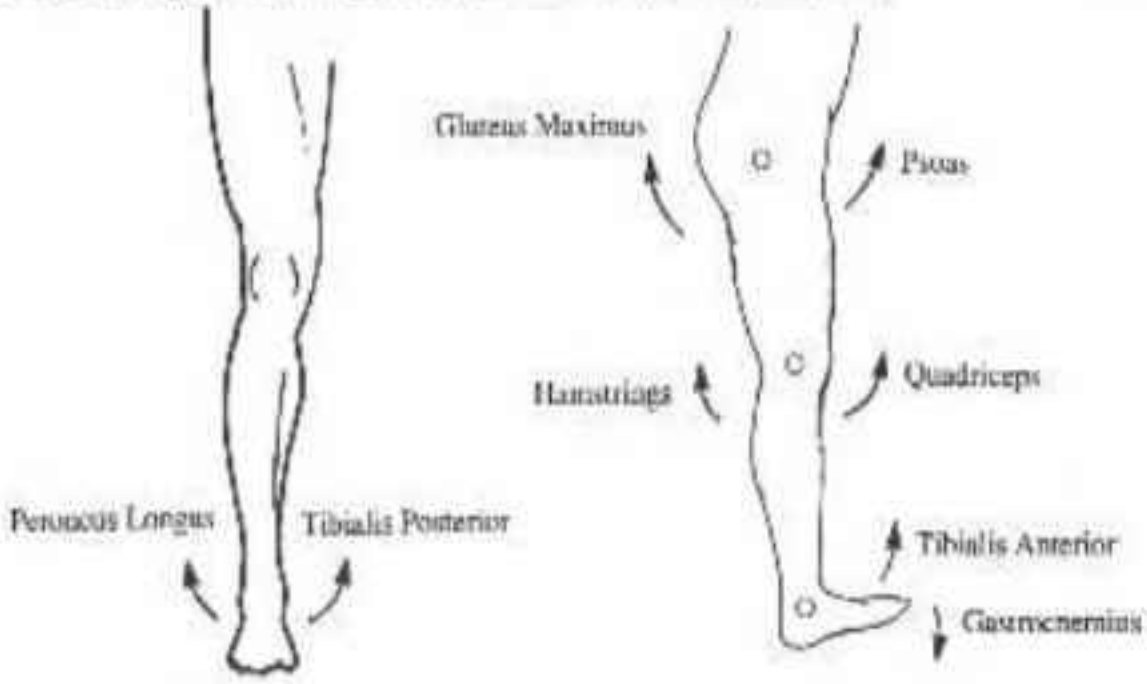
Red Nucleus: One of the basal ganglia.

Lesions Below the Motor Strip: Another place the pyramidal tract is 'pure' (untainted by basal ganglia or brainstem fibers) is in the medulla. Lesions here also produce relatively flaccid limbs.[5]

Individual Muscles

Pyramidal tract dysfunction does, however, usually affect some muscles more than others. The *less* affected muscles are the 'antigravity' muscles if you were doing a chin-up. This means that in the arm the wrist extensors become weaker than the wrist flexors and the triceps become weaker than the biceps. In the leg, the less affected, antigravity muscles are the ones that extend the leg at the hip, knee, and ankle: gluteus maximus, quadriceps, and gastrocnemius.

Each joint in the leg has a flexor and an extensor. The hip flexor is the psoas; the extensor, gluteus maximus. The knee extensor is the quadriceps; the flexor, hamstrings. The ankle dorsi-flexors are tibialis anterior and extensor hallucis longus; the ankle plantar-flexor, gastrocnemius. In addition to a flexor and an extensor, the ankle has an everter (peroneus longus) and an inverter (tibialis posterior).



Another way to look at the leg muscles is: three down the front and three up the back—psoas, quadriceps, and tibialis anterior down the front, and gastrocnemius, hamstrings and gluteus up the back. Helping out tibialis anterior is extensor hallucis longus, the big toe extensor, a clinically very useful muscle for a number of reasons. Extensor hallicus longus is a pure L5 muscle (chapter 23), and small enough that it can always be overpowered, allowing detection of even subtle weakness. In fact, a lot of times you can spot extensor hallucis longus weakness before even touching the patient. When you ask the patient to cock his feet back, the big toe on the weak side doesn't fully curl back nor does the extensor tendon stand out as well. Similarly, in a supine patient you may spot an externally rotated foot, evidence of medial thigh weakness and a frequent sign of a hemiparesis.

In the leg, then, pyramidal tract weakness is worse in the hip flexors (psoas), knee flexors (hamstrings), and foot dorsiflexors (tibialis anterior and extensor hallucis longus). The pattern of pyramidal tract weakness should be obvious if you have ever seen someone with an old stroke. The person holds his arm flexed at the elbow and wrist, his leg extended at the knee, and foot plantar (downward) flexed, a posture resulting, in part, from weakness of the triceps and wrist extensors in the arm, and psoas, hamstrings, and tibialis anterior in the leg. When he walks, the patient has to swing the overextended leg around—circumduct—so he doesn't look like he's stepping into a pothole every other step.





At rest, the hand is flexed at the wrist and elbow.

Circumduction: He has to lift his left hip to swing the left leg around. Note the brace necessary to overcome his footdrop (tibialis anterior weakness).

In mild pyramidal lesions the only gait abnormality may be a unilaterally diminished arm swing, a subtle sign you can often bring out by having the patient heel walk. Bilateral leg spasticity is recognized by watching the patient's knees when he walks—they don't bend. Instead of the knee leading the hip, the hips seem to throw the leg forward, to lead the knee. If the spasticity has been present from early childhood, the knees rub against each other with each step (scissor gait).

The search for a hemiparesis begins in the face. Look specifically at the depth and crispness of the nasolabial* folds. Slight flattening of one fold is a clue to weakness of that side of the face. Look for a droop of one corner of the mouth. When the patient speaks or gently smiles, count the number of teeth on each side of midline; fewer teeth on one side implies weakness on that side. Which eye is open wider? Since the orbicularis oculi muscle closes the eye, the wider open eye is the side of orbicularis oculi weakness. Do both eyes blink synchronously? The one that lags is weak. When the eyes are tightly shut, look for more eyelash showing in one eye implying incomplete (weak) closure of that orbicularis oculi muscle. The forehead won't be weak in a pyramidal tract lesion because each side of the forehead is controlled by *both* cerebral hemispheres; you'd have to knock out the pyramidal tracts (corticopontine fibers) from both hemispheres to get a weak frontalis (forehead) muscle.



Nasolabial: Labia is Latin for lips.

We'll get into testing specific individual muscles later in the chapters on roots and peripheral nerves, but for now just a few points about testing strength when looking for a hemiparesis. In the upper extremity begin in the hand for two reasons. First, it's easier to detect early weakness in the small hand muscles than in the larger, more powerful muscles of the arm or shoulder. Second, the hand muscles are affected early in pyramidal tract lesions because the pyramidal tracts were invented to improve finger dexterity, not to further strengthen our large, proximal muscles.[6] (Otherwise man, with the best developed pyramidal tract in the animal kingdom, would be the strongest animal on Earth for his size.)

Test a patient's grip with your grip. You shouldn't be able to open up the grip of anyone older than nine or ten years of age. Don't let the patient grab your fingers like he's milking a cow; it's more objective to oppose his grip with your grip. Likewise, check his opponens muscle by interlocking your thumb with his. Again, you should not be able to overcome a normal opponens muscle.



When testing any muscle, be sure that only *one* of the patient's joints is situated between your hands. This ensures that you're testing only one muscle at a time. Stabilize the limb by holding it (with your left hand) just proximal to the joint that's going to move. Just before testing the muscle's strength, allow the patient to contract the muscle to maximize its strength. Now test the muscle with your right hand positioned as far distal to the joint as possible without actually crossing another joint.

Another general point about testing the strength of individual muscles is not to yank them; try to overcome the patient's muscles smoothly. Also, you don't have to concentrate on the patient's strength. Paradoxical as this sounds, it's easier and more accurate to concentrate on your own gut muscles. Concentrate on how much strength and grunting *you* have to exert to fully oppose his strength. Finally, a person's strength is judged at the moment of peak effort. If you can threaten or intimidate a weak grip into a normal grip, even for a second, the grip is normal. The assumption is that the person wasn't trying hard enough until you started screaming encouragement.

You can't legitimately diagnose weakness if it hurts the patient to use the muscle. Unless you can get him to ignore the pain for a second and give a full effort, all you can say is that there is antalgic* (painful) weakness, not true weakness. Antalgic weakness gets a little tricky when the patient complains of back pain and bilateral leg weakness. You may never get the patient to ignore his pain, but don't throw the baby out with the bathwater by attributing all his weakness to pain. The consequences of your being wrong—that he in fact *does* have spinal cord or cauda equina compression—can be devastating. Within hours the patient may deteriorate from mild paraparesis to complete paraplegia.

Antalgic: Algesia means pain. Analgesics are pain killers.

Groups of Muscles

There's another way to look for weakness besides testing each individual muscle, and that's to look at groups of muscles. When you hold your arms out in front of you palms up, you're using deltoid, supinator, triceps, etc. If one arm drifts downward, or slowly bends at the elbow, or begins to pronate, you cannot attribute the weakness to any one muscle, but you can still conclude the arm is weak. Testing groups of muscles is most helpful when you most need the information—in the emergency room, when the patient is too stuporous to test individual muscles but with-it enough to hold his arms up with your loud and persistent encouragement.

The specific tests of grouped muscle strength are: arms outstretched with the palms up ("like you're balancing a glass of water on each palm"), standing on each foot with the other knee raised ("like a stork"), hopping on one foot, walking on toes (primarily testing gastrocnemius), walking on heels (primarily testing tibialis anterior), and deep knee bend (proximal hip muscles).

RAPID ALTERNATING MOVEMENTS

Fine precision movements, for which the pyramidal tracts were invented in the first place, are examined by observing the speed and accuracy of rapid alternating movements. Pyramidal lesions (and extrapyramidal ones, too, in the next chapter) cause rapid alternating movements to become slow but accurate. Cerebellar lesions, in contrast, cause fast but inaccurate, sloppy movements. Rapid alternating movements are easily tested by having the patient flipflop one hand in the palm of the other, but any rapid alternating movement will do: tapping his thumb with the index finger of that hand, finger snapping, rapidly touching the thumb with the tip of each finger, fist shaking ("like you're mad"), rapidly revolving the wrists around each other (the 'traveling' signal in basketball), or rapidly tapping all four fingers of one hand against those of the other hand with the thumbs resting against each other. Though pyramidal lesions are supposed to slow the movements without disrupting their accuracy, sometimes the rapid alternating movements are just plain clumsy and sloppy, resembling cerebellar movements. So don't reject a pyramidal site just because rapid alternating movements are not perfectly slow and accurate; clumsiness will also do in a pinch.

HYPERREFLEXIA

Hyperreflexia is by far the most overrated sign of a pyramidal tract lesion. For the amount of information obtained, more time is spent on the tendon reflexes[1] than on any other sign in neurology. It's common for someone to describe nuances of the reflexes and omit whether the patient can walk, or whether the patient knew that he was in a hospital. Of the five signs of a pyramidal tract lesion, hyperreflexia is the weakest. Only when seen with spasticity, weakness, slowing of rapid alternating movements, or a Babinski sign does hyperreflexia take on significance.

Having overstated a point to make a point, the reflexes can actually be quite important in detecting subtle pyramidal tract lesions, particularly if one side of the body is hyperreflexic and the other side is not. But when an obvious hemiplegia is staring you in the face, don't dwell on the reflexes—you already know there's a

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Tendon Reflexes: A muscle reacts to any sudden stretch with a brief reflex contraction. The easiest way to stretch a muscle is to rap the muscle's tendon with a reflex hammer.

pyramidal tract lesion (99 + % of the time). An intelligent history and physical should be used to answer specific questions. If your question is 'does the patient have a pyramidal tract lesion?,' once you've answered it to your satisfaction, go on to another question like 'where along the pyramidal tract is the lesion?,' or 'Is this a purely unilateral lesion?,' or 'Is this a purely motor, or mixed motor-sensory disorder?'

At any time in the exam I should be able to stop you and ask why you're looking for that particular sign. What question will it answer? Don't you already have enough information to answer that question? It's certainly admirable to do a complete neurologic exam on every patient, but most neurologists don't. If a neurologist did a complete neum exam on every patient, he'd be locked up in two years. It's simply too tedious, time consuming, and unproductively boring. You are not a secretary cataloging the physical findings. Use your head; use the exam to answer questions. The good doctor is one who asks the right questions, not the one who always does the complete exam. I recall one case in which a 65 year-old man came into the emergency room after fainting. He related four or five episodes of fainting all associated with coughing. The resident correctly identified the cause of his fainting as cough syncope. The resident had asked himself 'why is this man fainting?,' but he should have asked himself 'why is this man coughing?' A chest xray several weeks later revealed the benign tumor compressing a bronchus.

Back to hyperreflexia. If you asked ten doctors what they mean by hyperreflexia, all of them would say the reflexes are excessively brisk, but the word brisk has too many interpretations. With a little careful observation you should be aware of five separate components to the tendon reflex: threshold, latency, speed, amplitude, and spread. How hard must you tap the tendon to elicit the reflex (threshold)? How long does it take between the time you tap the tendon and the moment the muscle begins to contract (latency)? How rapidly does the muscle contract (speed)? How much does the muscle contract (amplitude)? Finally, is there spread of contraction* into other muscles?

To test the tendon reflexes, first get the patient to relax. Tell him to relax his shoulders (not his arms) which will relax the arms. Next place the arms in a symmetrical pronated position—whether the patient is seated or lying. Begin with the biceps reflex by placing your left thumb with a little tension on the biceps tendon. Now very gently tap your thumb with the reflex hammer*. Slowly increase the strength of the tap until you get a muscle contraction. Mentally note this threshold. As you tap several more times, concentrate on your thumb. You'll soon be able to tell you how long the biceps tendon takes to contract after the thumb is tapped. Your thumb will also tell you how fast the biceps contracts. You will be able to see the amplitude of contraction by looking at how much the wrist moves. Pay attention to the fingers. If they also contract, the biceps jerk has spread into the finger flexors, a sign of hyperreflexia. Now go to the biceps jerk on the other side. Gently press the biceps tendon with your left thumb again (not your index finger) even though you'll have to place

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Spread of Contraction: Though the spread of contractions may take place in the spinal cord,[1] there's another, peripheral explanation. When you tap a tendon, vibrations are transmitted along the bones to other taut tendons, causing their muscles to contract, too.[2]

With the Reflex Hammer: Instead of swinging the reflex hammer like a regular hammer (rotating at the wrist), you'll have better control and more force by pinching the handle between your thumb and forefinger and using the *handle* as the axis of rotation. To hit the tendon hard, lead with your wrist and snap the head of the hammer into the tendon.

your hand in a slightly different position. Concentrate on the same five features. Usually, you'll be looking for asymmetries so you may have to go back and forth between the two arms to recheck.





Find the biceps tendon with your thumb, and tap your thumb.

For the brachioradialis jerk pick up both of the patient's hands in your left hand and tell him to relax his shoulders. Now tap the radius bone at the wrist and look for the five features discussed above. Put the arms back on the patient's lap and tap the triceps tendon. Be sure to tap the tendons just above the elbow, not the belly of the triceps muscle. You're looking at tendon reflexes, not muscle reflexes.



To check the leg reflexes in a seated patient, ask him to put his feet together flat on the floor, out slightly from the chair. Put your left hand on his quadriceps muscle so you can feel when it begins to contract. Tap the quadriceps tendon below the kneecap and look (and feel) for the threshold, latency, speed, amplitude, and spread into leg adductors (both knees will jut together). The ankle jerks are tested by gently dorsiflexing the foot and tapping the Achilles tendon*. If the patient is supine, lift *both* knees with your left arm, and get the patient to relax enough so that the heels rest on the bed. Now tap each quadriceps tendon, looking for asymmetries. The ankle jerks are examined by letting the knee rotate out into a frog position. Dorsiflex the foot to put a little tension on the Achilles tendon. Tap the reflex and pay attention to both the latency and return phase of the reflex*. Clonus refers to rhythmic involuntary pumping of the foot after you either tap the Achilles tendon or snap the foot into dorsiflexion. Clonus only means that the ankle jerk is hyperactive, admittedly very hyperactive, but nothing more.

Achilles Tendon: Because he was held by his heel when dipped into the protective river Styx, Achilles was subsequently vulnerable at his heel. Sure enough, Achilles was killed during battle when an arrow, directed by the gods, struck his heel.

Return Phase of the Reflex: A slow return is often seen in hypothyroidism.







Those are the standard deep tendon reflexes sought in most patients, but you need not confine yourself to them because every muscle has a tendon and, therefore, a potential tendon jerk. The 'nonstandard' deep tendon reflexes—the supraspinatus, pectoralis, finger flexor, Hoffmann, thigh adductor, and hamstring reflexes—are absent in most people. Their presence usually implies hyperreflexia, but since some skinny people (a la Don Knotts) are diffusely hyperreflexic, the major significance of these nonstandard reflexes is either an asymmetry between the right and left sides or an association with other pyramidal tract signs.

The reflexes are graded by a numerical system. Zero is an absent reflex. Trace is palpable but not visible. 1+ is hypoactive, but present. 2+ is a normal reflex. A 3+ reflex is hyperactive. 4+ means there is unsustained clonus, and 5+, sustained clonus[4]. Sometimes reinforcement, such as clenching the jaw, may disclose an apparently absent reflex.

Another kind of reflex, called the cutaneous reflex, is *lost* in pyramidal tract lesions. A typical cutaneous reflex is the abdominal twitch when you gently stroke someone's stomach. The easiest way to elicit an abdominal reflex is to unfold a safety pin and gently but quickly brush the abdomen. Fat stomachs make the reflex tough to see, but what you're really looking for is asymmetry between the right and left sides of the abdomen. Another cutaneous reflex lost in pyramidal tract lesions is the cremasteric: a quick brush along the inner thigh causes reflex retraction of the testicle upward toward the abdomen. I rarely look for the cutaneous reflexes because other pyramidal tract signs usually suffice. Besides, the cutaneous reflexes do not affect function. You can't explain a patient's weakness or incoordination by a lost cutaneous reflex alone. You need to find spasticity, weakness, or slowing of rapid alternating movements to lay the motor problem at the doorstep of the pyramidal tract.

Sustained Clonus: Sustained clonus means that as long as you maintain some pressure on the sole, the foot will continue to pump. For more on the physiology of clonus, see Dimitrijevic.[9]

BABINSKI REFLEX

Now the Babinski reflex.[6] My boss used to say he wished Babinski had gone into architecture. And for good reason. You can never elicit it when you want it, and it's always there when you don't need it. Nevertheless, the Babinski is an important sign and one you simply have to know how to elicit. Get the patient flat on his back relaxed. Hold his foot in a slightly inverted position and gently stroke the lateral side of the sole with something firm like a key. Do it gently at first because a lot of people have sensitive feet and you'll end up with a voluntary withdrawal response instead of a Babinski reflex. If the sole is too sensitive, stroke the less sensitive outside edge of the foot. If that doesn't work, simultaneously stroke the outside of the foot and rub your knuckles down the tibia. If that doesn't work, forget it. The response you're looking for is for the big toe to gracefully ('majestically') dorsiflex. In a full-blown Babinski reflex, the whole foot will withdraw and the knee will even bend, but if you stroke the sole gently just above threshold, only the big toe will dorsiflex. This avoids confusion with voluntary knee and toe withdrawal because of sensitive feet.

MINIMAL SIGNS OF A PYRAMIDAL TRACT LESION

Ideally, pyramidal lesions produce all five signs—spasticity, weakness, slowing of rapid movements, hyperreflexia, and a Babinski, but often only one or two of them are found. What are the minimal signs that allow you to call a pyramidal lesion? Well, a Babinski alone is enough. Asymmetric hyperreflexia alone is suspicious, but hyperreflexia with any of the other signs is probably enough. (Fortunately, spasticity and hyperreflexia usually occur together.) Slowing of rapid alternating movements is not enough even if it involves the hand and foot, because the patient may be faking (welcome to the real world, doctor). A patient may even fake weakness, but he can't fake spasticity, hyperreflexia, and a Babinski. However, until you're in the business awhile, give the benefit of doubt to the patient and at least suspect a pyramidal lesion if you find weakness or slowing of rapid alternating movements.

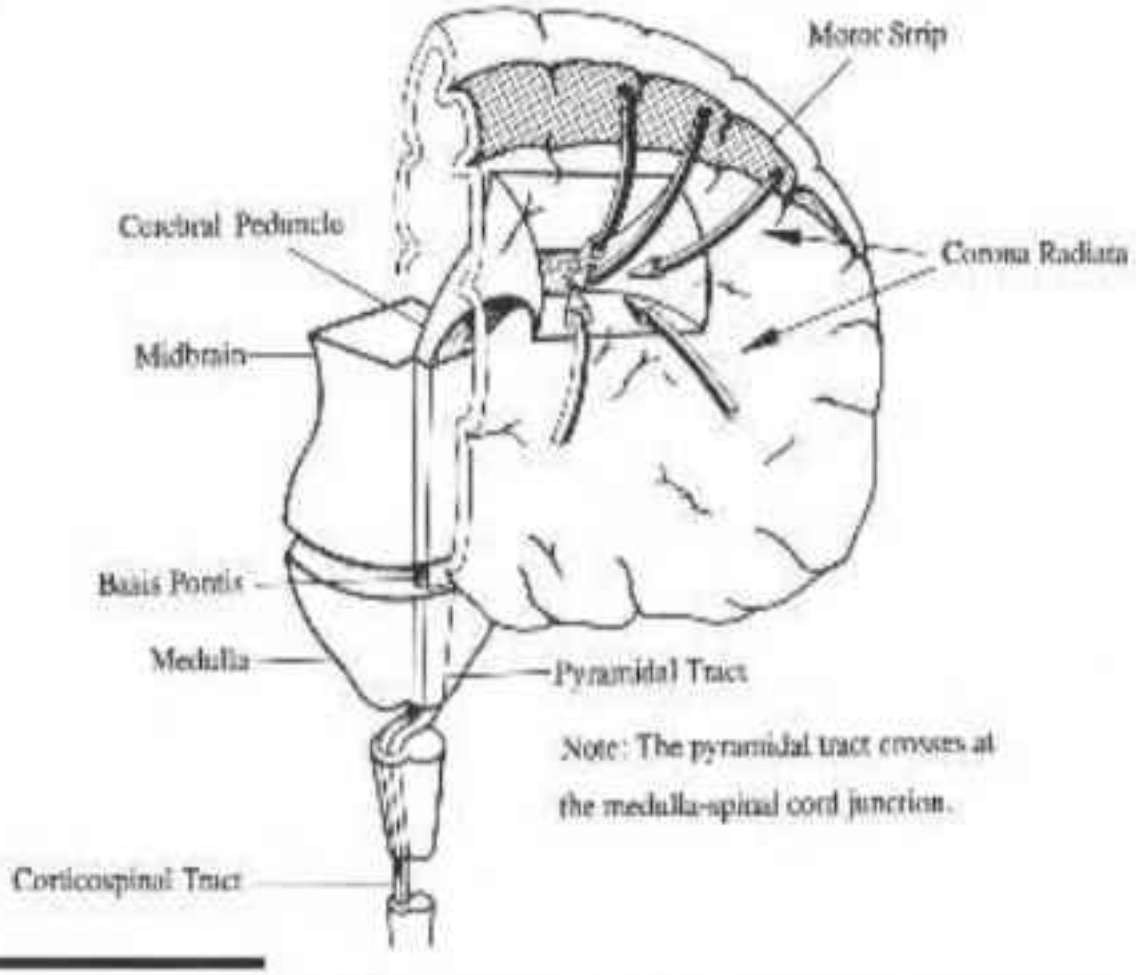
Despite the specificity of a Babinski sign for pyramidal tract lesions, recognize that, like the cutaneous reflexes, a Babinski sign does not impair function—only spasticity, weakness, and slowing of fine movements do. If a patient has trouble walking, and all you find is a Babinski sign or hyperreflexia *without* spasticity or weakness, be very cautious about attributing any gait difficulty to pyramidal tract dysfunction. The true explanation for the gait problem probably lies at another site in the neuromuscular system, or even in another organ system altogether, such as joint pain.

PYRAMIDAL TRACT LOCALIZATION

The pyramidal tracts are one of three vertical 'long tracts.' (The posterior columns and spinothalamic tracts are the other two long tracts.) Localizing a lesion to a particular spot along the pyramidal tract requires finding signs in an intersecting horizontal subsystem. Unfortunately, life being what it is, the horizontal signs are frequently absent. There are, however, certain helpful clues to pyramidal tract localization even without simultaneous horizontal signs. For example, the more spasticity,

the more likely the pyramidal tract lesion is in the spinal cord*. This is especially so if the spasticity is bilateral: since the pyramidal tracts are closest together in the cord, a single spinal cord site allows you to account for bilaterality with a single anatomic lesion. Conversely, it's unusual for a pyramidal tract lesion in the spinal cord lesion to produce a hemiparesis or monoparesis. The spinal cord is so small in diameter (a dime), that it's difficult to find a lesion discrete or polite enough to confine itself to only one side of the cord.

Reasonably accurate pyramidal tract localization on the basis of vertical signs alone can also be made in a patient with a *dense* (severe) hemiplegia unaccompanied by aphasia, Gerstmann's syndrome, seizures, confusion, or unconsciousness. Having thus spared the cortex, the lesion is almost certainly deep, either in the internal capsule or brainstem where a small lesion can intercept the bottleneck of converging pyramidal tract fibers*. If the patient has a mild hemiparesis and a homonymous hemianopia, the lesion likely involves the very posterior part of the internal capsule adjacent to the spot where the optic radiations leave the lateral geniculate body.

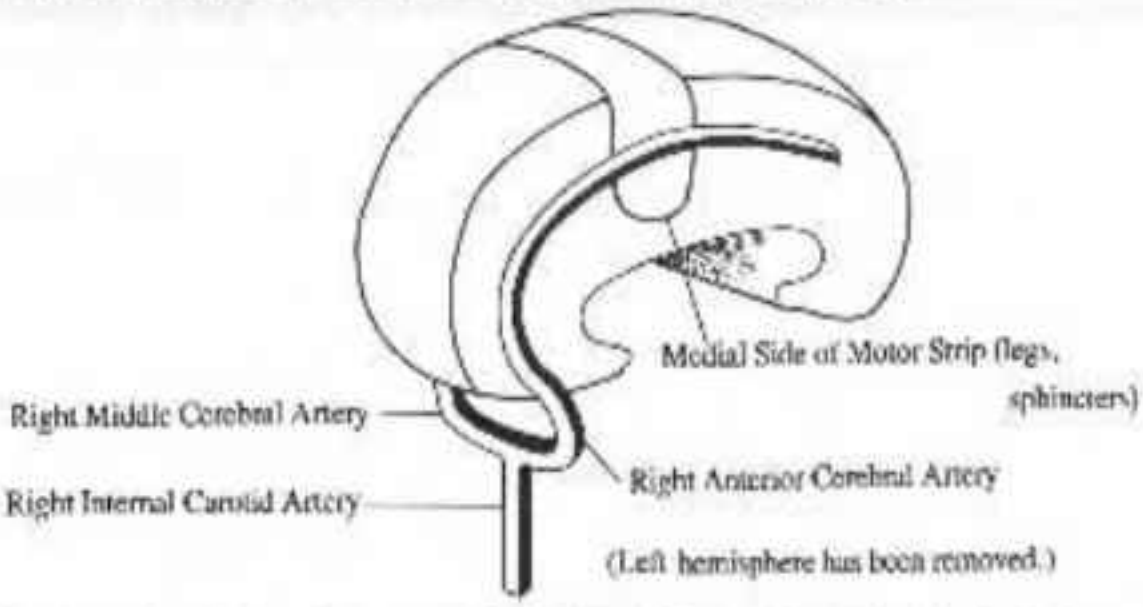


Spinal Cord: An exception to this occurs with prefrontal lesions (anterior to the motor strip). Lesions here often make the limbs quite stiff and spastic.

Converging Pyramidal Tract Fibers: The best example of a small lesion deep in the internal capsule is a small 'lacunar' infarction (lacune = lake). A common consequence of long-standing hypertension, lacunes may occur anywhere along the pyramidal tract—internal capsule, cerebral peduncle, or basis pontis.[11] Instead of picking off descending motor fibers, lacunes may in some instances pick off sensory fibers ascending in the internal capsule to produce contralateral hemihypesthesia (numbness of one half of the body).[12]

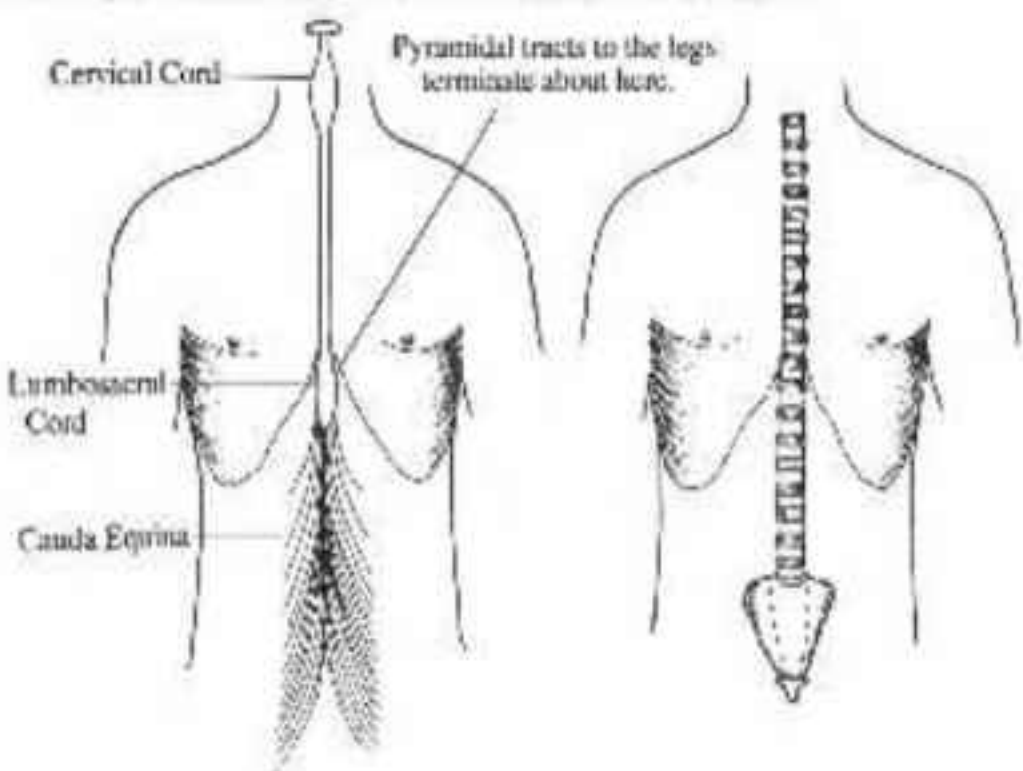
Lacunes accumulating in both internal capsules produce difficulty swallowing and, interestingly enough, a curious disturbance of emotions: patients cry, or less commonly, laugh at the slightest provocation, called emotional incontinence. Pseudobulbar patients are also frequently demented.

In a hemiparetic patient whose leg is weaker than his arm, the lesion is usually along the medial side of the motor strip where the leg fibers hang in the interhemispheric fissure. A stroke in this region is due to occlusion of the anterior cerebral artery which supplies the medial side of the motor strip (chapter 31).

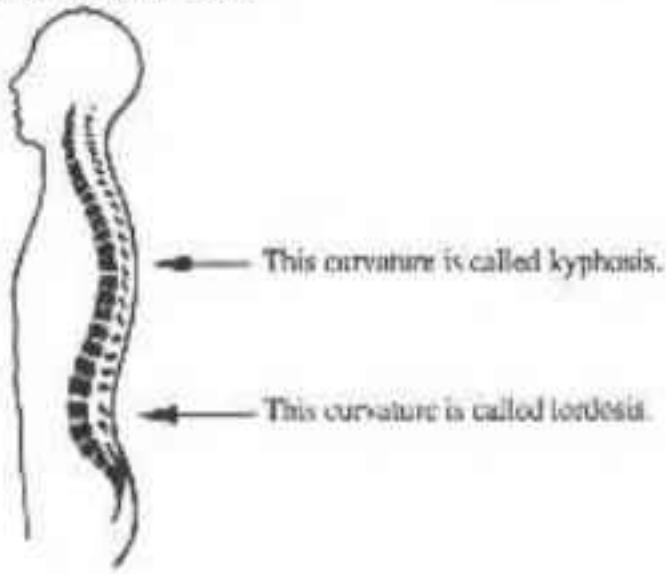


In attempting to pinpoint a pyramidal lesion without the benefit of horizontal signs, be careful to avoid a couple of tricky anatomic pitfalls. For example, a hemiparesis that extends into the face naturally places the lesion somewhere above the facial nerve nucleus—in the cerebral peduncle, internal capsule, corona radiata, or motor strip. But the converse is not true. If the hemiparesis spares the face, the lesion does not have to be below the facial nerve nucleus. A small lesion in, say, the internal capsule or cerebral peduncle may have missed the corticopontine fibers headed for the facial nerve nucleus.[15] Likewise, a spastic paraparesis alone, without involvement of the arms, does not automatically place the lesion between the cervical and lumbar spinal cord. Not uncommonly, a tumor or intervertebral disc pressing on the *cervical* spinal cord injures the leg fibers well before those to the arms,[16] probably by interrupting the vascular supply to the spinal cord.[15]

Another frequent mistake is to forget that the spinal cord terminates behind the L1 vertebral body, and that the pyramidal tracts terminate neurologically at about L5. Neurologic L5 is *anatomically* in the lower thoracic region.



In other words, don't settle for a lumbar myelogram* with pyramidal tract signs in the legs! You've got to run the dye at least into the thoracic spinal canal, keeping aware of the normal thoracic kyphosis. In the usual prone position, myelographic dye will roller-coaster past a thoracic lesion. To prevent this, remove the spinal needle and flip the patient supine to pool dye in the thoracic region allowing better visualization of the thoracic cord, especially its dorsal surface.



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*Myelogram: An xray test in which a spinal tap (lumbar puncture) is performed on a patient lying prone on an xray table. Myelographic dye is then injected through the spinal needle into the sac of spinal fluid (subarachnoid space) surrounding the spinal cord. The heavier-than-water dye is made to flow rostrally by tilting the xray table head down. Xrays of the dye-filled subarachnoid space can detect tumors, discs, or bony overgrowths compressing the cord or roots within the spinal canal.

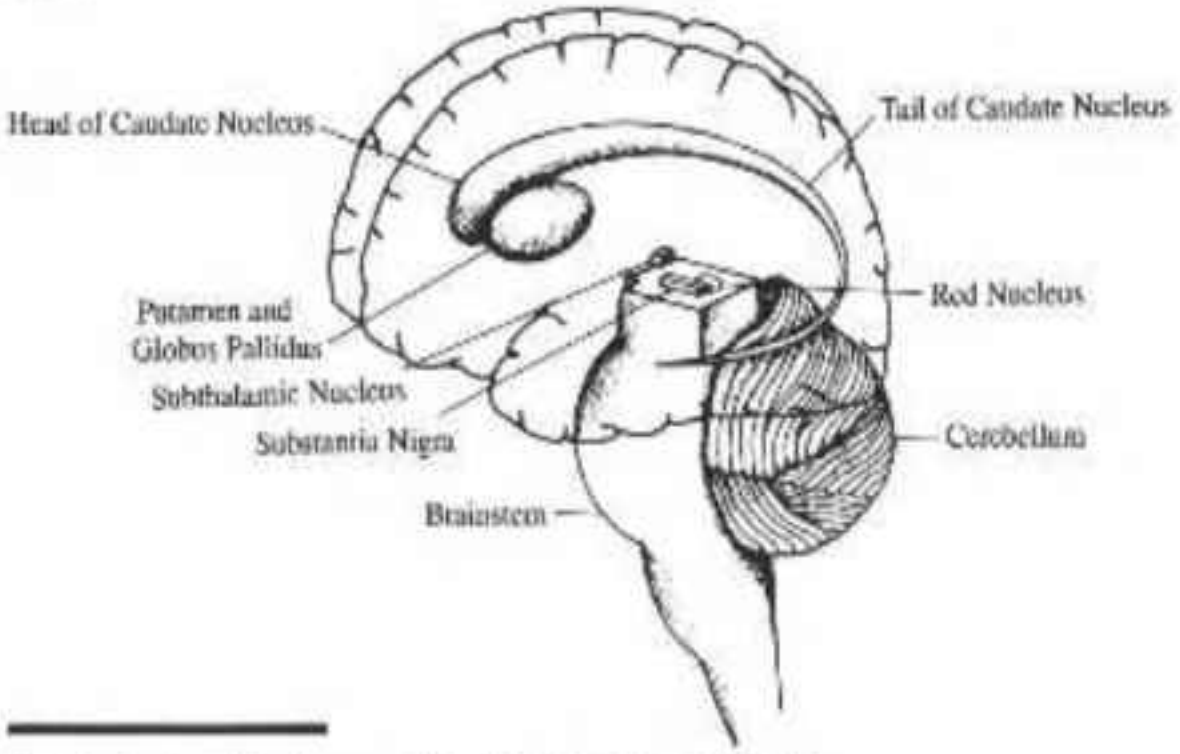
In the head the meninges lie on the surface of the brain, but in the spinal cord the meninges and dura are plastered up against the surrounding vertebral bone. This anatomic arrangement provides a relatively large subarachnoid space around the spinal cord and cauda equina, large enough to safely tap with an LP needle.

BASAL GANGLIA

THE NEXT CENTRAL NERVOUS SYSTEM SUBSYSTEM to be considered is the basal ganglia, a collection of gray matter structures deep within the brain. Ganglia are clusters of nerve cell bodies, and basal refers to their subcortical location—hence, basal ganglia. Unlike the pyramidal tracts which govern strength and fine dexterity, the basal ganglia govern the speed and spontaneity of movements, which also means there are no sensory signs in basal ganglia diseases. The basal ganglia are much older phylogenetically than the pyramidal tract, and in fact, still serve as the highest motor control center in reptiles. Another term for the basal ganglia is the 'extrapyramidal system,' a term coined by Kinnier Wilson (who also described Wilson's disease in 1912) to distinguish the basal ganglia from the pyramidal tract system.

ANATOMY

Six separate structures comprise the basal ganglia: caudate nucleus*, putamen, globus pallidus*, subthalamic nucleus, red nucleus and substantia nigra*. The caudate, the largest one, sits far forward, its head indenting the lateral ventricle and its tail arching gracefully backward into the temporal lobe, terminating near the amygdala*.

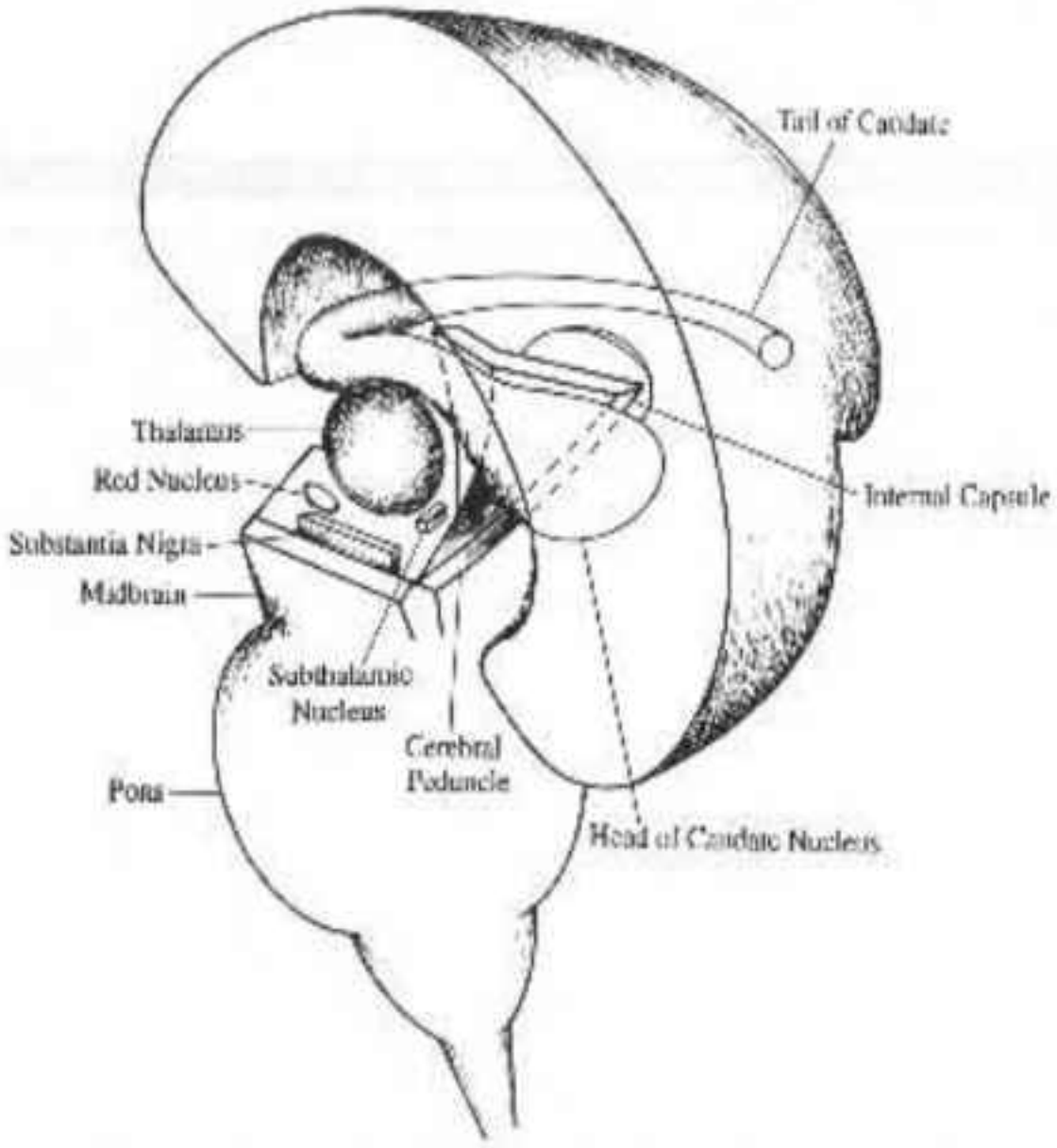


Caudate Nucleus: Cauda means tail in Latin. Caudate means tailed.

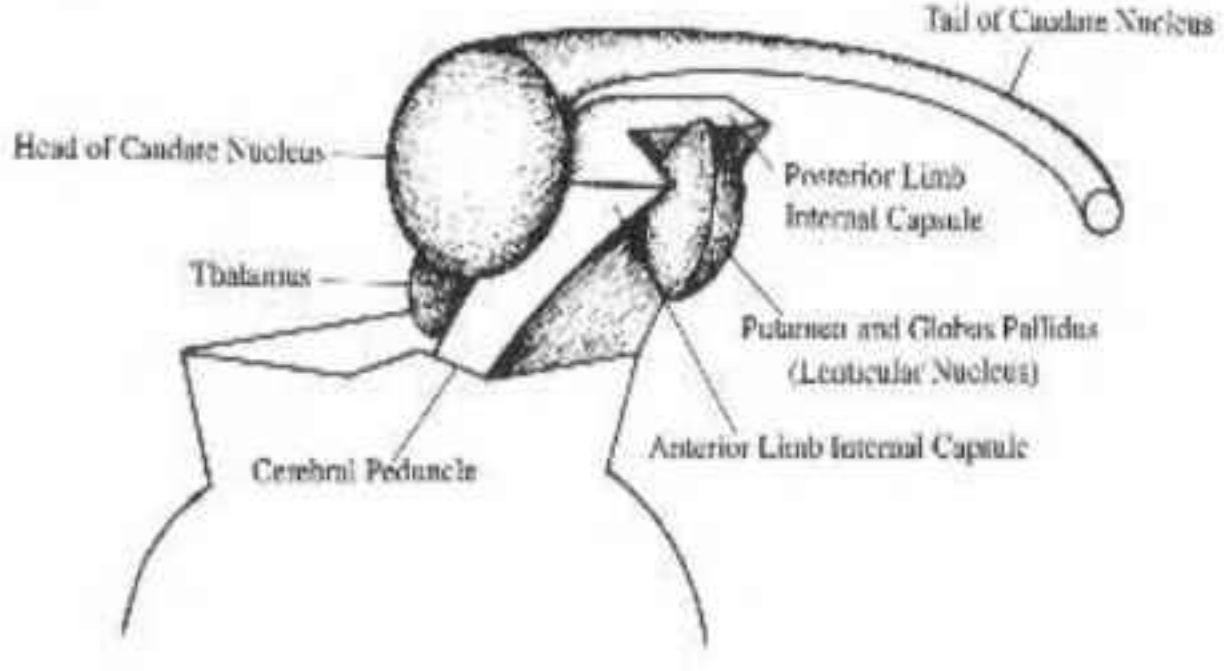
Globus Pallidus: Globus is sphere (globe), pallidus is pallid or pale.

Substantia Nigra: Black substance. The pigment in the substantia nigra is neuromelanin, similar to the pigment that darkens our skin. Why the substantia nigra should need neuromelanin is unknown.

Near the Amygdala: The tail of the caudate is made up of neuronal cell bodies, not axons. Don't let the tail of the caudate fool you into thinking that the head of the caudate is projecting to the amygdala.

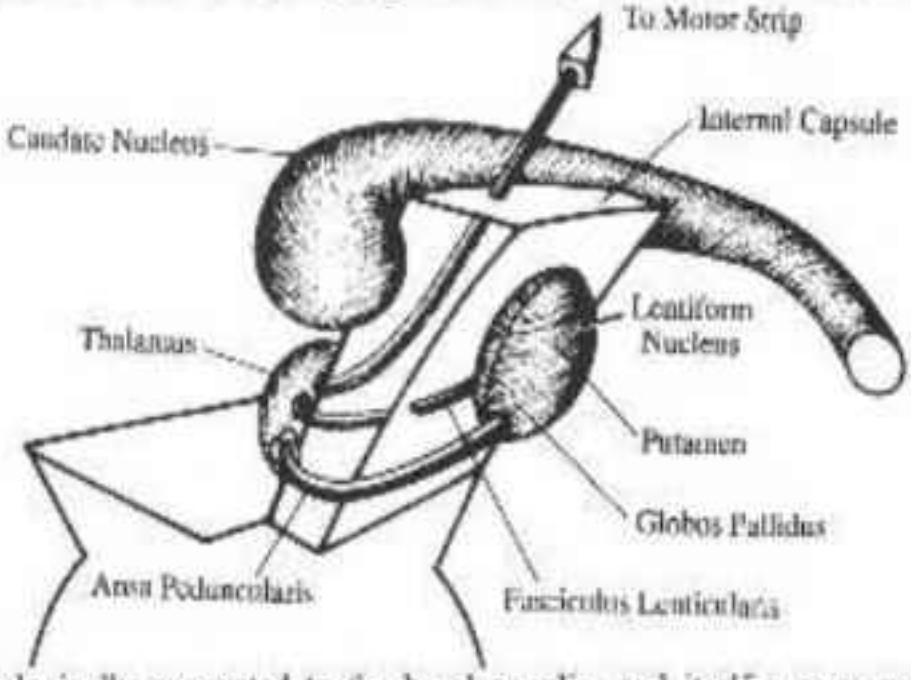


The caudate and putamen, located on opposite sides of the internal capsule, are partially connected to each other by numerous small bridges of gray matter. In cut section these gray matter bridges make the internal capsule look striated (striped). Because of these striations, the caudate and putamen, taken together, are known as the striate nucleus, or corpus striatum.



The globus pallidus is nestled just medial to the putamen*. The putamen and globus pallidus, together, in the uncut state look like a lens, and from that, the lentiform nucleus. Note how close the internal capsule skirts medial to the putamen and globus pallidus. It's no wonder that in intracerebral hemorrhages, which occur most commonly in the putamen, a hemiparesis is practically unavoidable.

The spokesman for the basal ganglia is globus pallidus. Virtually all outflow from the basal ganglia is funneled through globus pallidus which, after contributing its own analysis, forwards the messages across and around the internal capsule to the thalamus. The thalamus, in turn, thrusts its axons upward through the internal capsule to the prefrontal cortex, where the basal ganglia exert their influence over the motor strip.[1]



Though physiologically connected to the basal ganglia, and itself a gray matter structure, the thalamus is not considered part of the basal ganglia. There is, however, a tiny structure beneath the thalamus that is a member—the subthalamic nucleus. For such a tiny structure, an uncooperative subthalamic nucleus can cause suicidal misery. Patients with subthalamic lesions suffer from ballismus*: spontaneous and uncontrollable movements of an arm, a leg, or both. The actual movements are rather coarse, often of such large amplitude that the limbs fling wildly about.

The two pigmented (black and red) nuclei, substantia nigra and red nucleus, lie in the midbrain, at the top end of the brainstem. The substantia nigra deserves our undying gratitude. This lowly structure boosted neurochemistry into orbit in the mid-1960's. Deterioration of the substantia nigra causes Parkinson's disease, an illness treated with the drug L-dopa. Axons from the substantia nigra connect up to the putamen and caudate nucleus where they release a chemical called dopamine. As the substantia nigra degenerates, less dopamine is released and symptoms of Parkinson's disease gradually appear. The solution is to goose the remaining nigrostriatal axons to make more dopamine. Since dopamine, possessing an electrical charge, cannot get

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Putamen: Putamen means shell in Latin.

Ballimus: Shares the same root as ballistic, which should remind you of bursting, chaotic, flinging movements. Myoclonus differs from ballismus by being faster, lightning fast. Myoclonus is also more stimulus-sensitive, frequently precipitated by an examiner's shout, hand clap, or skin pinch; ballismus is more spontaneous and less altered by external stimulation (though it may worsen as the patient attempts to use the ballismic limb).

across the blood-brain barrier* into the brain, the neutral precursor to dopamine, L-dopa, must be given instead. L-dopa is then metabolized* inside the brain to dopamine, and the substantia nigra work overtime restoring the patient to normal. . . . sorta.

More recent drugs (like bromocriptine) completely bypass the nigrostriatal neurons by directly stimulating the dopamine receptors situated on post-synaptic membranes in the caudate and putamen.[3]

SIGNS

Bradykinesia

What happens when the basal ganglia decide to quit working? Two basic patterns emerge—the patient either moves too much or not enough. Too little movement is called bradykinesia*. The face loses its natural range of expressions, including eye blink frequency.[4] The blank expression is called a 'masked face.' When quietly sitting or standing, the patient no longer shifts his weight or changes the position of his arms and legs. And when he does move, he moves slowly and deliberately. Concentrate separately on the amount and speed of spontaneous movements. A paucity of spontaneous movements is not always accompanied by a slowing of movement. Sometimes a patient may sit motionlessly, but *move* relatively quickly.

The opposite of bradykinesia, too many movements, may also result from basal ganglia dysfunction. The patient cannot keep still even when instructed to, because of a resting tremor, chorea, ballismus, or athetosis. These movements—which are best noticed when the patient is distracted—may be voluntarily suppressed, but only temporarily; the involuntary movements quickly break through the patient's attempts to suppress them.

Blood-Brain Barrier: When ink is injected intravenously into animals, every organ of the body stains blue except the brain. Intracerebral blood vessels are impermeable to all but a few select molecules. The blood-brain barrier helps prevent every punk molecule in the bloodstream from disrupting the brain. The three major structures involved in the blood-brain barrier are the capillary endothelial cells, the 'tight junctions' between the capillary endothelial cells, and specialized astrocytes surrounding the capillary endothelial cells.[2]

Metabolized: Every molecule in the body is either assembled or disassembled—metabolized—to another molecule. L-dopa, a metabolite of the amino acids phenylalanine and tyrosine, is itself a precursor to dopamine, norepinephrine, and epinephrine:

Phenylalanine ⟶ Tyrosine ⟶ L-dopa ⟶ Dopamine ⟶ Norepinephrine ⟶ Epinephrine.

The L means levo (left), a chemical label. D-dopa (dextro, right) is less potent than L-dopa.

Bradykinesia: Brady(slow) kinesia(movement).

Tremor

The number one characteristic of basal ganglia tremor is its presence at rest and disappearance (or diminution) when the limb attempts a specific feat like reaching for a fork*. This is in diametric contrast to cerebellar tremor which is minimal at rest and brought out by specific intended movements—an intention tremor. The other characteristic of an extrapyramidal tremor is its coarseness—maybe two or three beats per second of relatively large amplitude. The fine hand tremor* while waiting to see the boss is not from the basal ganglia; it's too fast and not coarse enough. An extrapyramidal tremor should be coarse enough and slow enough to almost wind an automatic-winding wristwatch.

Chorea and Ballismus

Chorea*, or choreiform movements, are involuntary random flickers of small muscles of the hands, feet, or face, as if the patient were fidgety*. Chorea may be proximal enough to cause a whole arm to gently jerk, but typically only a finger, eyebrow, corner of a mouth, wrist, or ankle twitches. Remember that choreic muscles twitch randomly. If the same muscle twitches repetitively, it's called a tic* (or perhaps a focal seizure). If, instead of small distal muscles, larger more proximal muscles involuntarily flinch, producing chaotic flinging and jerking of an arm or leg, the patient has ballismus. Ballismus can be unilateral, but chorea is almost always bilateral.[6]

Athetosis and Dystonia

Athetosis* is a distorted movement, a contorted writhing. You can mimic it by moving a limb while contracting every muscle in the limb simultaneously.[10] A snapshot of athetosis is a posture, a dystonic posture (as opposed to an athetoid *movement*).[11]



Dystonic Hand Posture

Reaching for a Fork: Some Parkinsonian patients manifest a tremor when holding their arms outstretched—an action tremor—which may resemble a cerebellar intention tremor.[3]

Fine Hand Tremor: Nervous tremor is probably due to the effect of circulating epinephrine (adrenaline) on muscle or peripheral nerve.[5]

Chorea: From the Greek, to dance.

Fidgety: Some fidgety patients are actually suffering from akathisia—an inability to keep still. This is a state of restlessness, not a true movement disorder (though the pathophysiology may indeed lie in the basal ganglia).[7]

Tic: A tic is a simple, purposeless movement which, though stereotyped, occurs with a random cadence. A more complex habitual movement, one that does serve a purpose, is called a mannerism or habit spasm, like Rodney Dangerfield stretching his neck and adjusting his tie.[8]

Athetosis: From Greek, without a fixed position (i.e., in constant motion).

A common example of dystonia is torticollis ('wry neck') in which one sternocleidomastoid muscle contracts continuously (for unknown reasons), making the patient turn his head as if he were looking up over his shoulder.[12] More dramatic acute dystonia, called oculogyric crisis, may suddenly occur after a dose or two of phenothiazines*. The patient strikes a bizarre posture usually involving the eyes, face and neck. He may, for example, be unable to close his mouth or lower his eyes which have rolled upward. Rather typical dystonia may also occur after severe birth trauma, severe enough to damage the pyramidal tracts and basal ganglia; the child develops a stiff, scissored gait (pyramidal tracts), and dystonia of the neck, trunk, and limbs*. Even writer's cramp, in which the hand becomes so stiff and awkward that writing is impossible, is thought to be a form of acute dystonia of the hand.[13]

Posture and Gait

The posture and gait of extrapyramidal disorders is most diagnostic in Parkinson's disease, described in 1817 by Dr. James Parkinson, a London practitioner.[16] Even just standing, the Parkinsonian patient is easy to recognize. Besides a blank expression and infrequent blinking, the patient is bowed slightly at the waist to help compensate his terribly insecure balance: even modestly nudging the patient's sternum may send him reeling backward, called retropulsion. To walk, he leans forward, challenging his feet to prevent him from falling forward. The feet respond with festinating steps*, and the patient shuffles forward barely balanced on the balls of his feet. Once in gear, he needs frank assistance to stop. Turning is a precarious 'en bloc' maneuver: instead of the head leading the body, both the head and body turn together. Add to this image a set of arms flexed in front of the stomach, the hands coarsely shaking three times a second, and you'll have a gait that's hard to miss.[17]

Speech

Parkinsonian patients speak without moving their lips or taking a deep breath. The speech comes out soft and twittery; it speeds along devoid of the normal changes in pitch and cadence, forcing you to listen carefully to discern individual words and phrases*.[18] You can see how easy it might be to look at such a motionless person staring away, drooling, taking a long time to answer with barely audible speech, how

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Phenothiazines: The major tranquilizers for schizophrenia, including drugs like chlorpromazine (Thorazine) and trifluoperazine (Stelazine). Though initially discarded in the early 1950's because of its sedative side effects, chlorpromazine was just the drug needed by an attentive French surgeon looking for a pre-operative sedative. He passed this apparent sedative on to his psychiatric colleagues who quickly discovered Thorazine's powerful antipsychotic properties.[13] Thorazine spawned a revolution in psychiatry, miraculously eliminating the need for prefrontal lobotomies—operative sectioning (cutting) of the prefrontal white matter.

Though not chemically a phenothiazine, haloperidol (Haldol) also reverses schizophrenic symptoms by a mechanism similar to Thorazine's: by blocking dopamine receptors.

Neck, Trunk, and Limbs: These children have, in popular terms, cerebral palsy: mixed, but stable, pyramidal and extrapyramidal signs stemming from birth injury.[14] Most neurologists avoid the term cerebral palsy because the signs are too variable (including even cortical and cerebellar signs) to present a consistent clinical picture.

Festinating Steps: Literally means running. Refers to a running-shuffling gait.

Individual Words and Phrases: Listening to Parkinsonian patients makes you realize how much we depend on lip reading, facial expressions, and breathing patterns to understand the spoken word.

easy it might be to mistakenly call such a person demented*. Their intelligence is apparent after a little L-dopa. I recall one stone-frozen 82 year-old patient (a World War I Veteran to boot) who wrote bawdy limericks after his L-dopa.

Tone

The tone of basal ganglia disease is either hypotonic†, as occurs in choreiform disorders, or increased (rigid), as in the bradykinetic varieties. Bending a rigid arm is like bending a malleable lead pipe or a piece of soft plastic—stiff throughout the entire range of motion, back and forth.[20] This lead pipe (or plastic) rigidity contrasts with the free interval and spastic catch of pyramidal lesions. Rigidity is also easily detected at the wrist by flexing and extending the hand. As you do this, you may also feel ratchety, bumpy catches called cogwheeling. Sometimes it helps to bring out subtle cogwheeling by having the patient rapidly tap his knee with his other hand. The going explanation for cogwheel rigidity is a Parkinsonian tremor superimposed on rigidity.[21]

Strength and Reflexes

The strength and deep tendon reflexes are normal in extrapyramidal diseases, and there's no Babinski sign. Rapid alternating movements, however, are slow. The subtle difference between pyramidal and extrapyramidal rapid alternating movements (both of which are slow) is that extrapyramidal movements 'wind down'—that is, they become progressively smaller in amplitude and speed. This is most characteristically seen in the handwriting which may start out with reasonable size but quickly grinds into illegible micrographia.

There is one curious extrapyramidal reflex, the glabellar reflex (Myerson's sign), brought out by tapping just above the nasal bridge between the two eyebrows (the glabella).[22] A normal person may blink a few times but quickly stops after only a few glabellar taps. Not so in basal ganglia diseases, especially Parkinson's disease: the patient will continue to blink despite your instructions not to.

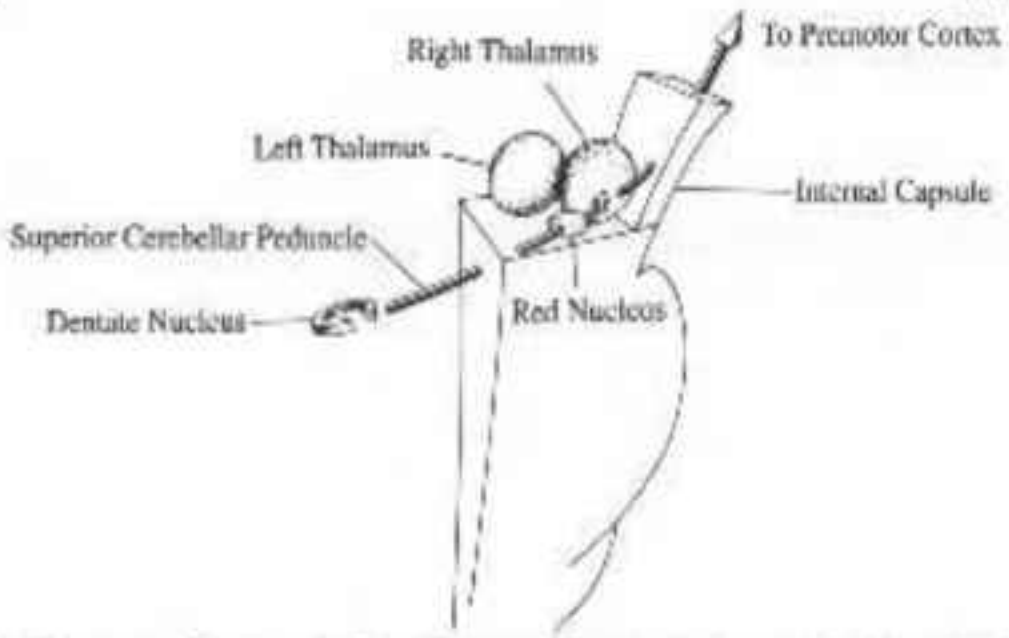
CLINICAL-ANATOMIC CORRELATION

The correlation between extrapyramidal signs and basal ganglia anatomy is only fair. Degeneration of the substantia nigra correlates with Parkinson's disease; the subthalamic nucleus correlates with ballismus‡.[24] A lesion in the red nucleus causes a hybrid of subthalamic nucleus, substantia nigra, and cerebellar signs: a coarse and somewhat proximal (like ballism) resting tremor (like a Parkinsonian tremor), which worsens with intention (like cerebellar tremor).[25] Situated directly in the mainstream of cerebellar outflow fibers targeted for the contralateral thalamus (see next chapter), the red nucleus cannot help but superimpose an intentional (cerebellar) component onto a resting (extrapyramidal) tremor.

Demented: Some Parkinsonian patients *are* modestly demented (and depressed), but not as much as their bradykinesia would suggest.[23]

Hypotonic: Diminished tone—floppy, flaccid.

Ballismus: Some patients with ballismus have had lesions outside the subthalamic nucleus.[22]



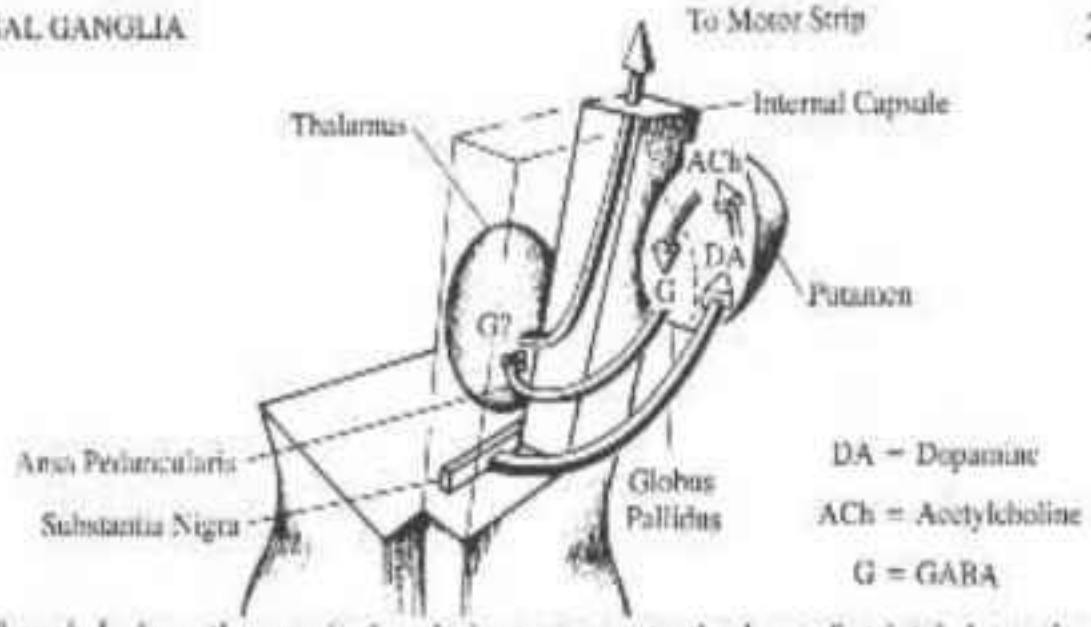
So far, chorea,[26] athetosis,[27] and dystonia[28] have no clear anatomic substrate, apparently because their dysfunction is chemical, not structural. The bradykinesia and rigidity of Parkinson's disease is somehow related to loss of dopamine released in the putamen and caudate nucleus (corpus striatum) by axons from the substantia nigra. These nigrostriatal fibers normally inhibit a small cell confined to the striate nucleus. This small cell, when not inhibited by the substantia nigra, releases acetylcholine which in turn stimulates a third cell. This third cell only extends as far as globus pallidus where it releases the inhibitory neurotransmitter, GABA, onto a fourth neuron. From the globus pallidus, this fourth neuron extends across (and circles around) the internal capsule to synapse in the ventrolateral and ventroanterior nuclei of thalamus. Like the third order neuron, this fourth order neuron may also release GABA*. The ventrolateral and ventroanterior nuclei, meanwhile, project their output up the internal capsule to the premotor cortex*, providing the entire basal ganglia with a wide open channel to modulate voluntary movements*.[29]

GABA: Besides sending a neuron across the internal capsule to the thalamus, the globus pallidus also sends a GABA-ergic neuron back down the midbrain to cool off the substantia nigra (feedback inhibition).

Premotor Cortex: The area of frontal lobes anterior to the motor strip. The premotor cortex, in large part, directs the motor strip.

Modulate Voluntary Movements: The basal ganglia do more than just modulate motor activity. There's good evidence that many movements, especially routine ones like walking, running, even perhaps copulation and fighting, are preprogrammed in the basal ganglia[24] (i.e., no conscious thinking is necessary to execute them). Sudden movements, too, are probably preprogrammed at a subcortical level. For example, in sudden danger, we freeze or flee. We don't think about it—we just do it. Freezing up is every bit a "movement" as fleeing; we freeze because agonist and antagonist muscles contract with equal force. Fleeing and freezing are preprogrammed, simply waiting to be sprung into action by any sudden, intense emotion. The neurologic trumpet calling for sudden action is probably nucleus accumbens, part of the mesolimbic system in front of the caudate nucleus. With direct connections to the substantia nigra and to the ventral tegmental area lying adjacent to the substantia nigra, nucleus accumbens can rapidly usurp the entire motor system with highly charged instructions to freeze or flee.[25]

Another good example of preprogrammed extrapyramidal movements occurs with damage to an internal capsule. The patient's paralyzed face may suddenly light up with a normal smile when the patient is told a funny joke. Presumably, emotional movements (like facial expressions) detour around the infarcted internal capsule through alternative routes in the basal ganglia.



Though L-dopa therapy is the obvious answer to the loss of striatal dopamine in Parkinson's disease, another useful therapy is anticholinergic medication like Artane and Cogentin. These drugs specifically counteract the acetylcholine released by the intrastriatal small cell.

When too much L-dopa is administered, chorea develops, presumably because the small intrastriatal cell is overly inhibited and not enough GABA is released by the third and fourth order neurons. In Huntington's chorea* the small cholinergic cells degenerate, contributing to a paucity of GABA.[33] In other forms of chorea—Sydenham's chorea* and familial chorea—the chemistry is less clear.

The treatment rationale for chorea would be to 1) reduce dopamine (by withdrawing any L-dopa therapy), 2) block dopamine, which is what phenothiazines do, 3) pump the striatal small cell to make more acetylcholine by giving precursors to acetylcholine,[34] or 4) increase the GABA levels to cool off the substantia nigra.[35]

Another common choreiform movement disorder is tardive dyskinesia*, a side effect of phenothiazine tranquilizers.[36] The extra movements involve the face, mouth, tongue, but can also affect the hands and even the feet. At times the movements are rhythmic, similar to a Parkinsonian tremor. In fact, a second look may reveal more than just a semblance of Parkinsonian tremor; the whole patient may look Parkinsonian with a masked face, diminished eye blink frequency, and bradykinesia. The chemical explanation for this Parkinsonian picture stems from phenothiazine's blockade of dopamine receptors in the striate nucleus. To counteract this clinical side effect, anticholinergics (Cogentin or Artane) are often administered as an adjunct to phenothiazines.

Huntington's Chorea: An incurable, genetic (autosomal dominant—half the patient's children will develop it) illness brought to America from England in 1630. It took until 1872 before George Huntington, a Long Island physician, wrote its first clear description. Though caudate atrophy is the most striking and characteristic autopsy finding, the cortex also suffers the ravages of this invariably fatal disease. Patients develop personality disorders (irritability, depression, irrational outbursts) and progressive dementia in early to middle life along with uncontrollable chorea.[37]

Sydenham's Chorea: One of the cardinal signs of acute rheumatic fever.

Tardive Dyskinesia: Tardive is related to the word tardy. Dyskinesia refers to jerky incoordination resulting from volitional movements broken up by chorea. Tardive dyskinesia is a movement disorder which begins after the patient has been on phenothiazines for a while—usually a year, but sometimes only after a few months. Also known as oral-facial dyskinesia.

If you spotted the paradox in the last paragraph, congratulations. On the one hand phenothiazines can cause a paucity of movement (not enough L-dopa) and on the

other hand chorea (too much L-dopa). How can phenothiazines do both? Neurochemists have been stroking their beards over this one for a long time. The best explanation so far is that the blockade of normal dopamine receptors somehow supersensitizes them to dopamine, and also stimulates the synthesis of new dopamine receptors.[37] Chorea develops because dopamine from the substantia nigra and dopamine circulating in the bloodstream now exert a more powerful effect in the caudate and putamen. And if the phenothiazines are ever withdrawn, the supersensitive dopamine receptors are exposed to the normal flow of dopamine from the substantia nigra, to which they respond with excess activity, or chorea*.

Because of the widespread use of phenothiazines, it should be clear why the major cause of extrapyramidal signs is iatrogenic (caused by doctors). But, iatrogenic or not, the pathognomonic signs of basal ganglia dysfunction are still: rigidity, masked face, infrequent eye blinks, bradykinesia, festinating gait, retropulsion, soft twittery voice, resting tremor, chorea, ballismus, athetosis, dystonia (snapshot of athetosis), and the glabellar reflex. Most of the time the signs are bilateral, but on occasion the signs are unilateral, especially ballismus. In such cases the cerebral pathology is contralateral to the abnormal movement or posture.

Chorea: Isn't it interesting that phenothiazines, so effective against schizophrenia, cause Parkinsonian signs? In fact, the more effective the phenothiazine, the more severe the Parkinsonian side effects.[38] Why should dopamine blockers be so effective against schizophrenia?

There are high concentrations of dopamine receptors at the termination of the nigrostriatal pathway in the caudate nucleus and putamen.[39] Right next to the substantia nigra lies another midbrain structure, the ventral tegmental area, which also projects a richly dopaminergic pathway, this time to the nucleus accumbens and anterior perforated substance, part of the mesolimbic system at the anterior tip of the caudate nucleus.[40] As critical parts of the limbic system, these two structures have long been associated with emotions and moods.

An interesting parallel was pointed out by Dr. Janice Stevens between the dopamine-containing striate nucleus and the dopamine containing nucleus accumbens and anterior perforated substance (NAAPS).[41] Both of these dopamine sensitive structures receive input from the midbrain: the striate nucleus from substantia nigra and the NAAPS from the ventral tegmental area lying just in front of the substantia nigra. Dr. Stevens reasoned that if both nuclear complexes receive dopamine-containing axons, then just as the striate nucleus inhibits the substantia nigra with GABA (via globus pallidus), so might the NAAPS inhibit the ventral tegmental area with GABA. She tested this hypothesis by dripping minute amounts of a GABA inhibiting drug onto the ventral tegmental area of a live cat's brain. This presumably allowed the ventral tegmental area to escape from normal inhibition by the NAAPS, and thereby release large amounts of dopamine into the NAAPS. Though she didn't look for a rise in dopamine levels in the NAAPS, the cats became about as schizophrenic as a cat can get. Similarly, when they directly stimulated the ventral tegmental area, Stevens and Livermore elicited fearful behavior.[42]

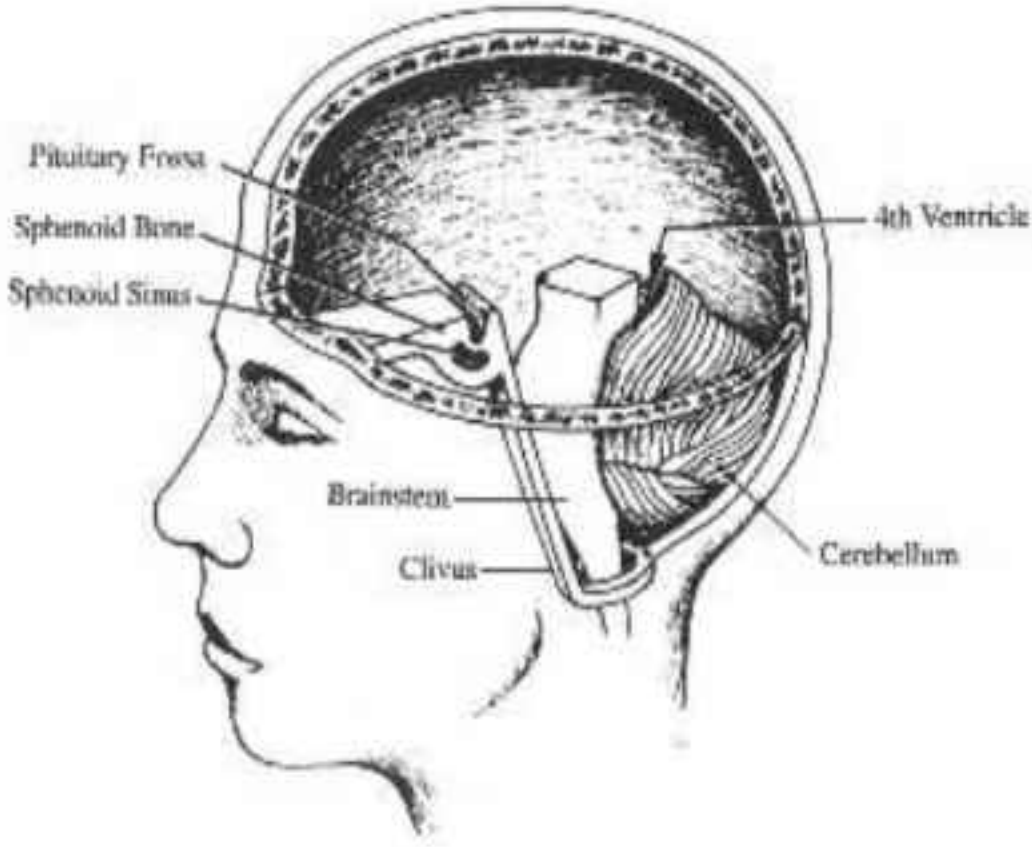
There is also evidence that phenothiazines work their magic in the nucleus accumbens.[43] So far, however, no one has been able to attribute schizophrenia directly to faulty dopamine receptors even though elevated dopamine and dopamine receptors have been found in the brains of schizophrenics off phenothiazines.[44]

Part of the difficulty working with dopamine receptors is that they're found in a large number of sites; and depending on what it's connected to, a dopamine receptor in, say, nucleus accumbens may produce an entirely different set of signs than the same dopamine receptor in the caudate nucleus. To make matters worse, there are at least two kinds of dopamine receptors.[45] So, dopamine-blocking drugs may affect one or both dopamine receptors in one or more separate sites, all of which make it difficult to draw definite conclusions about dopamine receptor function.

Iatrogenic: Caused by doctors.

CEREBELLUM

We now have under our belt the pathognomonic signs of three important areas of the nervous system. Let's go on to the cerebellum, another pure motor structure. The cerebellum sits right behind the fourth ventricle, a pyramid-shaped fin of cerebrospinal fluid snugly cloaking the backside of the brainstem. The brainstem, in turn, stands like a ski jumper in flight, bellied up against the gently inclined clivus*. The

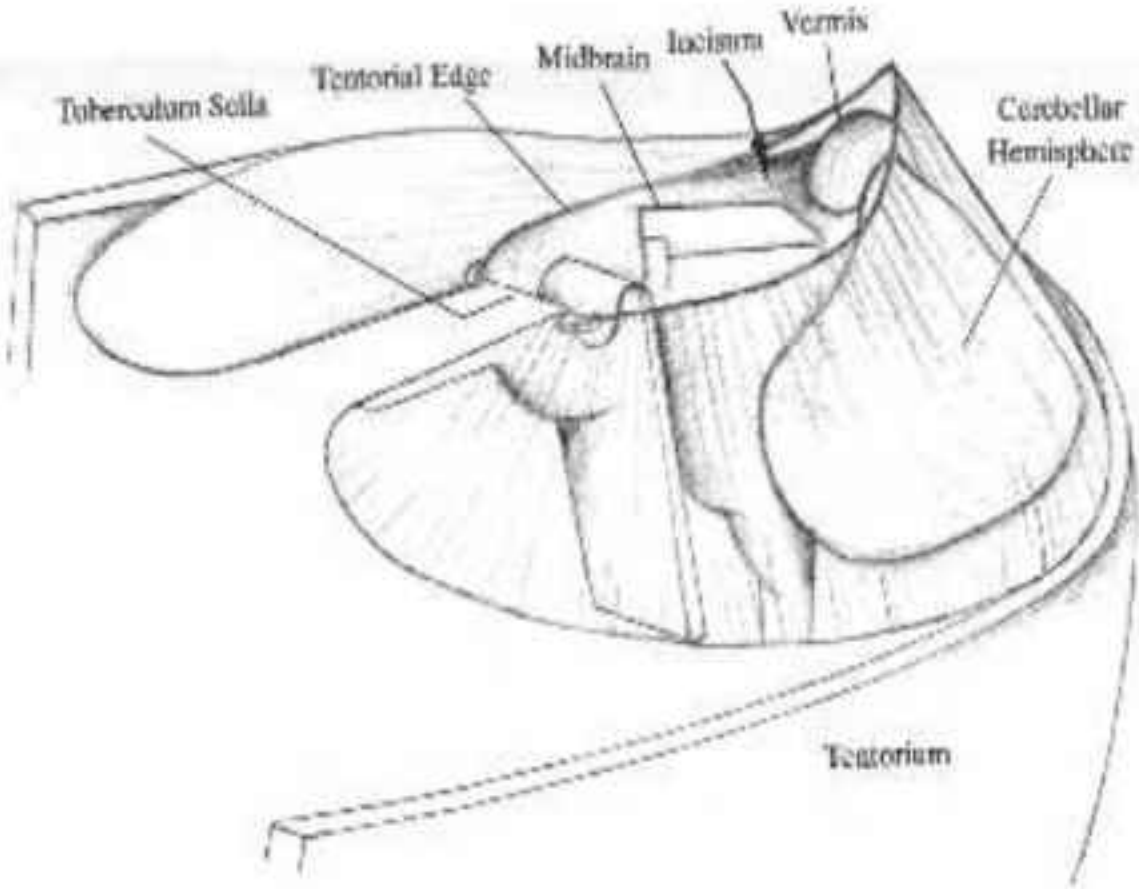


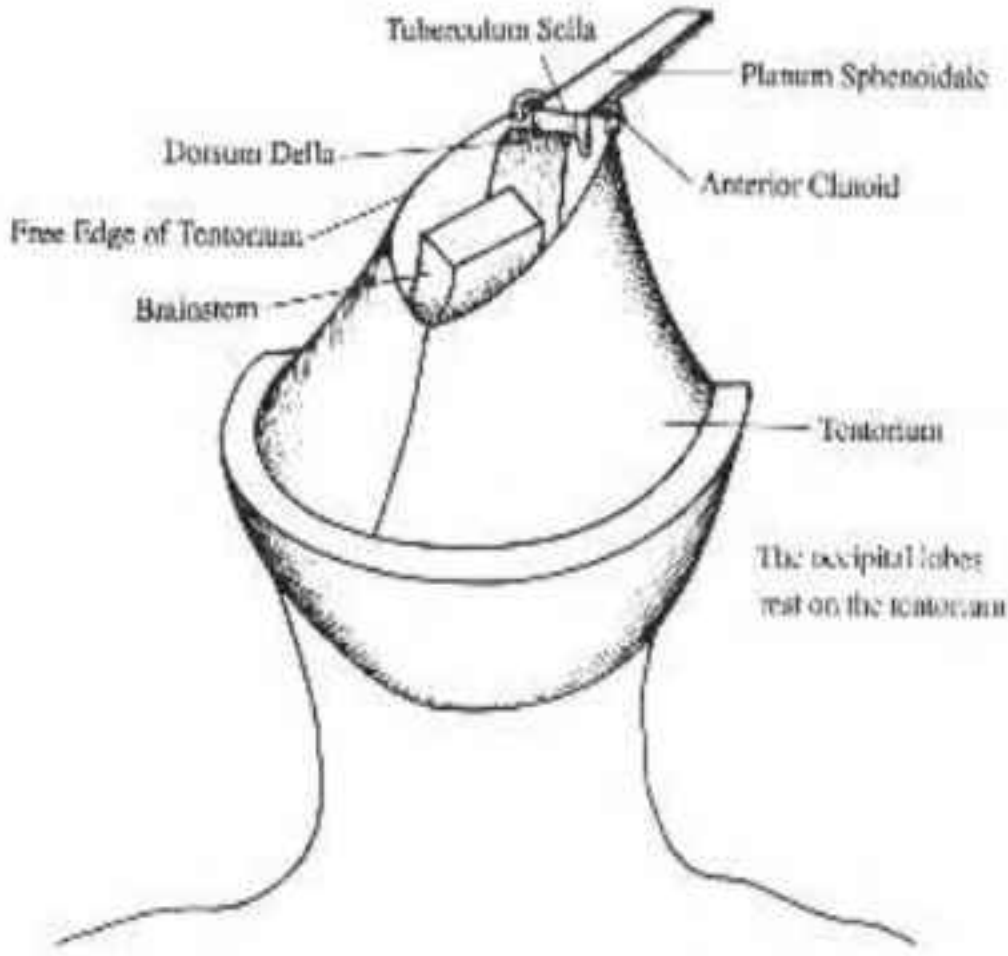
area behind the clivus, below the tentorium*, and above the foramen magnum is the 'posterior fossa,' containing the three posterior fossa* structures: cerebellum, fourth ventricle, and brainstem.

Clivus: Clivus means slope (which it does).

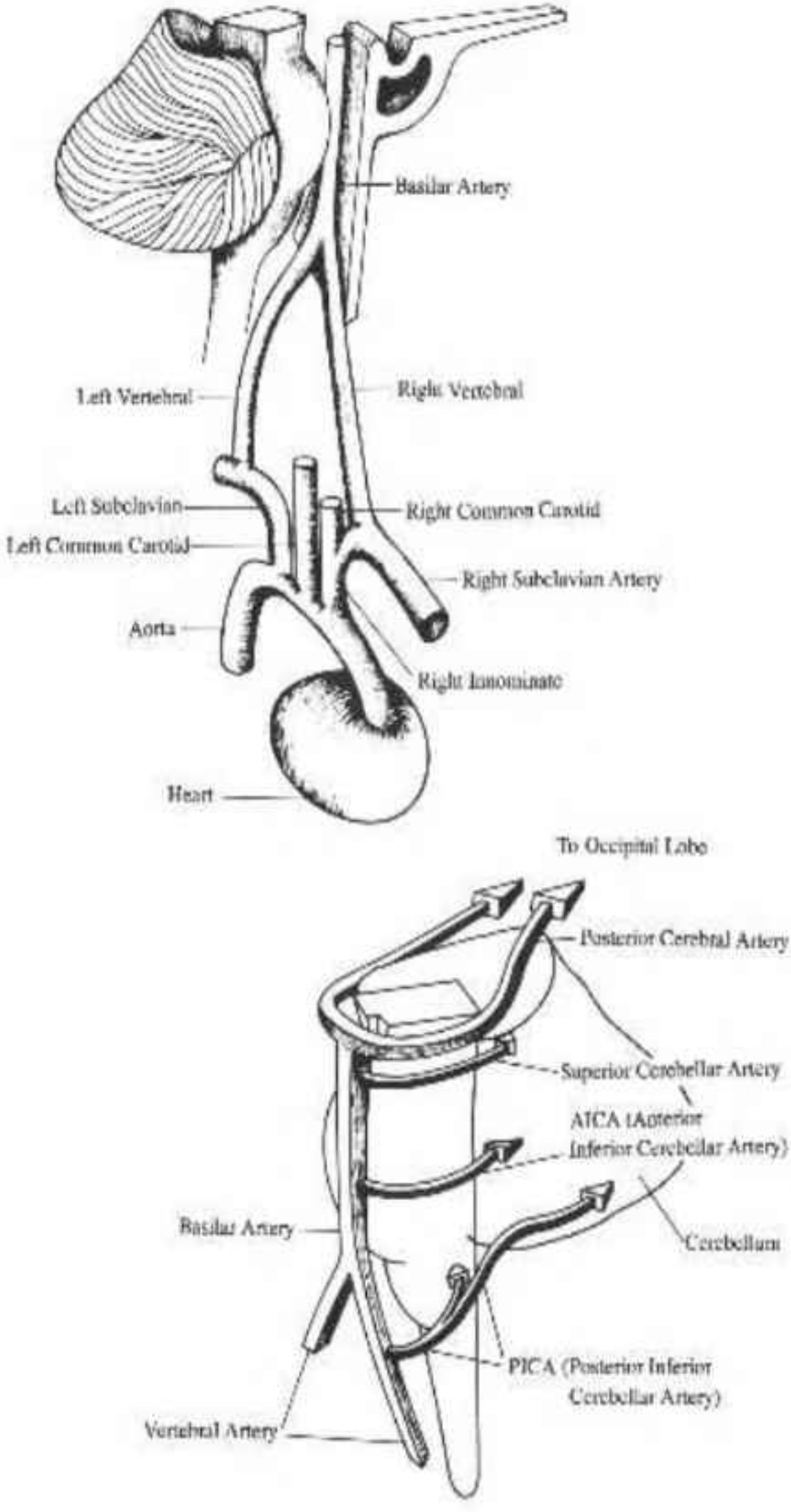
Tentorium: A tough membrane spread out over the top of the cerebellum, separating it from the occipital lobes (tentorium means tent). Anteriorly, the free edge of the tentorium wraps around each side of the midbrain, attaching itself to the anterior clinoids. The gaping passageway for the midbrain is called the incisura.

Posterior Fossa: (Fossa=trench) The middle fossa contains the temporal lobe; the anterior fossa, the anterior halves of the frontal lobes.





Between the brainstem and clivus slips the basilar artery bearing blood for the brainstem and occipital lobes.

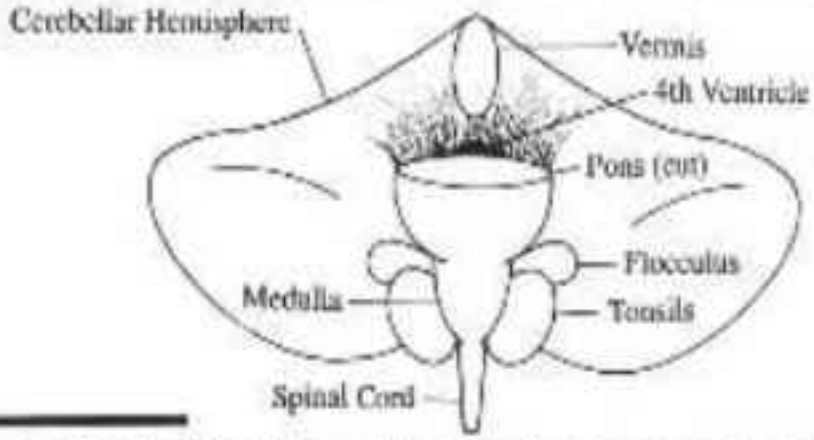

Basilar Artery
Left Vertebral
Right Vertebral
Left Subclavian
Right Common Carotid
Left Common Carotid
Right Subclavian Artery
Aorta
Right Innominate
Heart
To Occipital Lobe
Posterior Cerebral Artery
Superior Cerebellar Artery
AICA (Anterior
Inferior Cerebellar Artery)
Basilar Artery
Cerebellum
PICA (Posterior Inferior
Cerebellar Artery)
Vertebral Artery

SIGNS[2]

The job of the cerebellum is to smooth out movements, to make them more accurate by preventing under- or overshooting* a target. You can learn the signs of cerebellar dysfunction by sitting in any bar because alcohol fancies the cerebellum. Watch a drunk reach for his drink. His hand sways back and forth as it nears the glass—an intention tremor*, or cerebellar dysmetria*. Sometimes a cerebellar tremor is also present with the arms outstretched (postural tremor), but the tremor almost always worsens with intention.[3] A relatively common cerebellar tremor, called titubation, affects elderly people with a rapid, fine, bobbing motion of the head.

Our drunk friend has just gotten up to leave. He first spreads his feet apart to widen his base of support and staggers out the door. He tries to maintain the upright posture, but his trunk keeps under- or overshooting the vertical midline. The reeling, ataxic* gait resembles a sailor who first steps ashore after a long time at sea. This side-to-side imbalance of cerebellar ataxia stands in curious contrast to the front-to-back imbalance of Parkinsonian patients.

Limb dysmetria and gait ataxia correlate with the two major divisions of the cerebellum. The midline of the cerebellum, the vermis*, controls the midline of the body—truncal ataxia—while the periphery of the cerebellum, the cerebellar hemispheres, control the periphery of the body—limb dysmetria.[4] Unlike the crossed pyramidal and extrapyramidal systems, the right cerebellar hemisphere controls the right arm and leg; the left cerebellar hemisphere, the left arm and leg.



Under- or Overshooting: How the cerebellum smooths out movements is still unclear, but at least some investigators feel the cerebellum works by inhibiting antagonistic muscles during movement. Every joint in the body is controlled by two (or more) opposing muscles, a good example being the biceps and triceps. When either muscle contracts, the other one relaxes. This cooperation may in part be controlled by the cerebellum for smooth coordination.[4]

Intention Tremor: Many elderly people develop a fine hand tremor, different from a typical cerebellar intention tremor. The physiology is thought to be the same as that causing benign essential (idiopathic) tremor and familial tremor.[3] It's still not clear, however, whether essential tremor is due to central or peripheral nervous system dysfunction.[4]

Dysmetria: 'Mismeasured.' Dyskinetic movements are voluntary movements broken up by chorea; dysmetric movements are broken up by mismeasured efforts. Overshoot during an intended movement results when the cerebellum fails to activate the antagonist muscle in time to halt the limb on target. Each time the pyramidal tract tries to correct the overshoot by reversing direction, the hand overshoots again, causing an intention tremor.

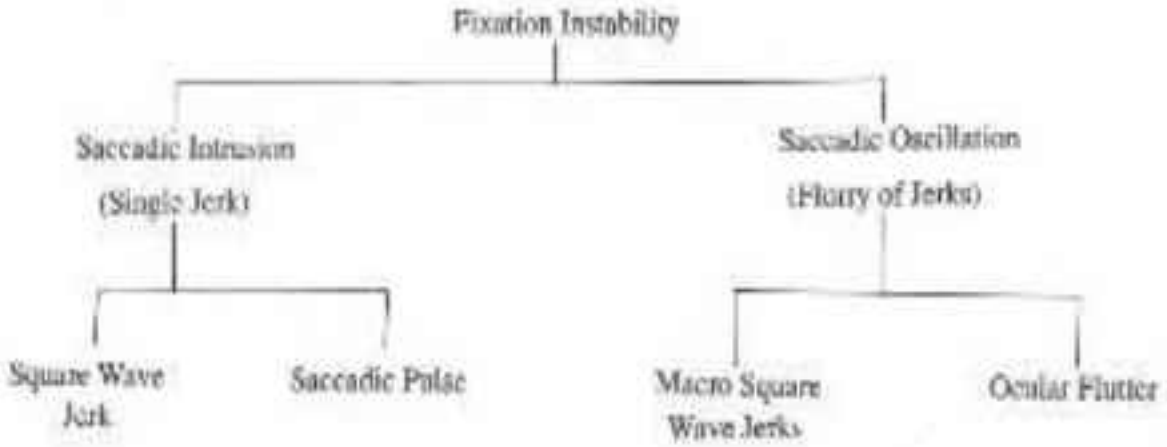
Ataxic: Disorderly in Greek.

Vermis: Worm-like, referring to its long, thin shape and its transverse ribs like those of a nightcrawler.

The cerebellar vermis and its flocculi (small outpouchings from the posterior vermis) comprise one of the busiest and most useful areas of the brain. Besides maintaining truncal coordination, the vermis and flocculi also have a major say in eye movements. Like the whole cerebellum, the vermis and flocculi work like a miniature computer to calculate the muscular effort necessary to maintain the eyes in a fixed position or, when glancing at a peripheral target, to reach that target without under- or overshooting it. If the vermis and flocculi aren't working properly, the patient's eyes intermittently 'shiver' back and forth when looking at a fixed or moving target, called fixation instability*. And when trying to maintain gaze off to one side, the eyes drift back to midline and must be jerked back to the target, which you see as coarse nystagmus. Glancing at something to the side, the patient's eyes consistently over- or undershoot and zero in with one or two small, ricocheting corrections—analogous to an intention tremor—called ocular dysmetria.[10]

Finally, wide receivers depend heavily on their cerebellar vermis and flocculi to maintain visual control while looking over their shoulder to catch a pass. Here's why. When you slowly rock your head back and forth while looking at a stationary target, your eyes must rotate in exactly the opposite direction to maintain visual fixation, called the vestibulo-ocular reflex.[11] When, however, you rotate your head to follow a *moving* target (like a football), you don't want your eyes to counter-rotate; you want your eyes keep up with the target. This requires that you suppress the vestibulo-ocular reflex, another job for the vermis and flocculi.[12]

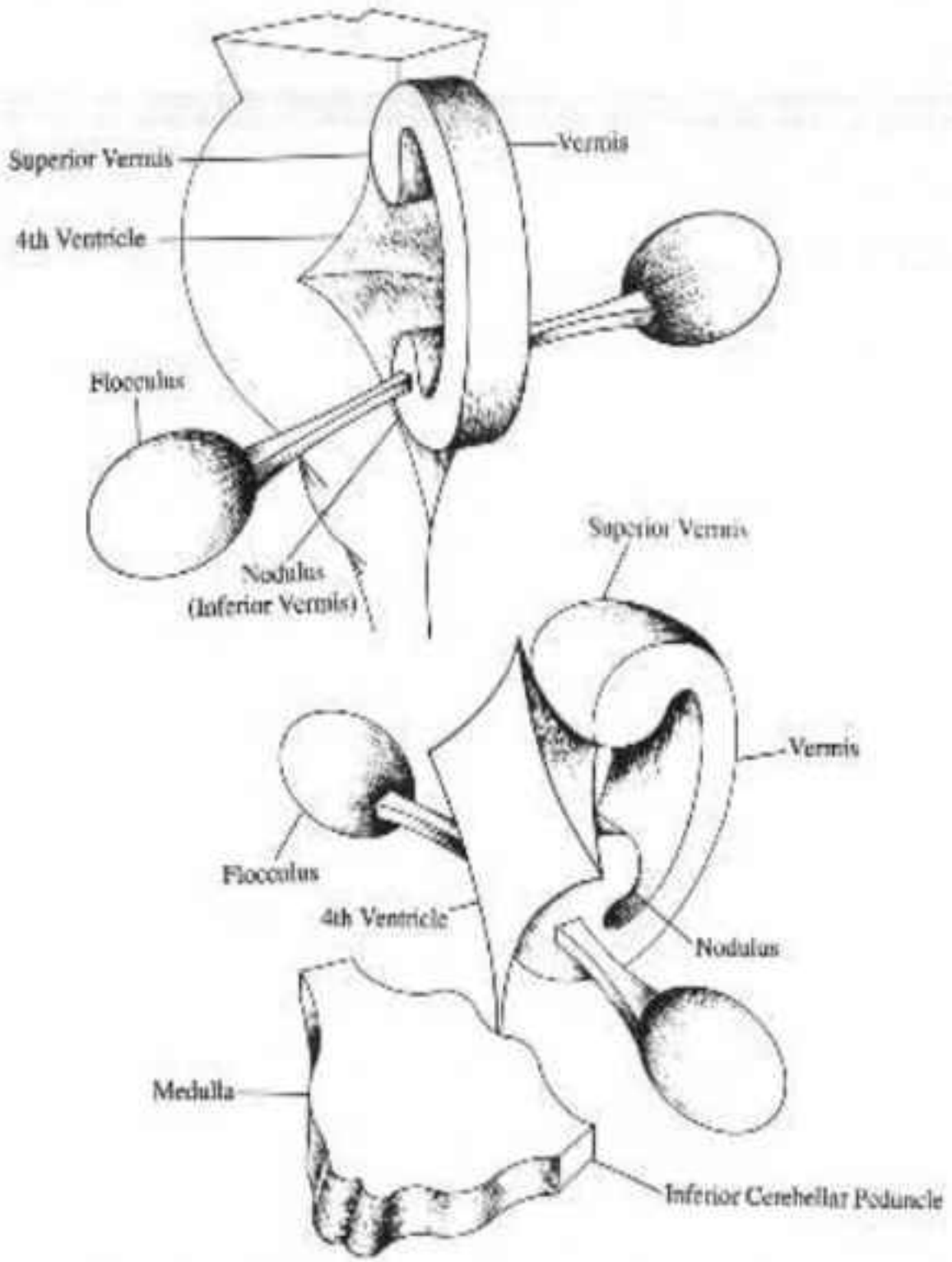
Fixation Instability: There are two main types of fixation instability.[7] In one type, called saccadic intrusions, the eyes dart off target to one side and quickly return. In the other type, called saccadic oscillations, the eyes briefly shiver back and forth before locking back on target. Saccadic intrusions and saccadic oscillations are further broken down into two groups, depending on how much time the eyes remain off target before darting back. (The pause, too fast for our eyes to measure, can be recorded electronically.)



As the names imply, square wave jerks and macro square wave jerks spend about 200-300 msec off target, while saccadic pulses and ocular flutter jerk back to the target without the 200-300msec 'intersaccadic latency.'

The most extreme example of fixation instability is opsoclonus (also probably of cerebellar origin), part of the 'dancing eyes, dancing feet' syndrome: truncal ataxia and wildly chaotic, lightning fast random eye movements.[9] In infants opsoclonus surfaces in some mysterious way as a remote effect of a distant neuroblastoma, a malignant tumor of primitive neural crest cells.[6]

During fetal life neural crest cells migrate to distant sites where they differentiate (specialize) into various tissues like the adrenal medulla. Neural crest cells destined to become neurons in sympathetic and parasympathetic ganglia are called neuroblasts.



Speech is also affected in cerebellar disorders. If you listen to cerebellar speech with your eyes closed, the volume, pitch, and cadence of the speech sound just like the gait—reeling and lurching. No longer are words clustered into well modulated phrases. Instead, prolonged emphasis is given to the syllables we normally slur over. The speech pauses when it shouldn't and then lurches forward with a blurted-out phrase. The chaotic pitch may suddenly rise too high and then unexpectedly plummet. This unmistakable ataxia of speech is called scanning speech.[13]

Though strength is virtually unaffected in cerebellar diseases, the limb may fatigue easily, a phenomenon called 'neurasthenia.'[14] The tone in cerebellar dysfunction is hypotonic.[15] Besides directly shaking the arms, you can also demonstrate cerebellar hypotonia by tapping a patellar tendon (knee jerk) with the leg hanging free. Instead of coming to rest after one or two swings, the leg continues to swing like a pendulum.

To test cerebellar function, all you have to do is listen to the patient's speech, look at his tandem walk (vermis), and watch him do finger-nose-finger and heel-shin (cerebellar hemispheres). Tandem walking is like walking on a railroad track, touching heel to toe. You have to use your head when testing tandem walk. A stooped Parkinsonian or a badly hemiparetic patient won't be able to tandem walk either, but in those two cases the inability to tandem walk is about as bad as their usual gait. Vermis dysfunction produces a disproportionate difficulty with tandem walking.

Finger-nose-finger simply means having the patient touch your finger then his nose, back and forth. If his finger wavers as it nears your finger or if he keeps missing the tip of his nose because of an intention tremor, there is something wrong with the ipsilateral cerebellar hemisphere*. Heel-shin means having the patient rub his heel up and down his tibia. Cerebellar dysfunction produces a course, irregular, sideways tremor of the heel as it slides up and down the tibia. You can also test the cerebellar hemispheres by having the patient tap a spot with his hand or foot*. If the tap sounds and looks like atrial fibrillation—varying irregularly in rhythm, force, amplitude, and accuracy—he has an ipsilateral cerebellar hemisphere lesion.

ANATOMY AND PHYSIOLOGY

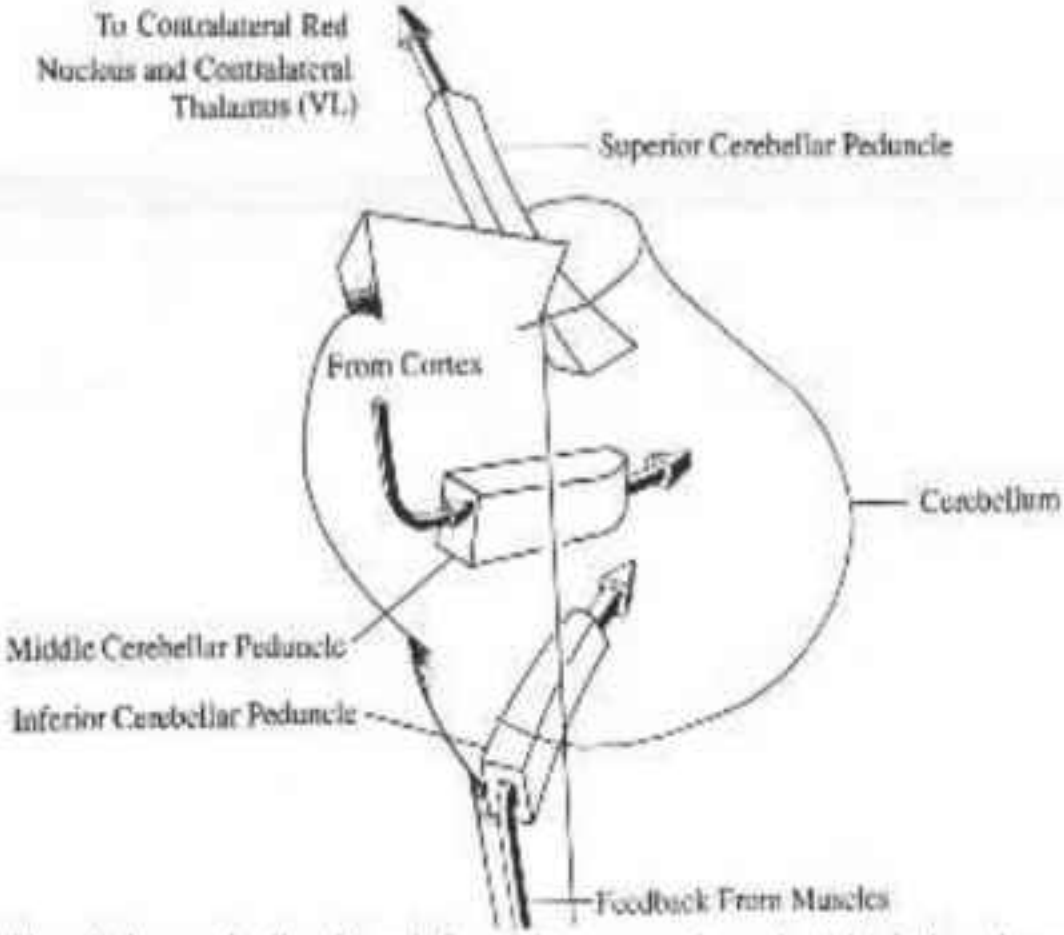
Cerebellar anatomy and physiology deserve a careful look-see because cerebellar dysfunction can be produced by lesions outside the cerebellum—either in the inflow tracts to or the outflow tracts from the cerebellum. With more cells in it than the rest of the central nervous system put together,[18] the cerebellum demands enormous input to keep it busy. The cerebellum has three major sources of information: labyrinths, muscles, and frontal cortex. The labyrinths provide the cerebellum with feedback for truncal balance. The muscles probably (no one has proved this yet) provide the cerebellum with feedback information during ongoing movements to keep the limb on course. The frontal cortex communicates with the cerebellum before a limb is moved probably to plan how much strength to exert and how long to exert that strength.

All information arriving and departing the cerebellum does so through one of three major tracts connecting the cerebellum to the brainstem. These three tracts are the inferior, middle, and superior cerebellar peduncles. In general, the inferior and middle cerebellar peduncles carry information into the cerebellum, and the superior cerebellar peduncle carries it out.

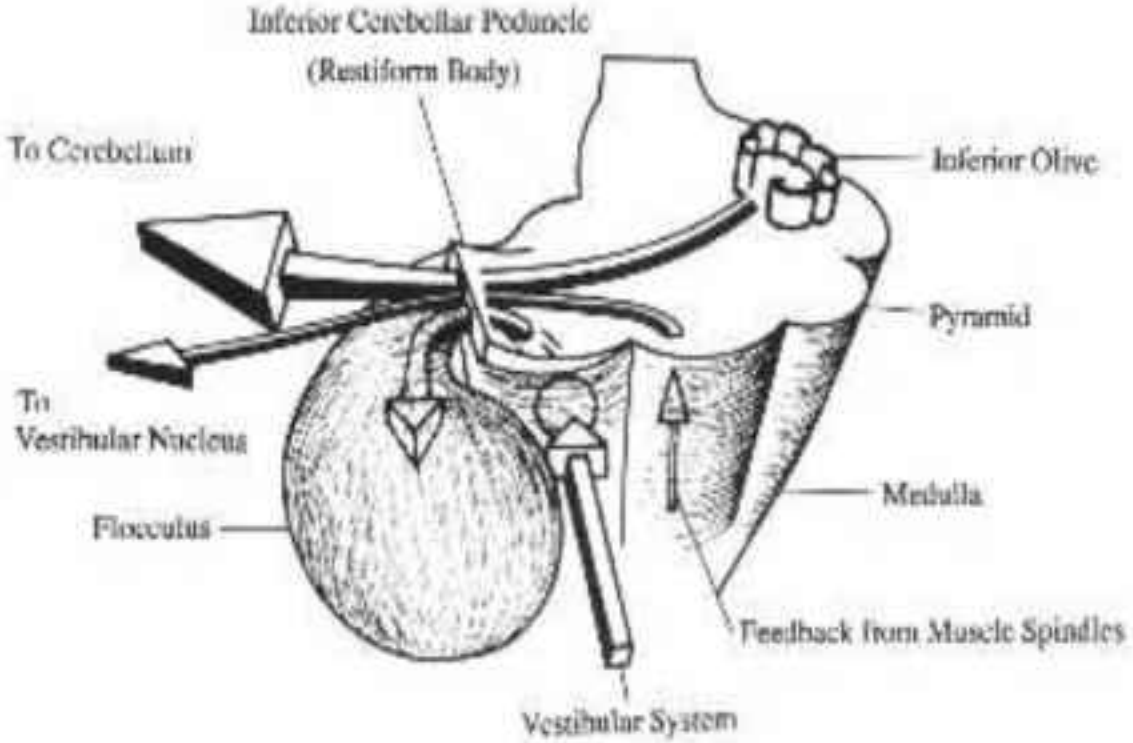
Ipsilateral Cerebellar Hemisphere: A patient with a cerebellar *hemispheric* intention tremor makes random mistakes to the right or left as he tries to touch his nose. Acute vestibular or cerebellar flocculus lesions will also cause the patient to miss his nose, but the mistakes are consistently off to one side (past pointing). Likewise, patients with vestibular lesions fall to one side rather than swaying back and forth like those with cerebellar vermis imbalance.[16]

A severe intention tremor begins to look a lot like intention myoclonus.[17]

Hand or Foot: Any rapid alternating movement will do, like flip-flopping one hand in the palm of the other, or rapidly revolving one hand around the other like a basketball referee signaling 'traveling.' Fast but inaccurate rapid alternating movements, varying in force, rhythm, amplitude, and accuracy, indicate ipsilateral cerebellar hemisphere dysfunction.

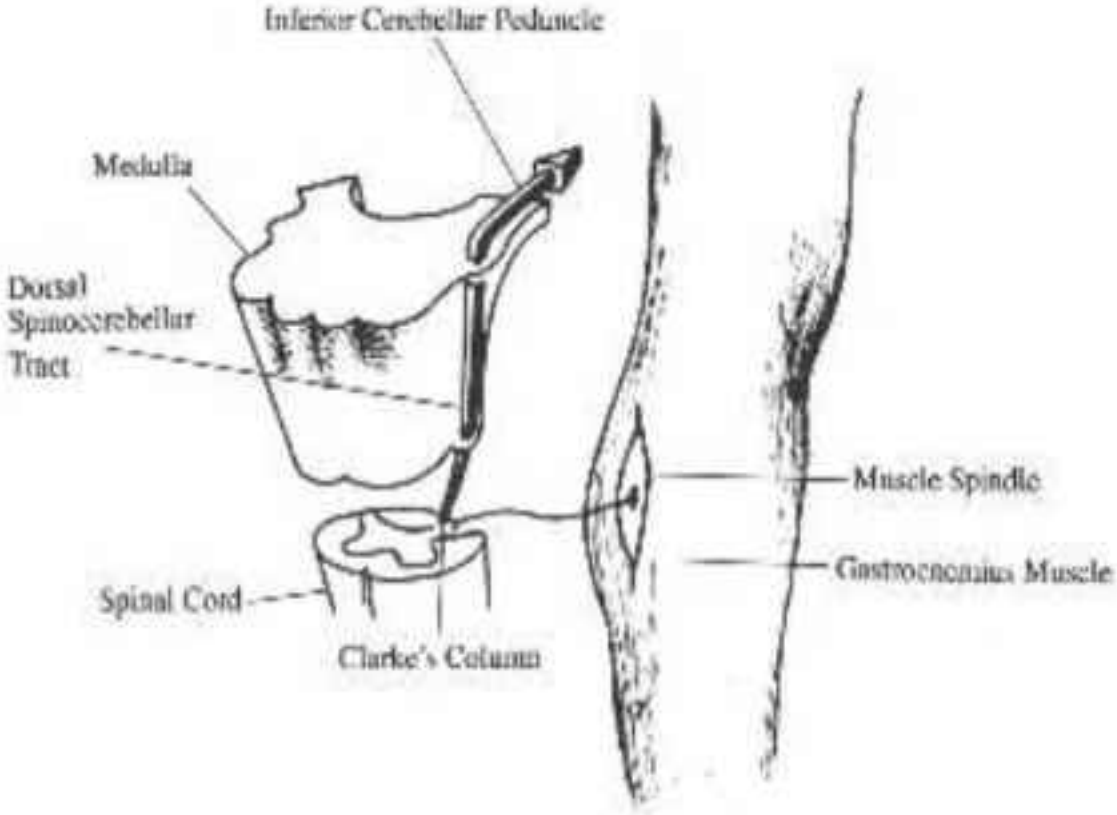


The phylogenetically oldest information comes from the labyrinth and projects by way of the inferior cerebellar peduncle to the phylogenetically oldest part of the cerebellum—the flocculo-nodular lobe.



Most of the input from the body's muscles travels up the cord in a tract called the dorsal spinocerebellar tract which also enters the cerebellum through the inferior cerebellar peduncle. The rest of the cerebellar-bound arm and leg fibers travel up the cord through another smaller tract, the ventral spinocerebellar tract, which continues upward, past the cut-off for the inferior cerebellar peduncle, to the superior cerebellar

peduncle where the ventral spinocerebellar tract takes a sharp curve backward into the cerebellum*.

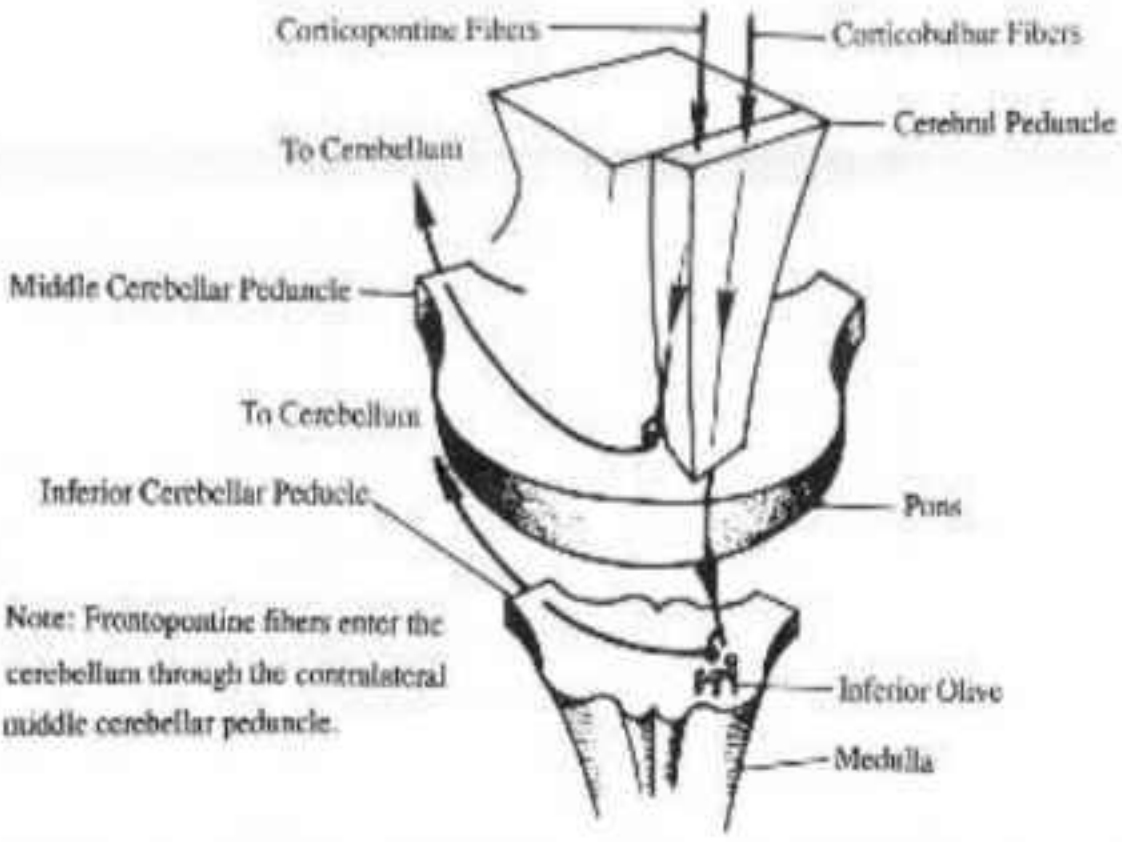


Information from the cerebral cortex reaches the cerebellum in two steps. Information first descends through the internal capsule, along corticopontine fibers to the pons and corticobulbar fibers to the inferior olive in the medulla. A second neuron then shoots back to the cerebellum, via the middle cerebellar peduncle from the pons, and via the inferior cerebellar peduncle from the inferior olive. To give you some idea of the intimate connections between the cerebral cortex and cerebellum, there are approximately nineteen million fibers descending through the cerebral peduncle, but only one million in the medullary pyramids.[19] Admittedly many of the missing eighteen million stopped at cranial nerve and other brainstem nuclei, but the great majority of those descending motor fibers bailed out in the pons and medulla to provide the cerebellum with important information for smoothly coordinated movements. This huge number of pontine fibers bridging* cortical information back to the cerebellum gives the pons its matronly midriff devoid of any cranial nerve nuclei.

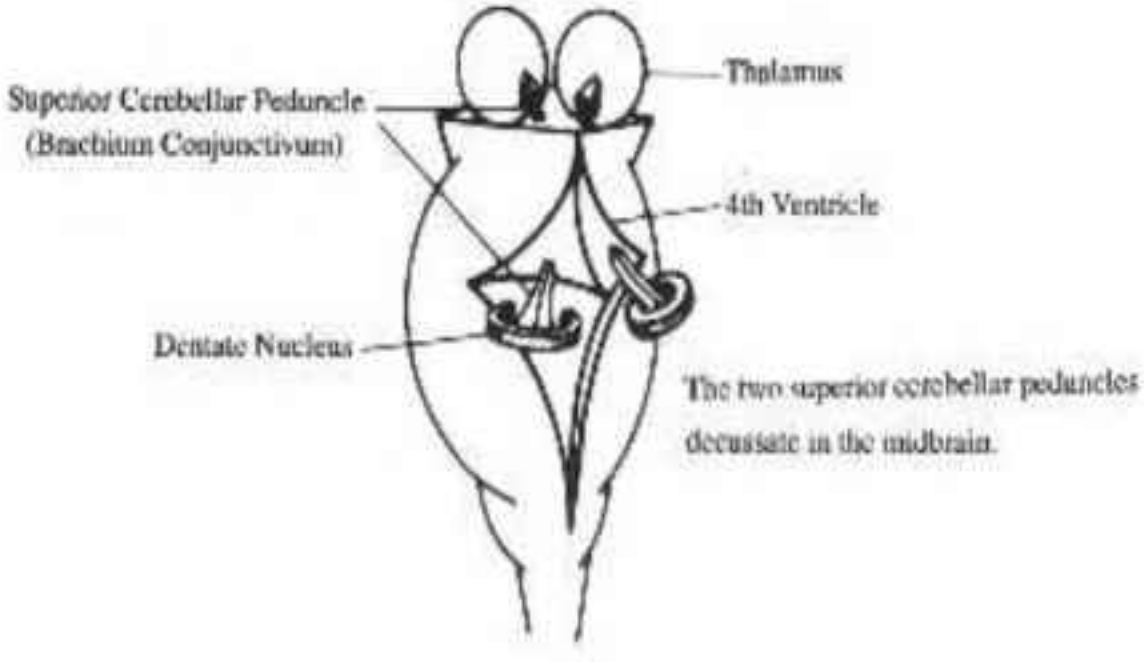
Into the Cerebellum: Despite providing such a prominent source of afferent fibers to the cerebellum, the spinal cord is rarely the source of cerebellar signs. Almost always cerebellar dysfunction is due to lesions within the cerebellum proper or its outflow tracts, occasionally in the pons (corticopontine afferent fibers), but almost never in the dorsal or ventral spinocerebellar tracts.

Information from the legs synapses in Clarke's column before ascending in the dorsal spinocerebellar tract to the inferior cerebellar peduncle. Unfortunately, there is no Clarke's column in the cervical cord, so input from the arms must first travel up the posterior columns of the spinal cord to the medulla before synapsing in the accessory cuneate nucleus. From the accessory cuneate nucleus cuneocerebellar fibers enter the inferior cerebellar peduncle into the cerebellum. The accessory cuneate nucleus, then, acts like Clarke's column for the legs.

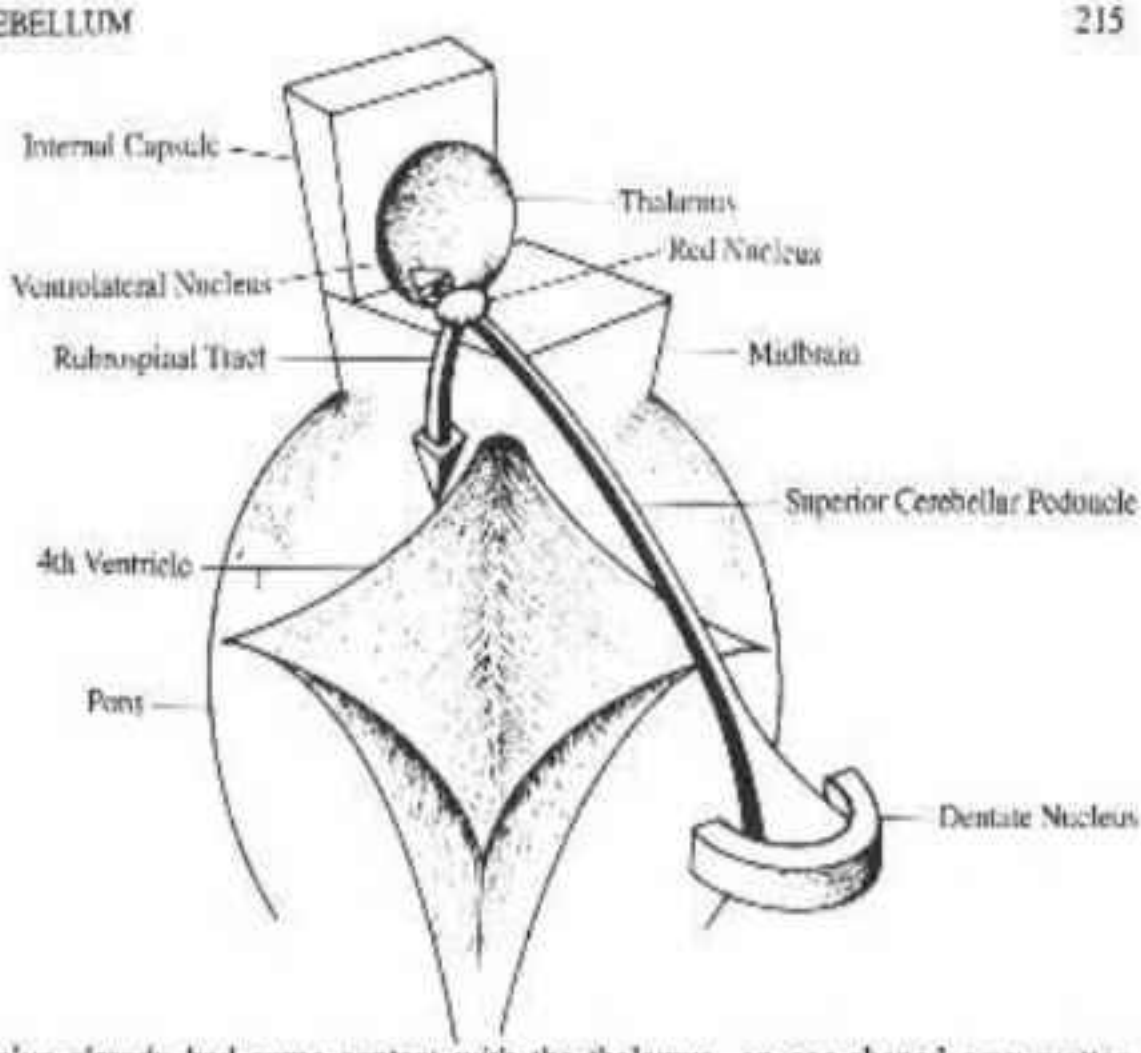
Bridging: Pons means bridge in French.



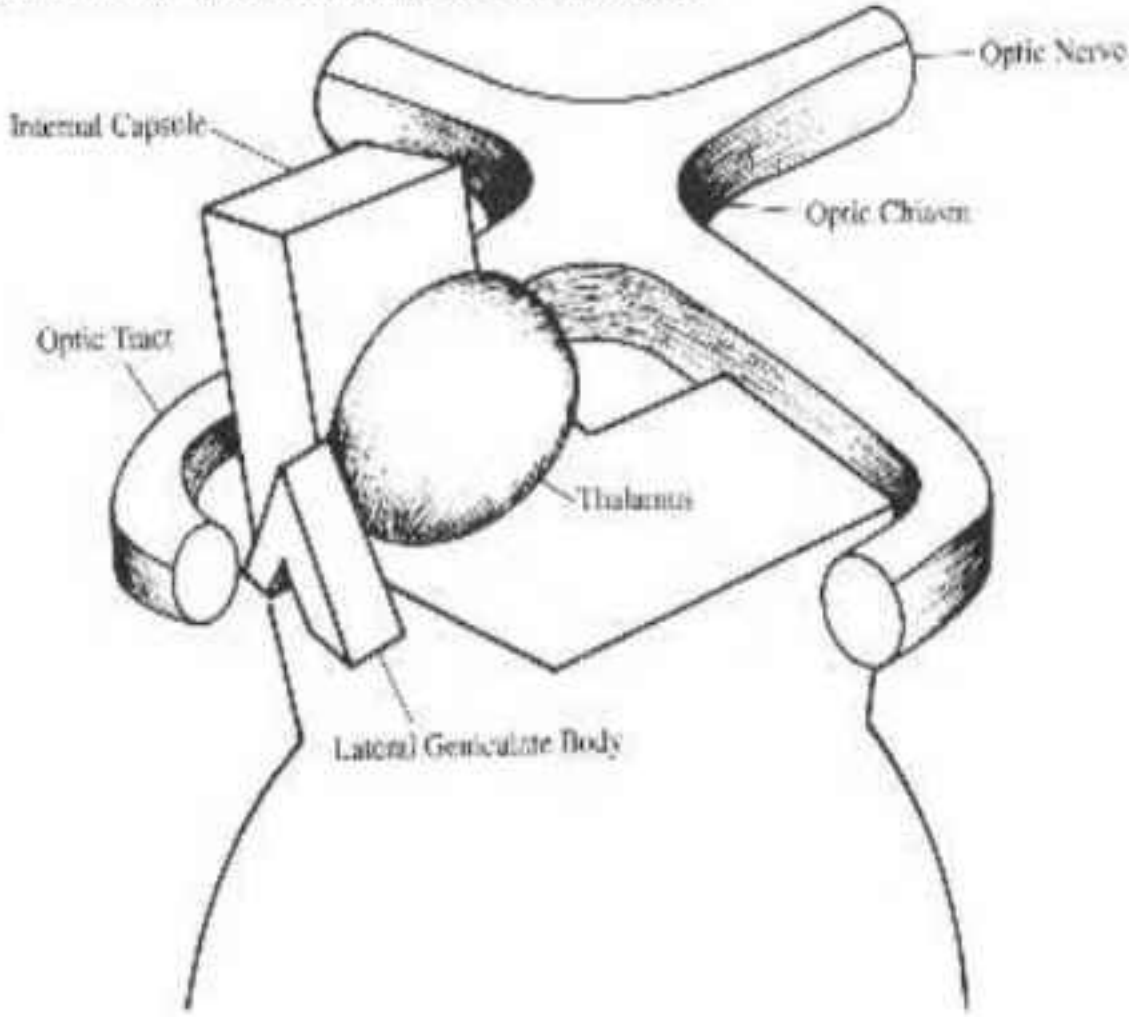
Cerebellar instructions exit via the superior cerebellar peduncle and head north(!) through the midbrain, en route to the contralateral motor strip to inhibit, smooth out, and modulate pyramidal (and extrapyramidal?) movements. The two superior cerebellar peduncles cross in the mesencephalon[4] before reaching their first synaptic destination in the contralateral thalamus. Some fibers don't make it all the way to the thalamus, synapsing instead in the contralateral red nucleus where instructions are then either relayed up to the thalamus or projected downward into the brainstem and spinal cord.

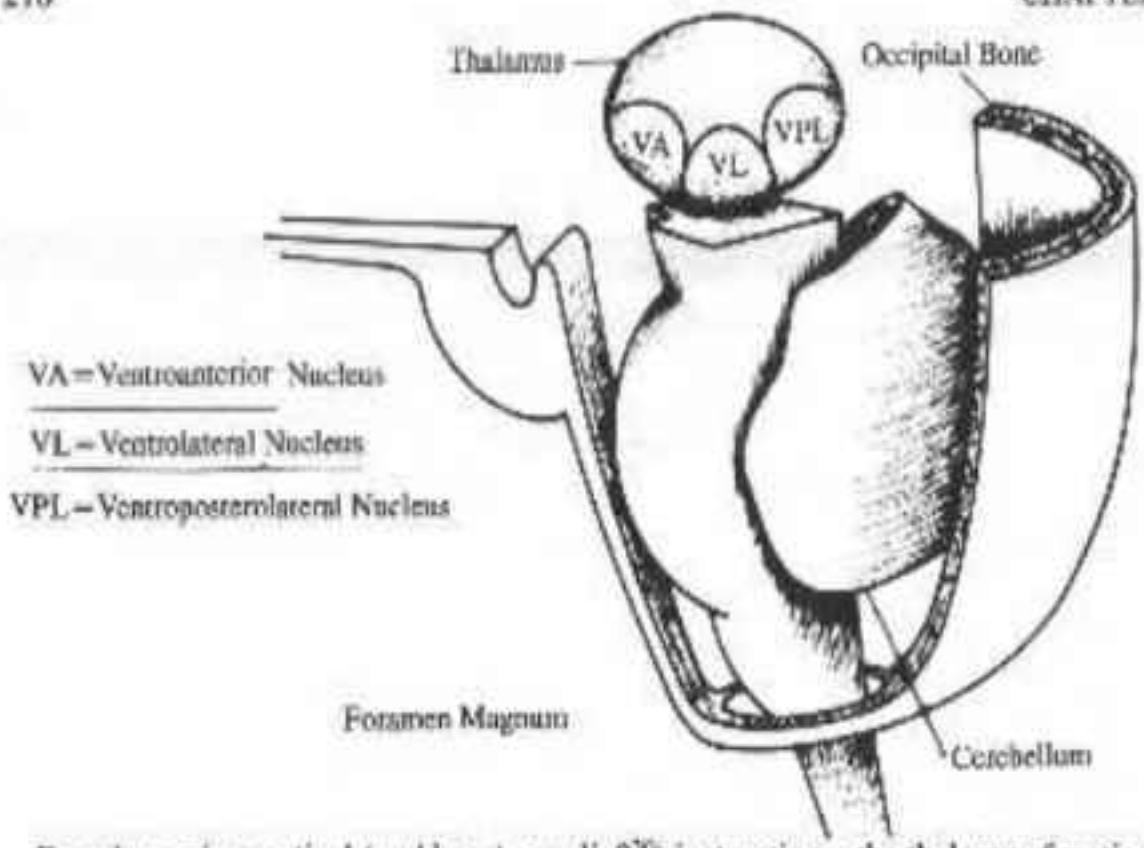


Mesencephalon: The mesencephalon is another name for the midbrain. The diencephalon is the thalamus and hypothalamus or any other structure bordering the third ventricle. The telencephalon refers to all hemispheric structures above the thalamus and hypothalamus.



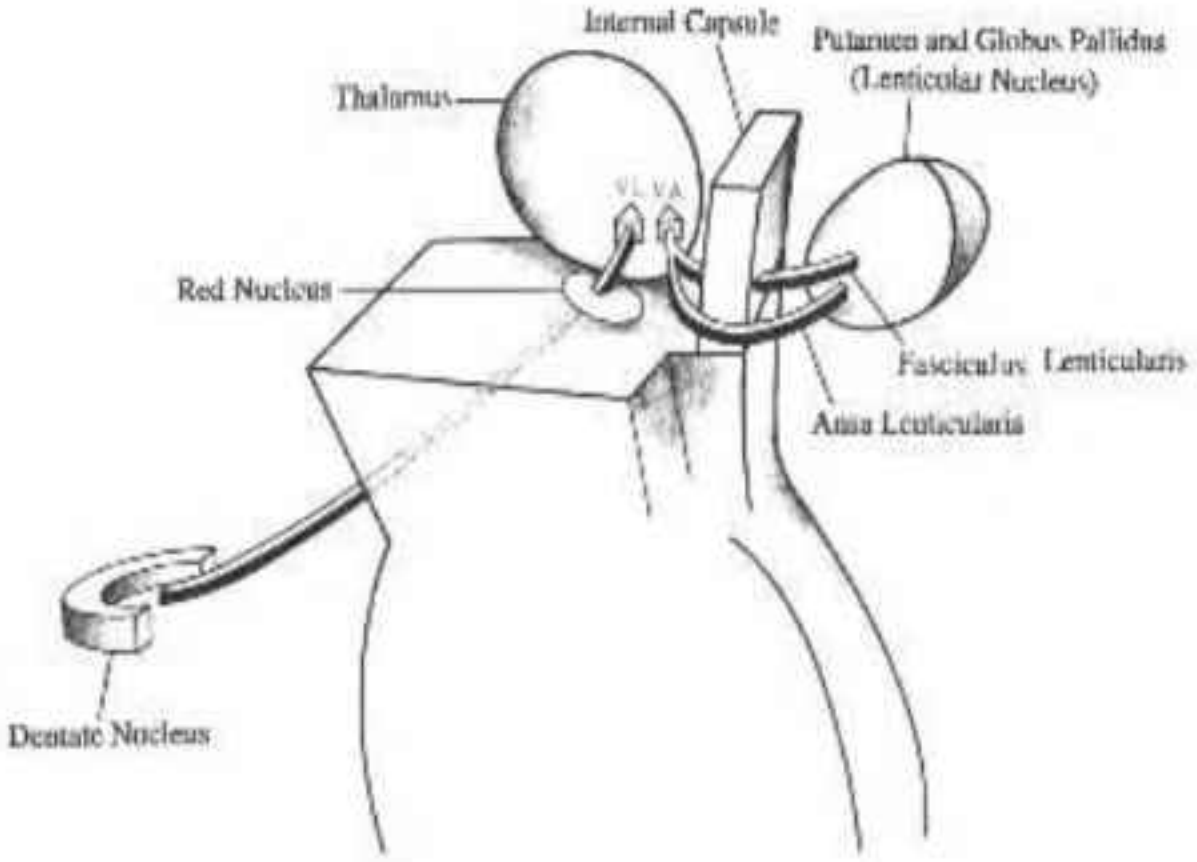
We've already had some contact with the thalamus, an egg-shaped gray matter structure perched atop the brainstem on either side of the third ventricle. While the optic tracts synapse in the lateral geniculate body at the back end of the thalamus, hearing, pain, temperature, touch, vibration, and proprioception ascend through the spinal cord and brainstem to synapse in three thalamic nuclei: medial geniculate body for hearing, ventral posterolateral nucleus for sensations from the body, and ventral posteromedial nucleus for sensations from the face.



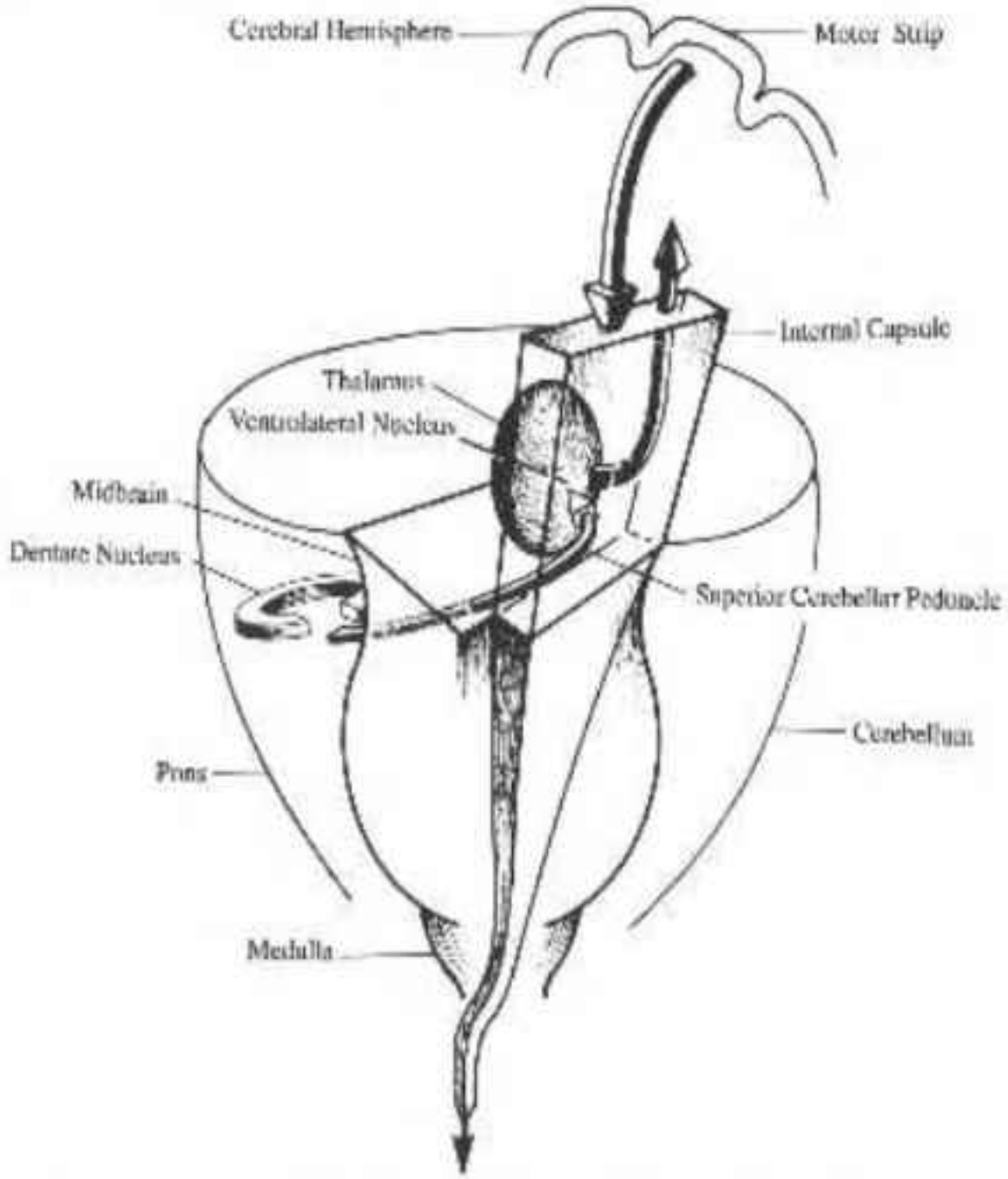


Based on prior cortical (and basal ganglia?[20]) instructions, the thalamus functions as a triage agent for the cortex. You'd think making important decisions about the bulk of sensory input to the brain would be enough for any one structure, but now we have the cerebellum, a motor structure no less, asking the thalamus to donate her ventrolateral nucleus to use as a stopover point on the way to the frontal lobe.

As you recall, the basal ganglia express themselves through the globus pallidus which projects a dense bundle of fibers across the internal capsule to the ipsilateral ventrolateral and ventroanterior nuclei of thalamus. You might expect globus pallidus fibers synapsing in the ventrolateral nucleus to interact with all those incoming cerebellar fibers, but as yet there's no clear evidence that cerebellar and basal ganglia fibers talk to each other en route to the frontal cortex.[21]



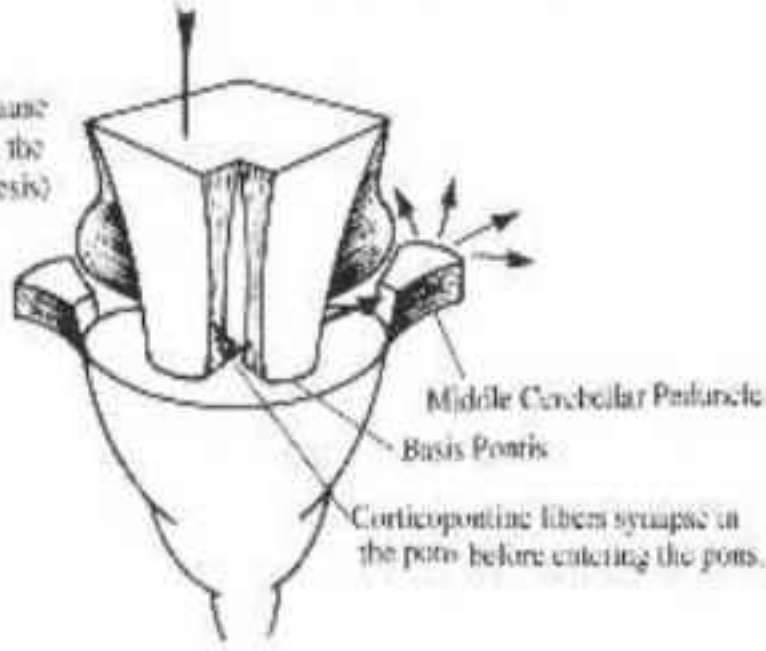
From these two thalamic check points, ventrolateral and ventroanterior nucleus, instructions are vaulted up to the frontal cortex where the cerebellum and basal ganglia exert their influence on the pyramidal system. Remember that cerebellar fibers decussate in the superior cerebellar peduncle; the right cerebellar hemisphere ends up in the left frontal cortex. Since the pyramidal tracts will be crossing at the medulla-spinal cord junction, the net result is that the right cerebellar hemisphere regulates function of the right arm and leg. This anatomic figure eight is known as the 'cerebellar double cross.'



The apparent purpose of all this crossing and re-crossing is to let the cerebellum know *in advance* what movement is about to be made so that the cerebellum can guide the motor strip. In other words, when the prefrontal cortex decides to move a limb, it first sends that inside info down the internal capsule to the pons which ships the message back to the cerebellum. The cerebellum rapidly calculates the effort needed to reach the target, and then scoots that information up the superior cerebellar peduncle to the thalamus, and from there up the internal capsule to the frontal lobe to modulate motor strip activity. A parallel system is probably used by the basal ganglia to influence the speed and spontaneity of movements generated from the motor strip.[27]

The long course of the cerebellar outflow tracts—reaching from the dentate nucleus through the superior cerebellar peduncle all the way to the contralateral thalamus and contralateral frontal lobe—complicates anatomic localization of cerebellar limb dysmetria. After all, is left hand dysmetria due to a lesion in the right frontopontine tract, left middle cerebellar peduncle, left cerebellar hemisphere, left superior cerebellar peduncle (i.e., brainstem), right thalamus*, or right frontal lobe?[23] This is the same old problem again which requires other signs to pinpoint the lesion. For example, a spastic, weak, and ataxic left arm suggests a right ventrolateral thalamic lesion, large enough to intercept the adjacent descending internal capsule*.[27] Limb dysmetria, then, is pathognomonic of cerebellar *system* dysfunction which includes the descending frontopontine tract, middle cerebellar peduncle, cerebellar hemisphere, superior cerebellar peduncle, contralateral thalamus, and sometimes even the contralateral cerebral hemisphere.

A lesion here in the pons would cause ataxic hemiparesis by interrupting the right pyramidal tract (left hemiparesis) and the adjacent fibers to the left cerebellar hemisphere (left-sided ataxia).



Right Thalamus: Helpful in localizing lesions to the thalamus (ventroposterolateral nucleus) is the contralateral loss of sharp pain. As will be described more fully in chapter 25, pain is conducted to the thalamus along two separate pathways: a fast one (for sharp pain) and a slow one (for dull pain). A *small* thalamic lesion may 'imbalance' these two types of pain. The patient won't immediately feel a sharp pin prick, but after several seconds, presumably when slow pain arrives, will feel the pain more intensely than usual. Without cortical analysis via the sharp pain pathway, he won't be able to localize or discern the nature of the painful stimulus. This situation can be quite uncomfortable when *non-painful* stimuli become misinterpreted as poorly localized, burning pain—a condition called 'thalamic pain.' A *large* thalamic lesion may interrupt all pain sensation from the contralateral half of the body, so that the patient cannot feel pain at all.

A parietal lobe lesion may also prevent patients from accurately localizing pain or accurately determining the nature of the pain (pin, knife, pinch, abrasion, burn, etc) but at least the patient knows it hurts. Thalamic patients can't even appreciate the sensation of pain when you first stick them with a safety pin. After a second or so, slow pain will be felt if the thalamic lesion is small, and no pain may be felt at all if the thalamic lesion is large.

Internal Capsule: Single lesions may cause ataxic hemiparesis in a number of different spots. A lesion in the internal capsule may (besides interrupting the descending corticospinal fibers) intercept fibers exiting ventrolateral thalamus bound for the cortex.[24] Similarly, a single internal capsule, or more commonly pontine, lesion could interrupt corticospinal fibers (hemiparesis) as well as corticopontine fibers bound for the contralateral cerebellar hemisphere (ataxia).[25] Finally, a unilateral midbrain lesion could simultaneously intercept one of the cerebellar outflow tracts and a cerebral peduncle.[26]

Gait ataxia is relatively specific for the vermis. Anterior vermis lesions (from chronic alcoholism, for example) cause gait ataxia by affecting coordination of the legs (abnormal heel-shin), while posterior vermis lesions cause gait ataxia by causing *truncal* imbalance (the patient can't even sit up in bed).[28] With suspected middle and posterior vermis lesions, look for ocular fixation instability and ocular dysmetria. Cerebellar dysarthria (scanning speech) is of some localizing value; the lesions are often in the cerebellar hemisphere adjacent to the vermis.[29]

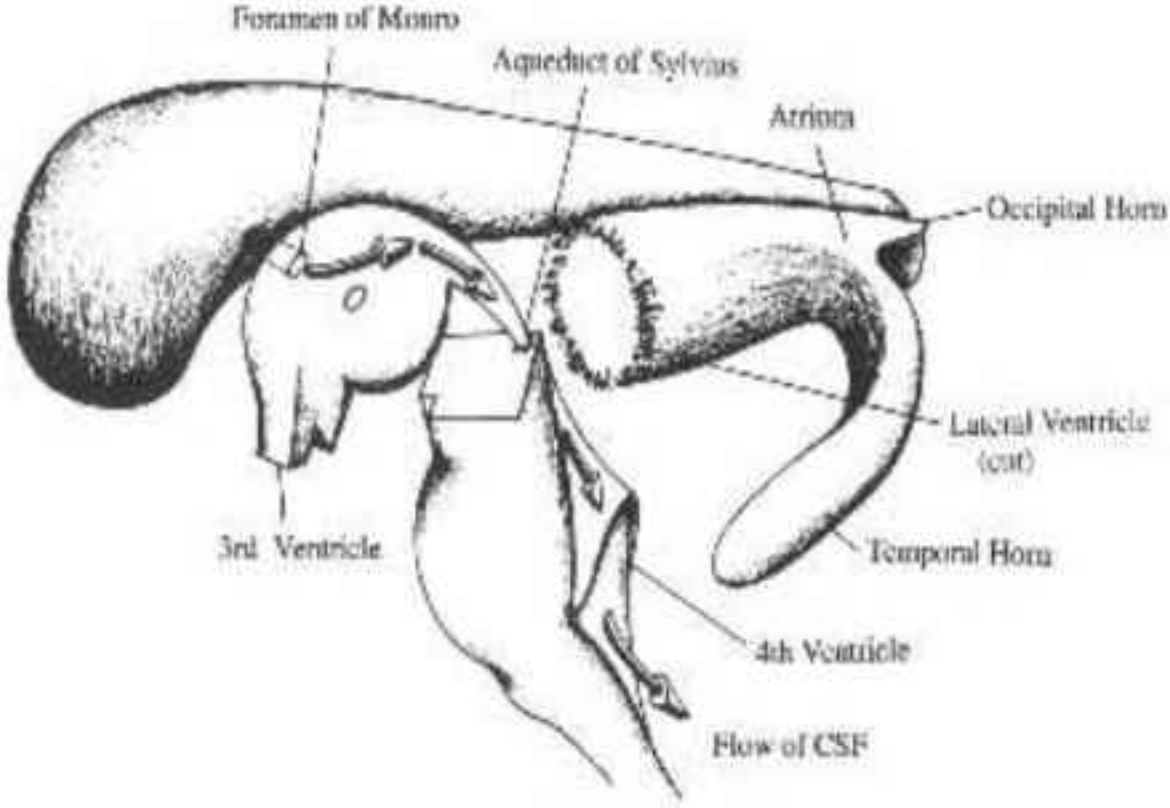
As the convergence center for cerebellar and basal ganglia outflow, the thalamic ventrolateral nucleus is a key spot for surgical therapy of cerebellar and basal ganglia dysfunction. Insufficient cerebellar or basal ganglia inhibition(?) of the ventrolateral nucleus allows unbridled bombardment of the premotor and motor cortex by second order cerebellar or basal ganglia fibers exiting the ventrolateral nucleus. It stands to reason, then, that many cerebellar and basal ganglia signs could be ameliorated by destroying the ventrolateral nucleus. Such an operation, called a thalamotomy*, can relieve patients of such varied (contralateral) signs as severe dystonia, ballismus, and incapacitating resting and intention tremors.[30]

Thalamotomy: First a half-inch size burr hole is drilled into the skull. A thin freeze probe is passed through the burr hole into the ventrolateral nucleus. With the patient awake, the ventrolateral nucleus is temporarily cooled. If the probe is properly placed, the abnormal posture or movement disappears without causing a hemiparesis (because of accidental cooling of the bypassing pyramidal tracts). A permanent freeze lesion can then safely be made.

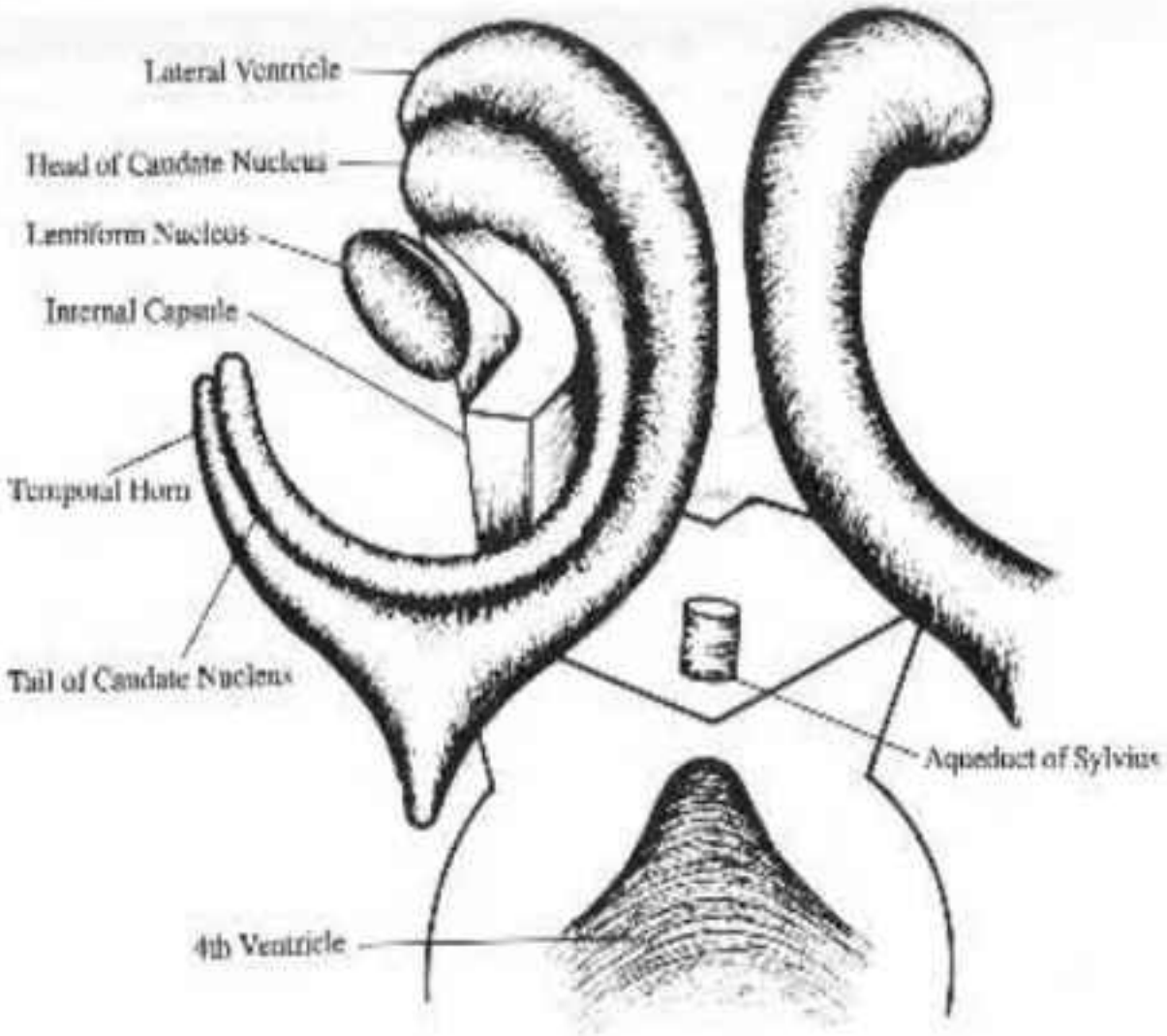
VENTRICLES

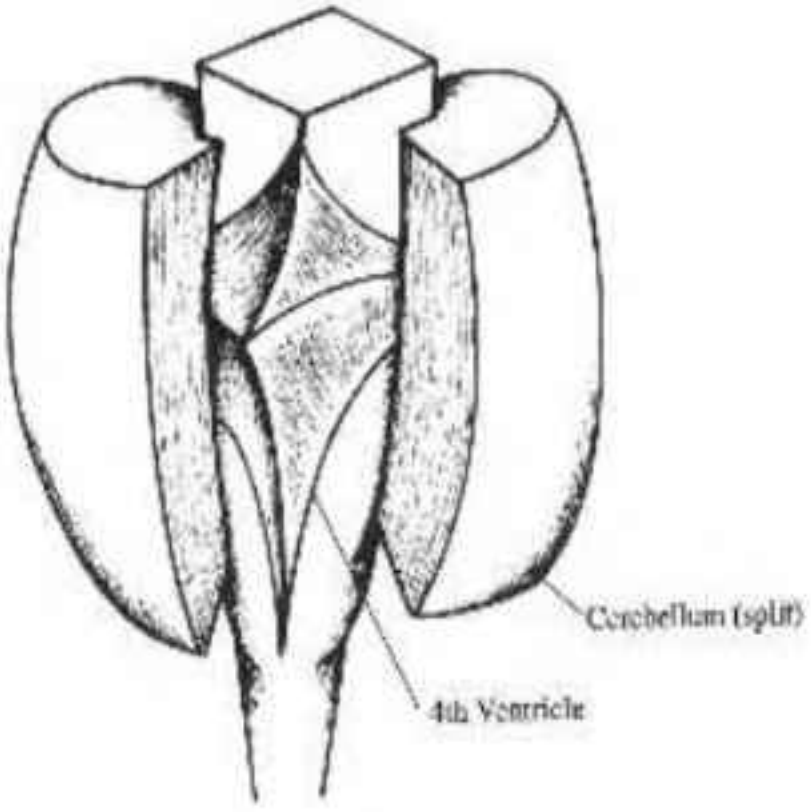
AMONG THE MANY INTERESTING FEATURES ABOUT THE BRAIN, one of the most interesting is that the brain is hollow. The interior cavity, the ventricular system, is filled with a clear-as-water fluid called cerebrospinal fluid (CSF). Spinal fluid trickles through the ventricles, draining away metabolites, cushioning the brain from sudden jolts, and perhaps even carrying neurotransmitters from one area to another.[1] After leaving the ventricular system at the base of the brain, CSF percolates up over the surface of the cerebral hemispheres to be absorbed.

That's the general idea of spinal fluid; now let's get closer. There are two lateral ventricles (I and II), a third ventricle and a fourth one. Extensions of each lateral ventricle, called horns, are named according to the surrounding lobe: frontal horn, temporal horn, and occipital horn. Where the frontal, temporal, and occipital horns meet (in the parietal lobe) is called the atrium of the lateral ventricle.

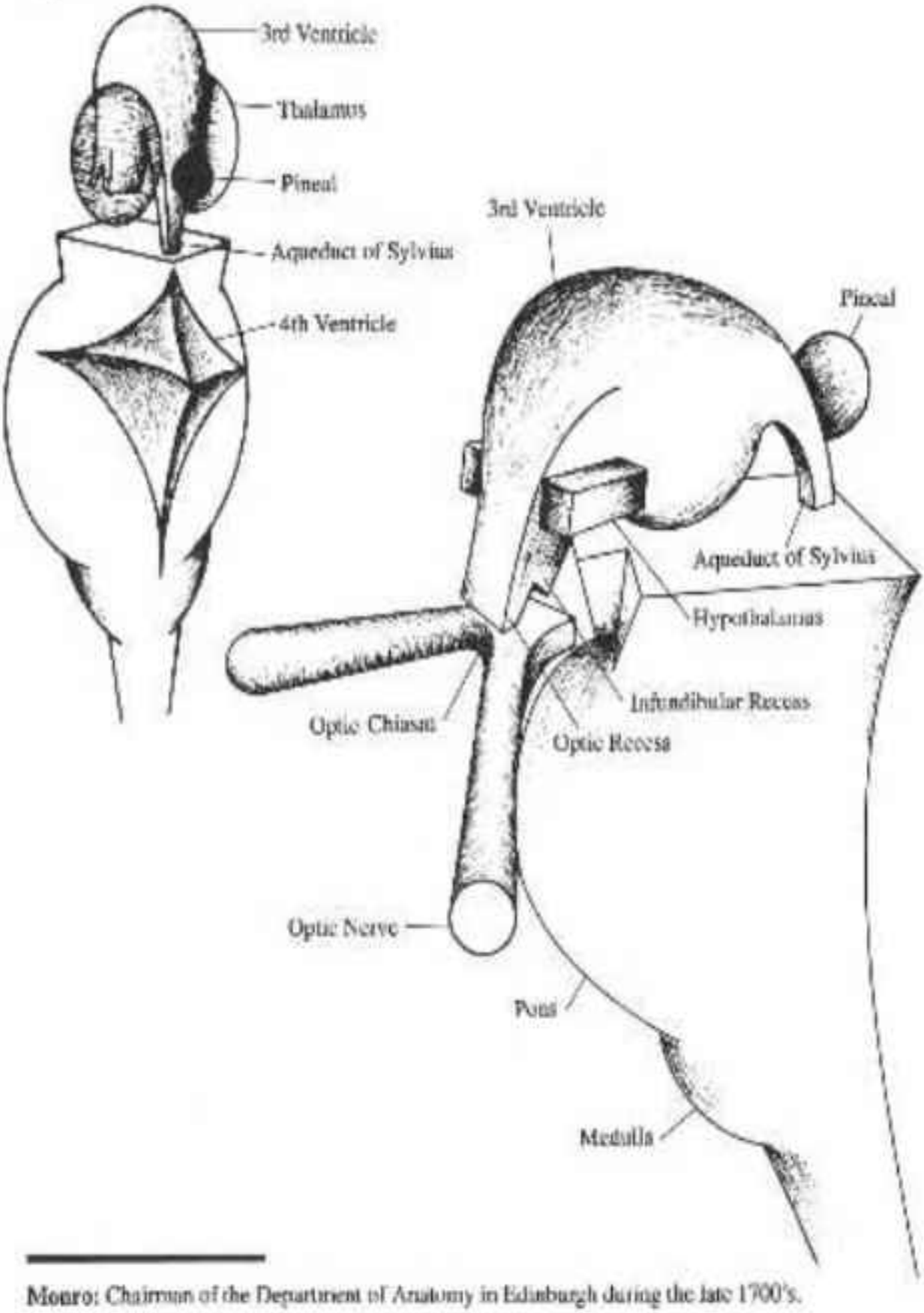


The frontal horn rests gently on the head of the caudate nucleus while the temporal horn, resting atop the hippocampus, arches gracefully behind the tail of the caudate.



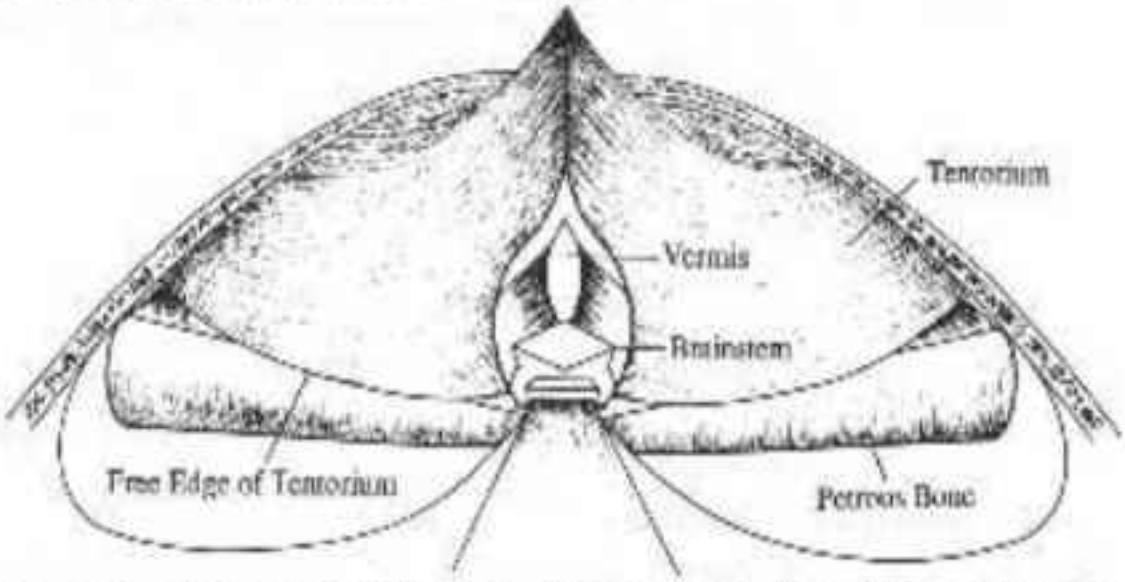


Slipping through the foramen of Monro*, CSF enters the midline third ventricle separating the two thalami. So the gray matter structure abutting the lateral ventricle is the caudate, astride the third ventricle, the thalamus. On either side of the anterior third ventricle lies the hypothalamic headquarters for the endocrine system. Tucked underneath the soft underbelly of the hypothalamus is the optic chiasm, nestled in the crotch of the optic and infundibular recesses of the third ventricle. From this vantage the optic chiasm can help mediate the effect of light on endocrine function and emotions (ask anyone from Alaska) via direct connections up to the hypothalamic suprachiasmatic nucleus.[2]

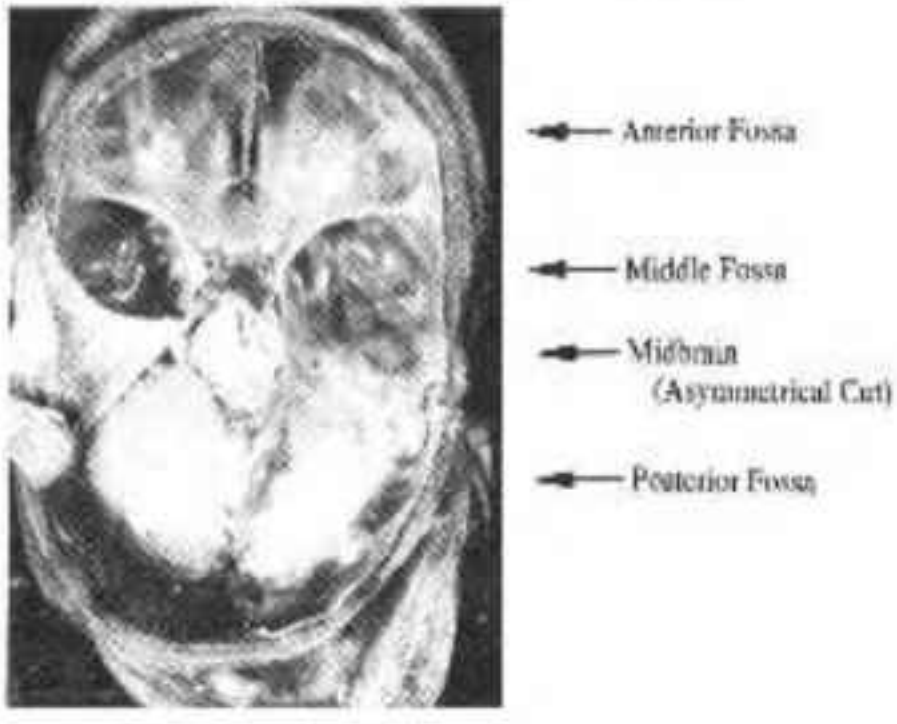


Monro: Chairman of the Department of Anatomy in Edinburgh during the late 1700's.

The tail of the third ventricle, called the aqueduct of Sylvius, connects to the fourth ventricle. Notice how the aqueduct slips through, not above, the midbrain. Just above the aqueduct peers the pineal gland*, originally thought to be the seat of the soul but now known not to be. And right behind the aqueduct spreads the tentorium separating the posterior fossa from the cerebral hemispheres.



The aqueduct leads us (and CSF) to the fourth ventricle, the pons' dorsal fin. Three small holes (foramina) in the fourth ventricle allow CSF to escape the ventricular system into the cisterna magna*. The two foramina of Luschka* are tucked into the lateral recesses of the fourth ventricle, far away from the single midline foramen of Magendie*. Note the convenience: lateral-Luschka, medial-Magendie.

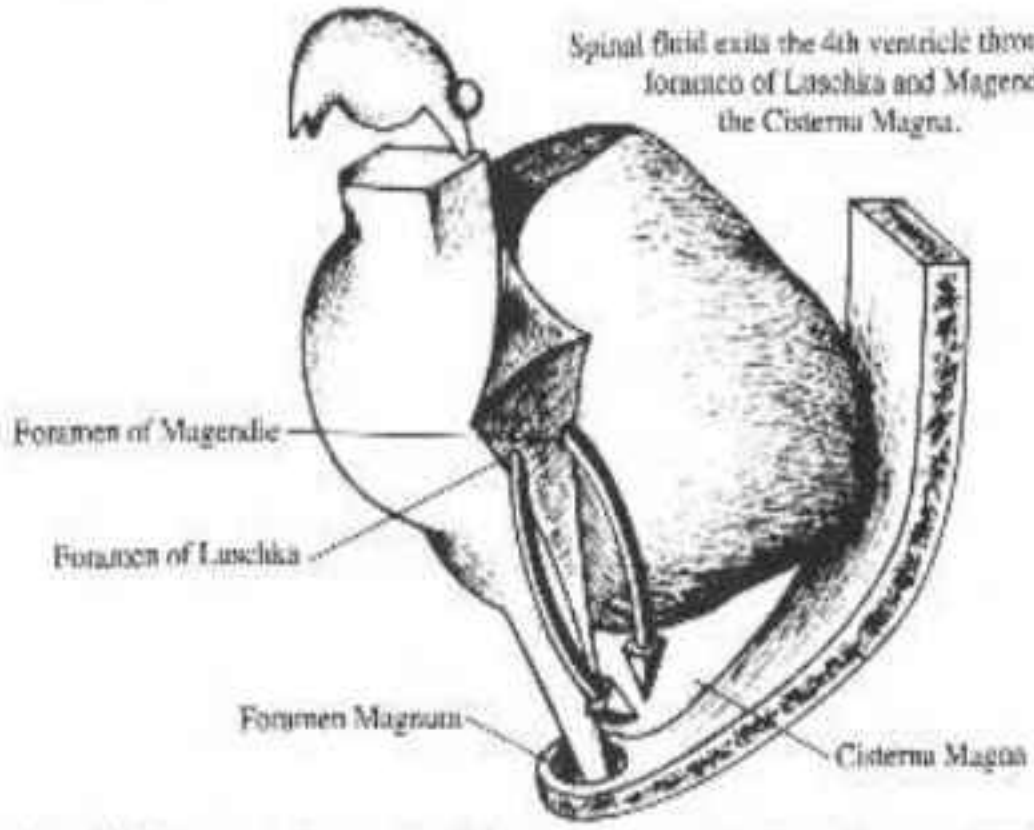


Pineal Gland: Probably helps mediate the onset of puberty. Its role in adults remains controversial.[3]

Cisterna Magna: Big cistern.

Luschka: Described the lateral foramen in the 1850's.

Magendie: A French physiologist in the early 1800's who, stimulated by Dr. Bell's (of Bell's palsy fame—chapter 20) demonstration of motor function in the ventral root (chapter 23), went on to localize sensory function to the dorsal root. Magendie also identified the midline 4th ventricular foramen. One of his students was the great physiologist, Claude Bernard.[4]



Spinal fluid is made in the choroid* plexus, a soft bluish ruffle attached all along the floor of the lateral ventricle, roof of the third, and lateral recesses of the fourth ventricle. CSF weeps from the choroid plexus into the ventricles, and window shops its way along the lateral ventricles, through the foramen of Monroe, into the third ventricle, through the aqueduct of Sylvius, into the fourth ventricle, and out the foramen of Magendie and Luschka into the cisterna magna. Now what? All that CSF in the cisterna magna must be gotten rid of because more is on the way and because it contains sewage the brain doesn't want. Though CSF in the cisterna magna has the option of going south to some absorption sites within the spinal canal, almost all the CSF bears north toward the major sites of absorption over the cerebral hemispheres. To get there, CSF creeps along in front of the pons midbrain where it slips around the midbrain through the perimesencephalic cisterns. Once CSF reaches the top of the brain, it's filtered through thousands of tiny nubbins, called arachnoid villi*, poking into the superior sagittal sinus* and its many tributaries.

Choroid: From the Greek word for skin: the suffix 'oid' (like) changed the meaning to a vascular membrane.

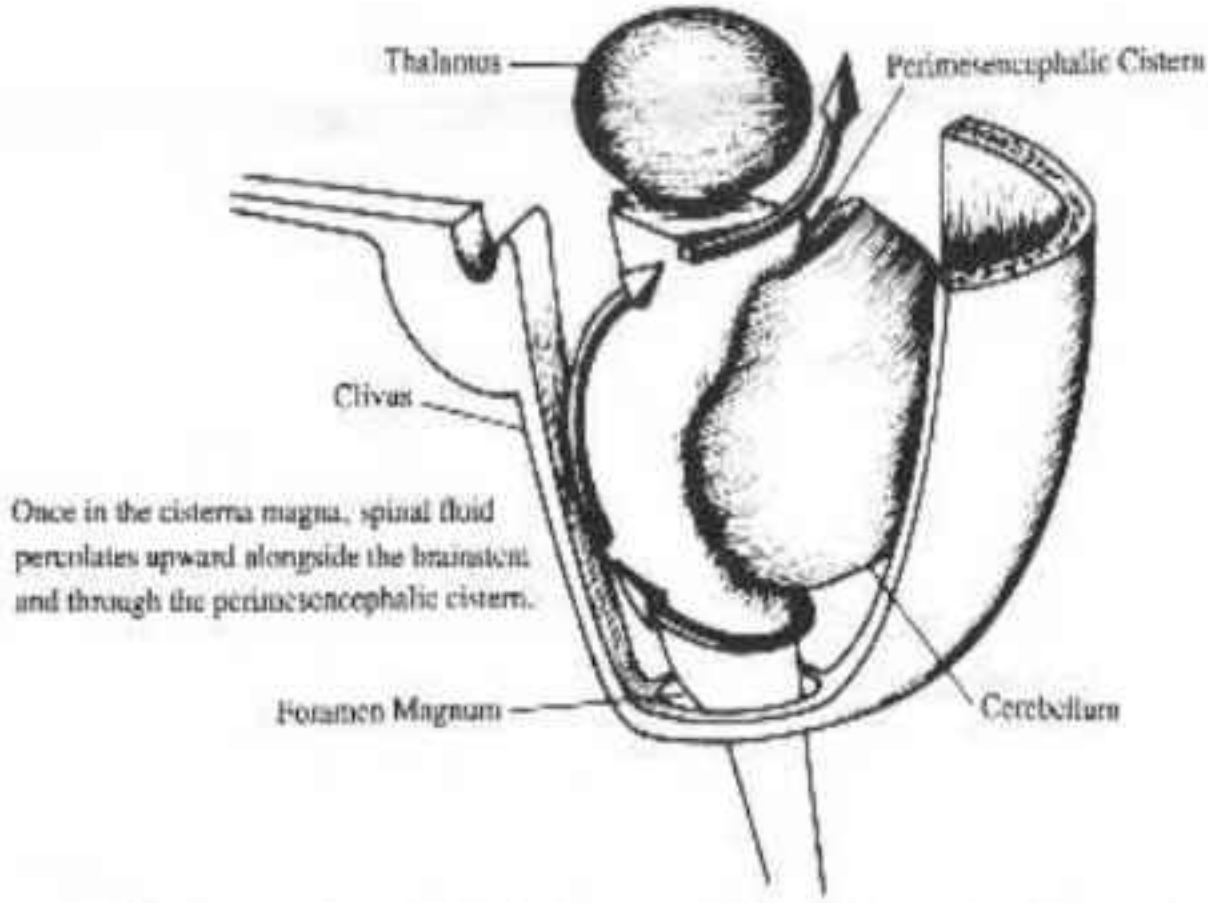
Arachnoid Villi: The name is derived from arachnida (spiders) because of spider like filaments in the arachnoid meshwork. Villus is Latin for tuft of hair.

Sagittal Sinus: Sagittal is from the Latin word for arrow. When the skull is viewed from above, its sagittal, lambdoidal, and coronal sutures resemble an arrow. (The sutures are the interdigitating borders between the skull bones.)

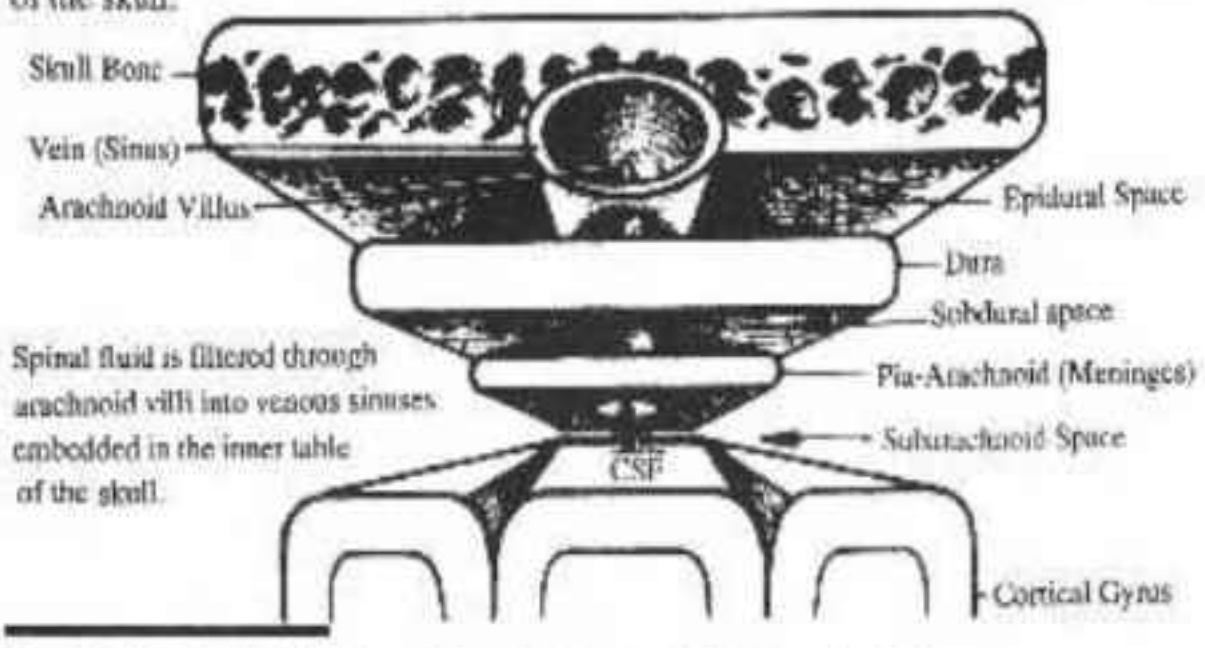
A sinus has can be a number of things: a large cavity, like the air-filled sinuses of the skull, a large vein without valves, or a sinus tract—a channel from the skin or from the surface of an organ into a deep-seated pocket, often a pocket of infection.

The sagittal sinus is not to be confused with the straight sinus which, lying deep in the falx* along the superior margin of the tentorium, drains blood from the ventricles, basal ganglia, and subcortical white matter (chapter 31).

Falx: The rigid vertical extension of dura between the two cerebral hemispheres. From Latin, meaning sickle.



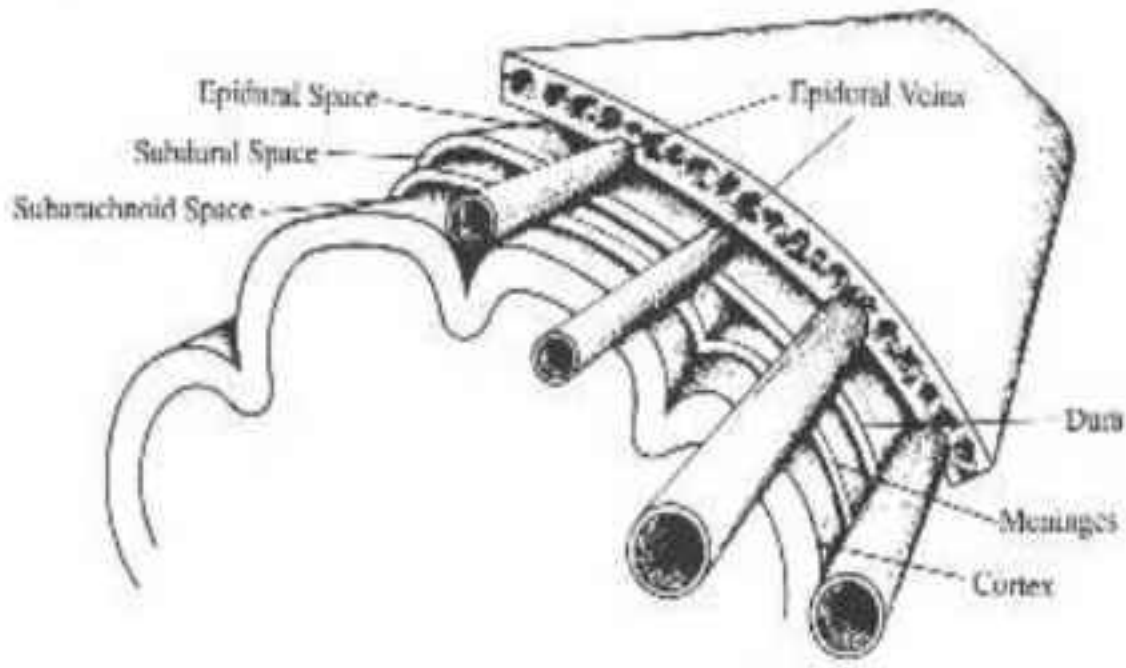
Wending its way up over the hemispheres, spinal fluid lies subarachnoid, underneath a thin, almost transparent membrane called the arachnoid. This delicate, gossamer membrane rests directly on the surface of the brain. Between the arachnoid and brain flows not only cerebrospinal fluid, but also arterial blood headed for the brain, which is why an arterial hemorrhage here is called a subarachnoid hemorrhage. Attached to the arachnoid is another very thin membrane, the pia*; together the pia-arachnoid are known as the meninges*. Outside the meninges is another, much thicker, tougher, more fibrous membrane—the dura*—plastered up against the inside of the skull.



Pia: Tender in Latin. The pial membrane dips into the sulci; the arachnoid does not.

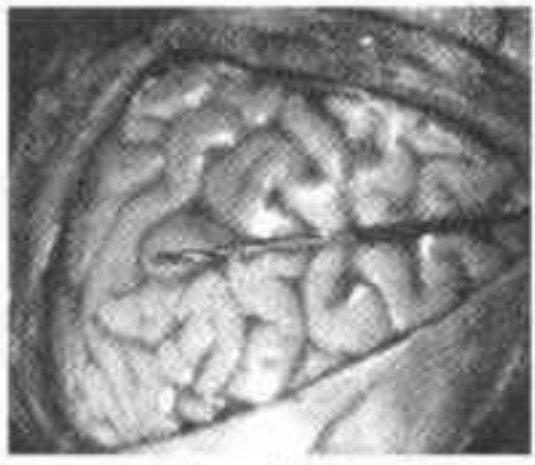
Meninges: Greek for membrane.

Dura: Means tough (durable) in Latin.



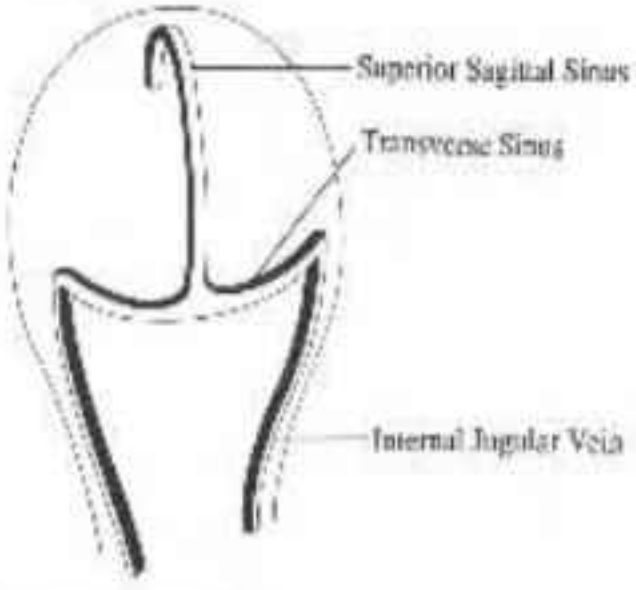


Dura



Meninges (Overlying Cortex)

Between the meninges and dura is a small subdural space across which thousands of small veins drain old blood away from the brain into larger veins embedded epidurally† along the inner surface of the skull. These veins converge on the superior sagittal sinus through which venous blood and CSF are drained back to the heart via the transverse and sigmoid sinuses and jugular veins.



Posterior View

†**Epidurally**: Outside the dura, between the dura and skull bone.

HYDROCEPHALUS

What happens if the CSF circulation is blocked? Like any dam, a lake forms behind it; the ventricles enlarge, producing hydrocephalus*. Your job is to suspect hydrocephalus, determine the site of obstruction, and ask a neurosurgeon to relieve the pressure built up behind the obstruction. You should suspect hydrocephalus when an infant's head enlarges faster than it should, when an adult develops difficulty walking associated with urinary incontinence and confusion, or when an adult sinks into coma for unclear reasons. Why the diverse presentations of hydrocephalus?

Part of the explanation lies in the structural development of the skull. To allow for brain growth, the skull begins at birth as a set of bony plates floating on the brain, a bit like the Earth's continental plates. Gaps between the plates, called sutures, fuse shut by about six years of age, after attainment of full brain size. Of the 500cc of CSF (one pint) made per day, the bulk is made in the lateral ventricles. So sudden obstruction at the aqueduct of Sylvius, for example, would quickly double or triple the size of the lateral and third ventricles. If this happens before the sutures have firmly fused, the massive increase in intraventricular pressure pops the sutures apart, allowing the skull to enlarge*. In adults, the skull won't budge, so the enlarging ventricles catch the cortex between a rock and a hard place: the cortical neurons simply stop working, resulting in coma. The other, and probably more important, explanation for the coma is the dilated third ventricle. Squatting right over the midbrain, the dilated third ventricle directly compresses the Reticular Activating System (the awakening center) scattered throughout the midbrain and upper pons (discussed more in chapter 21).

If the aqueduct of Sylvius is gradually and only partially obstructed, the ventricular dilation won't be so great or so sudden, and coma may not ensue. What *are* injured, however, are pyramidal tract axons coursing all the way round the lateral ventricles from the medial end of the motor strip. This produces impressive pyramidal tract

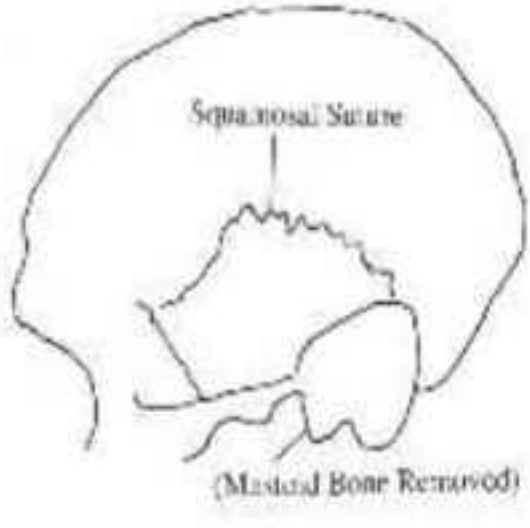
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Hydrocephalus: Hydro(water) cephalus(head). Strictly speaking, hydrocephalus only means enlarged ventricles from whatever cause. High-pressure hydrocephalus develops when the CSF circulation is blocked, but quite often the ventricles enlarge because brain tissue has withered away (usually from a degenerative illness like Alzheimer's disease). This type of hydrocephalus is called "hydrocephalus ex vacuo."

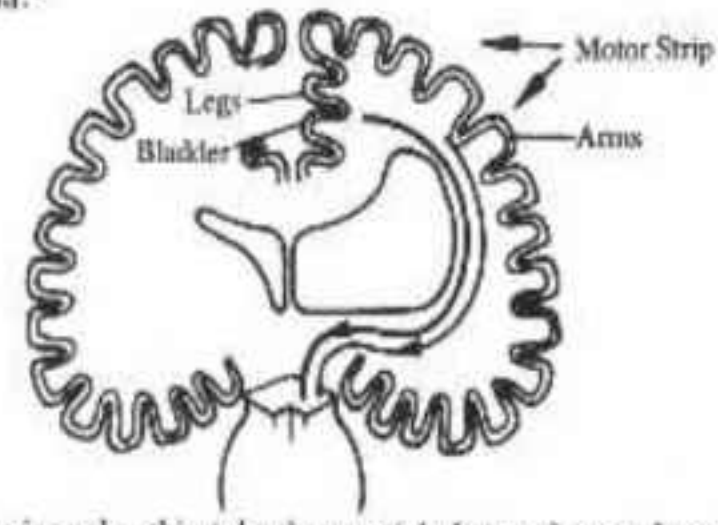
Enlarge: A good place to feel for popped sutures in an infant is just above the ear along the squamosal suture. Sometimes, tapping the skull with your finger will elicit the sound of a ripe watermelon or a cracked pot, both indicative of popped sutures.[2]

Children as old as twelve years of age have been known to pop their sutures from elevated intracranial pressure.



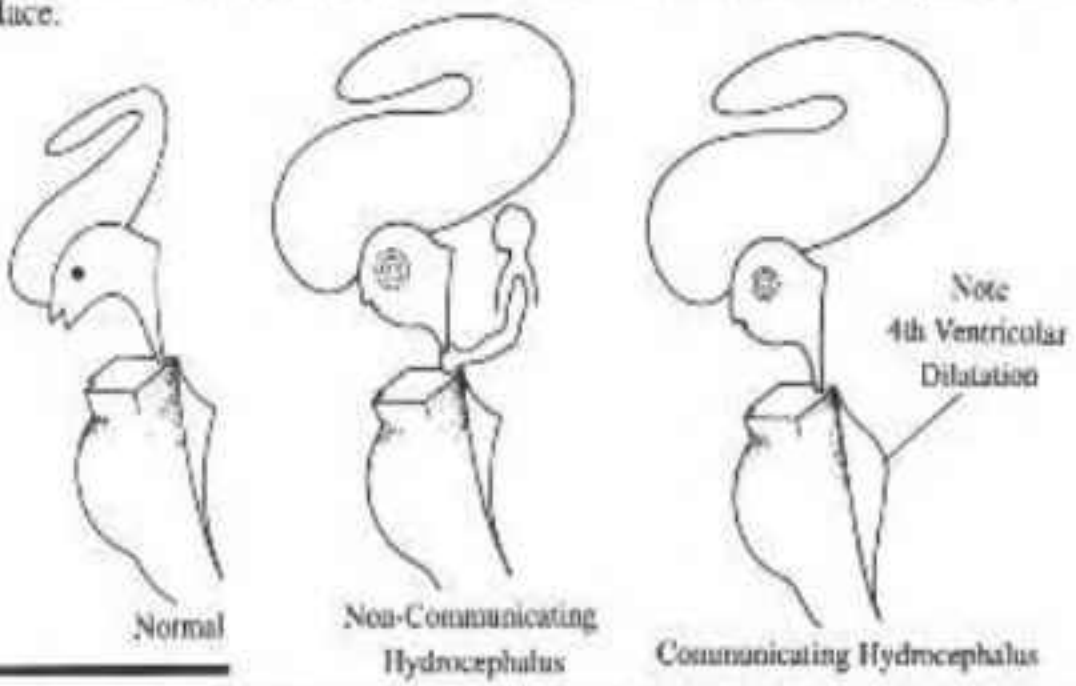


signs in the legs but, predictably, only mild signs in the arms. The legs become wobbly, unsteady, and intermittently weak.[6] The feet seem to develop a frontal lobe grasp reflex, and with it, a rather distinctive gait. The feet involuntarily 'grasp' the floor as if stuck. Like trying to walk on a steel floor with magnetized shoes, these patients have trouble starting their gait, but once they do unpry their feet and take a few initially tiny steps, their gait improves with longer, more natural steps. Unlike patients with marche a petit pas, patients with this low grade type of hydrocephalus *can* walk with relatively normal size steps (after the initial sticky ones); for this reason the gait is considered apraxic.[7] Bladder axons also get stretched by hydrocephalus, causing urinary urgency and incontinence. Cortical neurons get their share of increased pressure, too, but because the rise in pressure is neither too high nor too rapid, cortical neurons simply malfunction*, producing confusion, instead of shutting down into stupor and coma.[8]



Hydrocephalus stretches leg and bladder fibers more than arms fibers.

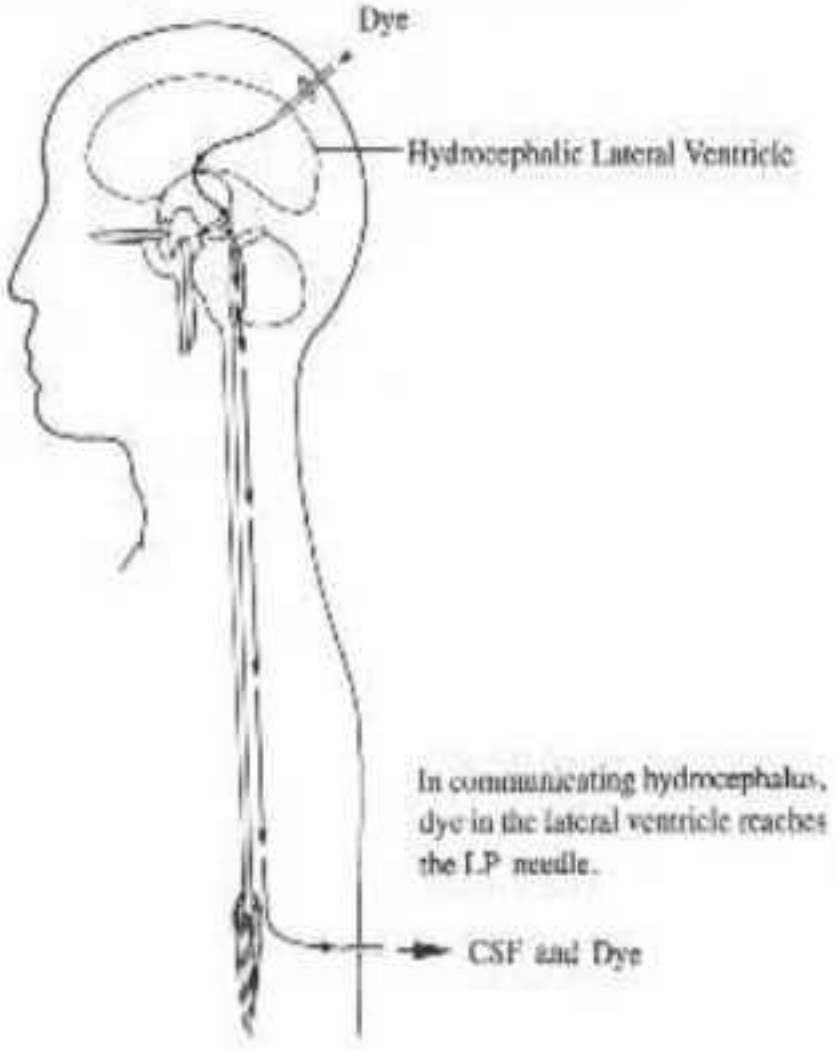
The aqueduct of Sylvius is such a thin tube that partial obstruction rarely occurs; it's either open or completely obstructed. But you can get the equivalent of partial aqueductal obstruction by damming up CSF further downstream along the base of the brain or in the arachnoid villi. A block at either one of these two places still allows enough CSF to enter the cisterna magna and either descend to absorption sites along the spinal canal or else drift up to the arachnoid villi where *some* absorption can still take place.



Simply Malfunction: It's likely, of course, that the intellectual changes also result from injury to the white matter, that is, to the subcortical axons which, by connecting different cortical areas, allow neurons in widely separate cortical areas to communicate with each other.

This second type of obstruction, at the base of the brain or within the arachnoid villi, produces 'communicating' hydrocephalus; obstruction at the aqueduct produces 'noncommunicating' (or internal) hydrocephalus. The term 'communicating' refers to a procedure begun around 1914 to diagnose hydrocephalus.[9] A small burr hole was drilled into the skull, a tube (catheter) passed through the brain substance (parenchyma) into one of the lateral ventricles, and a dye injected into the ventricle. Thirty minutes later a spinal tap* was done. If dye came out the spinal needle, there had to be free and open communication between the lateral ventricle and lumbar sac, which meant the obstruction to CSF flow had to be along the base of the brain or in the arachnoid villi*. If dye did not come out the spinal needle, no such communication existed. The block then must have been at one of the following locations: 1) one or both foramen of Monro, 2) within the third ventricle, 3) aqueduct of Sylvius, 4) within the fourth ventricle, or 5) foramen of Lushka and Magendie—all of which may produce noncommunicating hydrocephalus by preventing dye from escaping the ventricular system into the cisterna magna, and downward to the lumbar sac.

COMMUNICATING HYDROCEPHALUS



Spinal Tap: Lumbar puncture. By passing a needle through the back into the lumbar subarachnoid space, one can tap the spinal fluid (synthesized in the brain) for laboratory analysis—protein and glucose concentration, inflammatory cells, cancer cells, bacteria, fungi, etc. Analysis of lumbar spinal fluid can frequently diagnose the etiology of a cerebral problem two feet away.

Arachnoid Villi: Obstruction along the base of the brain (i.e., around the brainstem) commonly follows tuberculous, fungal, or sometimes, bacterial meningitis. Any prolonged meningitis may leave in its wake such dense scarring around the base of the brain that CSF cannot reach the arachnoid villi.[10] Obstruction at the arachnoid villi is a frequent complication of subarachnoid hemorrhage, which clogs up the arachnoid villi.[11]

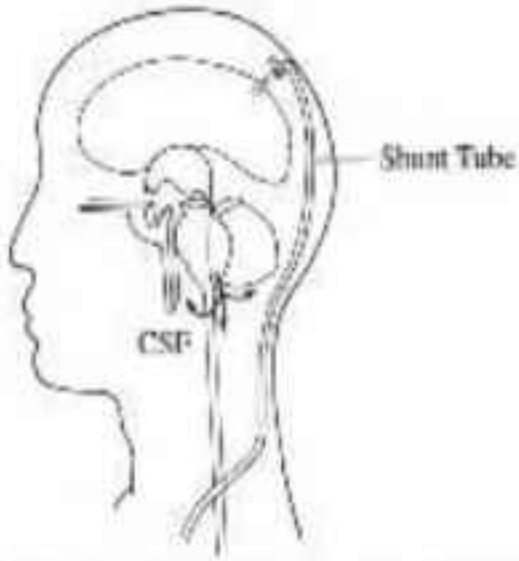
NON-COMMUNICATING HYDROCEPHALUS



The importance of determining the type of hydrocephalus is not only to help locate the site of obstruction, but also to decide how soon the pressure must be relieved. Noncommunicating hydrocephalus demands immediate attention because the pressure is much higher than in communicating hydrocephalus. Communicating hydrocephalus can often be observed for weeks if the patient is awake (i.e. not under much pressure).

High intraventricular pressure is relieved by inserting a catheter into one lateral ventricle (which communicates with the other lateral ventricle via the two foramina of Monro and midline third ventricle) and running the other end of the catheter under the skin into the abdomen or heart. Another plumbing solution is to run a catheter from the *lumbar* subarachnoid space into the abdomen. Of course, this would only work for communicating hydrocephalus: CSF would exit the fourth ventricle into the cisterna magna, see a blocked route to the arachnoid villi, and simply head south to the shunt tube.

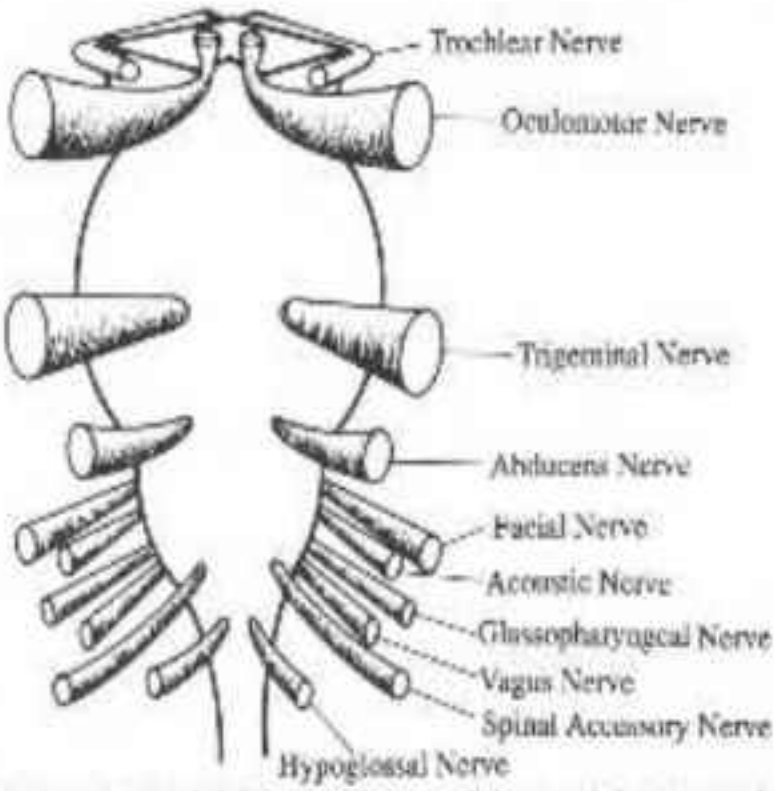
COMMUNICATING HYDROCEPHALUS



What non-communicating hydrocephalus really means is that a small tumor—critically placed—can amplify its symptomatology way out of proportion to its size. Conversely, unless an *intra*ventricular tumor obstructs the flow of CSF, that tumor can grow to the size of a baseball before becoming symptomatic.[12]

CRANIAL NERVES

THERE ARE TWELVE CRANIAL NERVES, but only III through XII enter the brainstem (cranial nerves I and II—smell and sight—do not). Diagnosing a cranial neuropathy* is only the beginning of an anatomic diagnosis. The lesion may lie anywhere along the cranial nerve, and for cranial nerves III through XII this means anywhere between the cell body in the brainstem and its termination in skin or muscle. The most important anatomic question for cranial nerves III through XII is whether the lesion is in or out of the brainstem.



How *do* you distinguish an extra-axial from an intra-axial* cranial neuropathy? In general, to localize a cranial neuropathy to the brainstem, you need to find signs of long tract dysfunction (pyramidal tract, spinothalamic tract, or posterior column) on the opposite side of the body. Since cranial nerves and long tracts only intersect in the brainstem, only a single intra-axial site can account for both a cranial neuropathy and long tract dysfunction. If you don't find the long tract signs, the site of dysfunction* may still be intra-axial, but you can't be sure.

Brainstem localization will be amplified later, after it is clear how to diagnose cranial neuropathies.

Neuropathy: 'Pathy' refers to any pathologic (abnormal) condition.

Intra-axial: Within the substance of the brainstem. A lesion confined to the cerebellum and pressing against the brainstem is extra-axial. So if a cerebellar tumor snakes a few infiltrating strands of tumor cells into the brainstem, the lesion would then be both extra- and intra-axial.

Site of Dysfunction: I've avoided the phrase 'site of the lesion' because the site of dysfunction may not always be the site of the primary lesion. For example, an extra-axial tumor may produce intra-axial signs (cranial nerve and long tract) by compressing the brainstem. The *presenting* site of dysfunction is intra-axial, but the lesion—the *primary* site of dysfunction—is extra-axial.

I: OLFACTORY NERVE

Cranial nerve I, the olfactory*, begins at the cribriform plate* high up in the nose and travels back underneath the frontal cortex to the temporal lobe. To test olfaction, pinch off one nostril and ask the patient if he can smell a test fragrance with the other nostril (almost any bar of soap is a handy test item). You don't have to ask him what the fragrance is; you're testing smell not memory*. Simply ask him if he smells a fragrance. If he wants to lie about his sense of smell, you won't be able to determine it unless you use a material like ammonia which irritates the nasal mucosa (cranial nerve V). If he can't smell ammonia, either I and V are both knocked out, or he's faking the absence of smell. Conversely, don't use a caustic material to test smell because you may be testing cranial nerve V by mistake.[1]

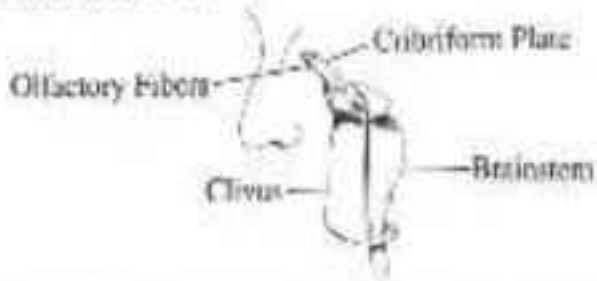
Though the most likely explanation for a unilateral loss of smell is local nasal obstruction, you should pursue a unilateral loss of smell if indicated. What does that mean "if indicated"? Well, since olfactory groove meningiomas* often become large enough to compress the ipsilateral frontal lobe and optic nerve, you have to investigate unilateral loss of smell if your patient has unexplained seizures, personality change, confusion, or visual loss. If he doesn't, and you find unilateral loss of smell without evidence of nasal obstruction, you're caught. Here you have an abnormal finding without a complaint to go along with it, an asymptomatic sign. A tough problem, because to pursue it with a CAT scan exposes the patient to the risk of anaphylaxis from the intravenous contrast dye*.

II: OPTIC NERVE

The second cranial nerve, the optic nerve, is the most complex, but also the most localizing of all the twelve cranial nerves. Nearly 40% of all fibers entering our brains do so via the optic nerves.[3] Testing involves five steps: visual acuity, color vision, Marcus Gunn, visual fields, and direct ophthalmoscopic observation of the optic disc and retina.

Olfactory: Olfacere in Latin means to smell.

Cribriform Plate: Cribra is a sieve in Latin. The olfactory bulb projects tufts of neuronal hairs through the cribriform plate to detect odors.



Smell Not Memory: Odor identification is unnecessary unless you run a smell clinic where patients with partial olfactory nerve damage complain that odors do not smell right.

Olfactory Groove Meningioma: A benign tumor compressing the olfactory nerve in the olfactory groove.

Intravenous Contrast Dye: I must admit I don't face this problem very often because I don't routinely check smell without complaints of loss of smell, impaired vision, or changes in frontal lobe function. Fortunately, olfactory groove meningiomas are pretty rare. I justify skipping the first cranial nerve by telling myself my time is more fruitfully spent on other *symptomatic* problems, but I know that someday I will miss an asymptomatic olfactory groove meningioma.[2]

Visual Acuity

Visual acuity is affected early in optic neuropathies for a number of reasons. First, fully 20-25% of all optic nerve fibers come from the macula*.[4] Second, macular fibers travel in the center of the optic nerve where many optic nerve lesions—immunologic lesions particularly—tend to attack.[5] Even buried within the center of the optic nerve, the metabolically active (and therefore more sensitive) macular fibers cannot escape the effects of optic nerve compression; tumors and aneurysms damage the entire cross section of the optic nerve.[6] Third, each cone receptor in the macula, unlike cones elsewhere in the retina, sees only a small area of the target with no overlap between neighboring cones. And each macular cone transmits its signal to a single ganglion cell deep in the retina. Cones outside the macula must share a ganglion cell with other cones.[7] This exacting architecture gives the macula high resolution, but at the expense of impaired visual acuity should anything happen to the optic nerve. In many ways, the optic nerve is a 'macular' structure.

Visual acuity testing is simple enough. First, have the patient put on his glasses on if he uses them for reading, and then cover one eye and read a near card*. Whichever line he reads without a mistake is his visual acuity. If he correctly identifies some but not all of the numbers, his visual acuity is that line with a little minus after it. If the patient's visual acuity is not 20/20* and can't be improved by refraction* or by looking through a pinhole*, his visual impairment is neurologic—and very likely an optic neuropathy—until proven otherwise. That is, ophthalmoscopy should reveal no corneal opacification or lens cataract*, a clear vitreous humor, and a normal macula and retina. Specifically, the retina should not be peppered with tiny flecks or clumps of black pigment, a sign of retinal degeneration. And the macula—which you can readily see by having the patient look directly at the ophthalmoscope light—should reflect back a small, shiny foveal reflex.

Macula: The central retinal spot where images are focused, lying about two disc diameters lateral (temporal) to the disc. The center of the macula is the fovea.

Near Card: An eye chart printed on a hand-held card.

20/20: The patient can see at 20 feet what any normal person can see at 20 feet. 20/80 means he has to get within 20 feet to see what a normal person can see at 80 feet.

Refraction: All lenses focus light by bending it, called refraction. The refractive strength of a lens is measured in units called diopters. The ingenious beauty of the eye is that, unlike the fixed refraction of a glass lens, ocular refraction can be continuously adjusted by a tiny muscle, the ciliary body. If more refraction is needed for close-up work, the ciliary body bunches up to relieve tension on the lens. The lens then rounds up to provide more refractive power.

Myopic (nearsighted) eyes are too short; light focuses behind the retina, a situation corrected by holding the object closer to the eye. Hyperopic (farsighted) eyes are too long; to focus incoming light on the retina, your parents hold the newspaper at arm's reach until they get bifocals. Astigmatism twists visual images, allowing part of the image to focus in front of the retina, and part behind.

Ophthalmologists and optometrists refract eyes by choosing the proper lens to focus the visual world sharply on the retina.

Pinhole: A pinhole sharpens the image before the image even reaches the lens.[8] A camera iris works the same way to expand the depth of field.

If the patient's visual acuity improves to 20/20 by looking through a pinhole, fine, but don't settle for less than 20/20 without an ophthalmologist's or optometrist's opinion about your patient's visual impairment.

Cataract: From the Greek term for waterfall, as if the patient were looking through one.



If both eyes have diminished visual acuity despite refraction, the lesion can be anywhere from both corneas to both occipital lobes. But if only *one* eye is affected, there must be—with rare exception*—something wrong anterior to the chiasm: in the cornea, lens, vitreous humor, retina, or optic nerve of that eye. As soon as the optic nerves reach the chiasm, fibers from both eyes intermingle and you can no longer (almost) have a disturbance of one eye alone.[10] There are four other ways to confirm a prechiasmal lesion (in the optic nerve or retina): color vision, Marcus Gunn pupil, visual fields, and ophthalmoscopy of the optic nerve head (disc) and retina.

Color Vision

The retina is made up of two types of light sensitive receptors: rods and cones. Rods, being much more light-sensitive than cones, are used for night vision. Cones, in contrast, are much more sensitive to color for daytime vision. No rods, only cones, are found in the macula which explains why at night you should look off to one side of whatever you want to see*.[11] Since the optic nerve is a 'macular' structure, color vision is a sensitive indicator of optic nerve function.

Test the patient's color vision by having the patient read a set of color plates with each eye*. If you don't have a set of color plates, simply cover each eye alternately,

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With Rare Exception: A mass compressing the chiasm from the right side may allow non-crossing macular fibers from the left eye to successfully reach the left occipital lobe, and hence normal visual acuity in the left eye. Not so with masses that compress the center of the optic chiasm: the crossing and non-crossing macular fibers from both eyes are injured, affecting visual acuity in both eyes.[9]

Want to see: This phenomenon is well known to fans of the Pleiades, the constellation of stars which increases in number if you look slightly off to one side. Next time you want to discern a moonlit object, verify the superiority of non-macular vision by looking slightly off target.

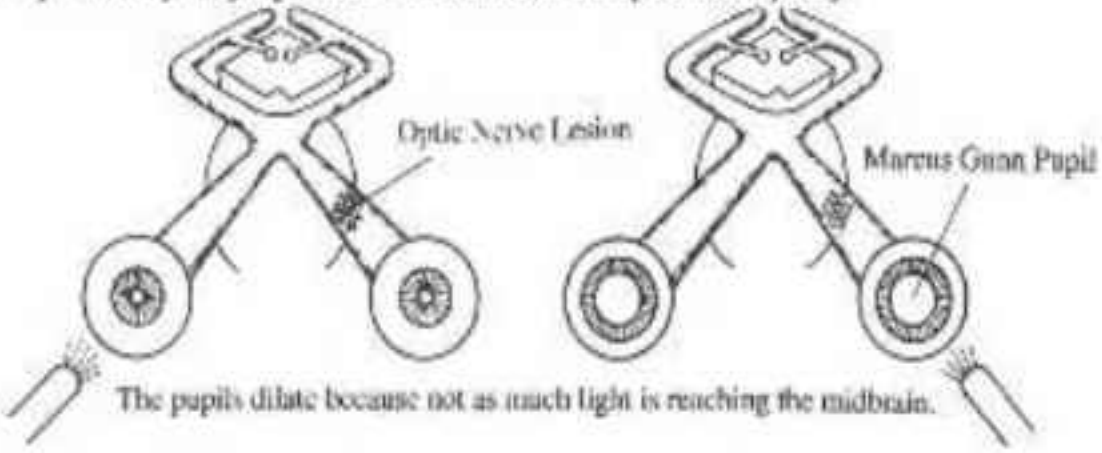
With Each Eye: A typical color plate has a colored number camouflaged amidst a differently colored background.

Since color-blind patients also can't read all the color plates, you may need an ophthalmologist to sort out color-blind patients with a superimposed optic neuropathy.[12] Of course, progressive loss of visual function (visual acuity, visual fields, color vision), or unilateral loss of color vision, would automatically imply a neurologic site if the cornea, lens, vitreous, and retina looked all right. Fortunately, most patients with color blindness still have pretty good sensitivity to red.[13]

and ask the patient if he is aware of a color change to a red target. Red is probably the best color to use, because the eye is quite sensitive to that end of the color spectrum; more importantly, red suffers the greatest fall-off in color sensitivity with optic neuropathies.[14] If the patient admits to a washout (lighter or pinker) or a darkening of the red target in one eye, he probably has an optic neuropathy, especially if he also has other signs of an optic neuropathy. Again, check the macula and retina to rule out, as best you can, local eye disease.

Marcus Gunn

Marcus Gunn, or the swinging flashlight test, is performed as follows: first have the patient look over your shoulder to prevent the pupils from constricting when looking at something up close (the accommodation reflex: see p. 267). Shine a somewhat dim* light in the right eye, and note how small the right pupil constricts (the left pupil also constricts). Now swing the light over to the left eye and carefully note the left pupil. If the *first* reaction* of that pupil is dilation instead of maintaining its previous small size (from the light in the right eye), there is something wrong with the left optic nerve*. To help confirm a Marcus Gunn, ask the patient if the light appears less bright in the suspicious eye, symptomatic evidence of an optic neuropathy.



Somewhat Dim: The easiest way to do this is to shine the light from below. This will not only allow you an unobstructed view of the pupils, but will also prevent the patient from looking at the light and accommodating (constricting) the pupils. You want the light to be dim because too bright a light makes it hard for the abnormal pupil to escape the light (by dilating).[15]

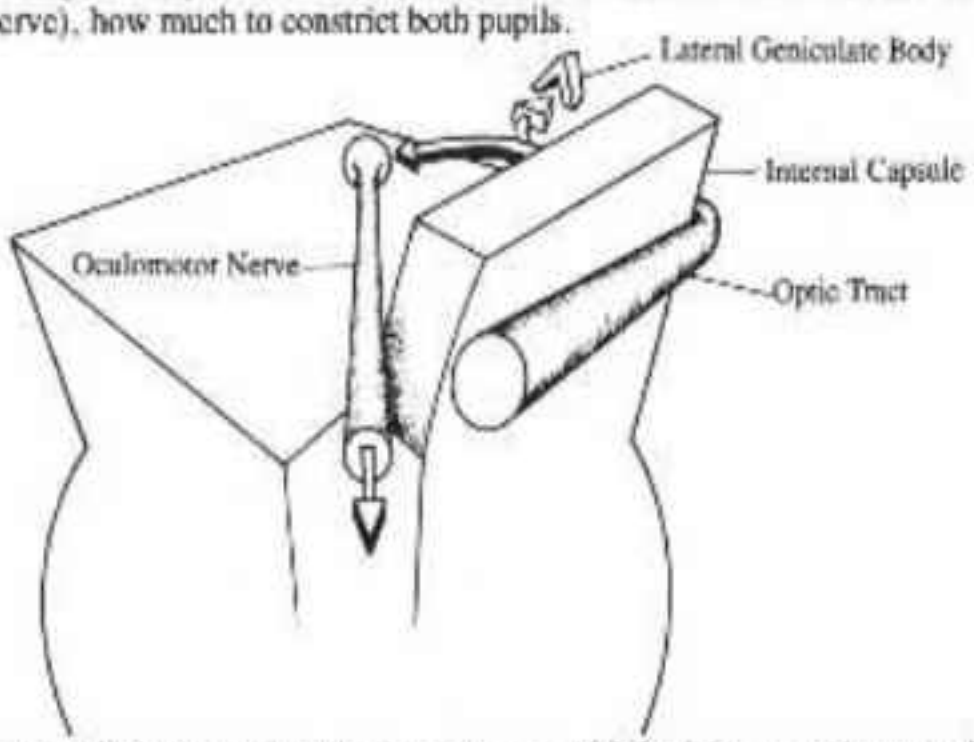
First Reaction: You shouldn't accept a Marcus Gunn if, when you swing the flashlight to the other eye, the pupil first constricts and *then* dilates. The very first reaction should be dilation. Constriction and then dilation may be Marcus Gunn, but it may also be normal.[16] If the pupil constricts and then redilates to a larger diameter than the opposite pupil did, be sure that that pupil wasn't larger to begin with. And don't let the light linger too long in one eye; that eye may adapt to the light, causing the pupil to redilate wider that the other pupil exposed to a briefer light.[17]

If you keep these caveats in mind, it's probably all right to diagnose a mild Marcus Gunn if one pupil constricts first but then redilates to a larger diameter than the contralateral pupil. Otherwise, stay on safer ground by calling Marcus Gunn only when the pupil *first* dilates.

Finally, ignore any hippus – a normal instability of the pupil that makes the pupil throb slightly with tiny waves of alternating constriction and dilation.[18]

Left Optic Nerve: Rarely, you may run across a Marcus Gunn caused by a retinal detachment[19] or severe macular disease.[20] Central retinal artery occlusion may cause a Marcus Gunn pupil by damaging the retinal axons entering the optic nerve (*see text below*). All three of these situations should be visible with an ophthalmoscope. In most situations, a Marcus Gunn pupil implies an optic neuropathy.

The anatomic explanation for the Marcus Gunn reflex is fundamental. Suppose the patient has a left optic neuropathy. Light striking the right eye fires retinal axons which pass through the optic nerve and chiasm into both optic tracts which, in turn, wrap around the midbrain to terminate in both lateral geniculate bodies behind the thalami. However, just before reaching the lateral geniculate bodies, each optic tract gives off a slip of fibers to the pretectal* nucleus in the midbrain, announcing how much light is striking the retina. Knowing that light intensity, the pretectal nucleus then tells the Edinger Westphal nucleus, a subdivision of the oculomotor nucleus (the IIIrd cranial nerve), how much to constrict both pupils.



When a moderate light was shined in the right eye, 100% of the axons in each slip fired at the pretectal nuclei. When the same light was shined in the left eye, only perhaps 75% of the axons fired, 75% because 25% weren't working from the optic nerve lesion. The Edinger Westphal senses the apparently less intense light and tells the pupils to open up a bit, which you see as paradoxical pupillary dilation when the light is swung from the good right eye to the abnormal left one*.

Visual Fields

Unilateral Field Cuts

The fourth way to corroborate an optic nerve lesion is with visual fields. Visual field testing at the bedside is probably the most tedious part of the neurologic exam, though it shouldn't be because most visual fields cuts, especially those due to optic neuropathies, can be detected by concentrating on the central 20–30 degrees surrounding central fixation. The central 30 degrees of the retina provides the optic nerve with 90% of its fibers.[21]

Pretectal: The pons and midbrain are divided, in a dorsal to ventral direction, into three sections: tectum, tegmentum, and basis. The basis is the area occupied by the pyramidal tracts. The tegmentum stretches from the basis to the 4th ventricle (or in the midbrain, to the aqueduct of Sylvius). The area above the 4th ventricle (or aqueduct) is the tectum. The most rostral part of the midbrain tectum is known as the pre-tectum, housing the midbrain's light-sensing center, the pretectal nuclei.

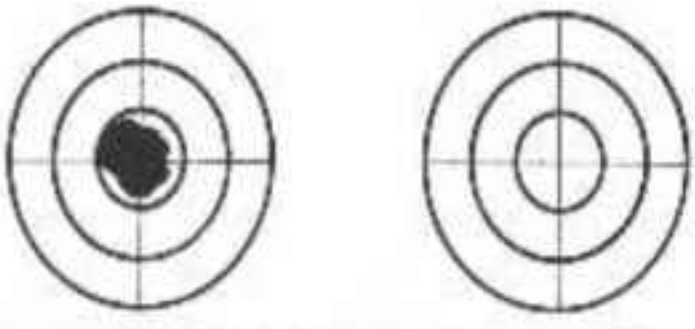
Abnormal Left One: Other names for the Marcus Gunn pupil are afferent pupillary defect, paradoxical light reflex, pupillary escape, and positive swinging flashlight test.

When testing each eye, ask yourself three questions: does the visual field loss respect the vertical midline? the horizontal midline? and does the field loss involve central fixation?

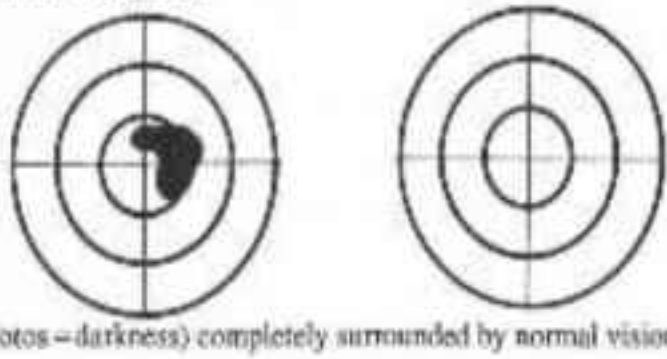
To test visual fields, sit the patient in front of you with one of his eyes covered. Ask him to focus either on your eye (his left, your right), or preferably, on your nose which is less distracting to him than looking you in the eye. Hold up both your hands close together in the superior visual fields on each side of midline. Ask if one hand is clearer. If one hand is absent or less distinct, move that hand toward the midline. If, as it crosses the midline, he notes an improvement, the defect 'respects the vertical.' Do the same for the horizontal midline, and repeat for the inferior quadrants.

To get at more subtle defects, hold each hand on either side of midline, then briefly wiggle both index fingers and ask him which one wiggled. Or flash a number of fingers in each hand and ask the patient to add them up. By changing the number of fingers flashed, you will soon be aware of any difficulty resolving the number of fingers in a particular visual field. Or, subtler still, hold a red target in the superior quadrants, asking if one looks washed out (pinker) or darker.[22] Again, see if this impairment respects the horizontal or vertical. If you're still unsure or suspicious, obtain formal visual fields with a tangent screen or Goldmann perimeter. Tangent screen will give you the central 30 degrees of vision, while Goldmann perimetry will display the entire visual fields.

What visual field pattern reflects an anterior, prechiasmal (optic nerve or retinal) lesion? First of all, any uniocular field cut (other eye normal) implies a prechiasmal lesion (with one rare exception described later). That makes sense; anywhere from the chiasm back—chiasm, optic tract, optic radiation, and occipital cortex—nerve fibers from both eyes mingle so that any chiasmal or retrochiasmal lesion should produce field cuts in both eyes. This certainly makes life easier—a field cut in one eye places the lesion somewhere between the retina and chiasm. But can the visual fields reliably distinguish a retinal lesion from an optic neuropathy? No. Strictly speaking, there is no visual field cut that will distinguish retina from optic nerve. One can always conjure up a retinal lesion to mimic any optic nerve visual field loss. For example, this:



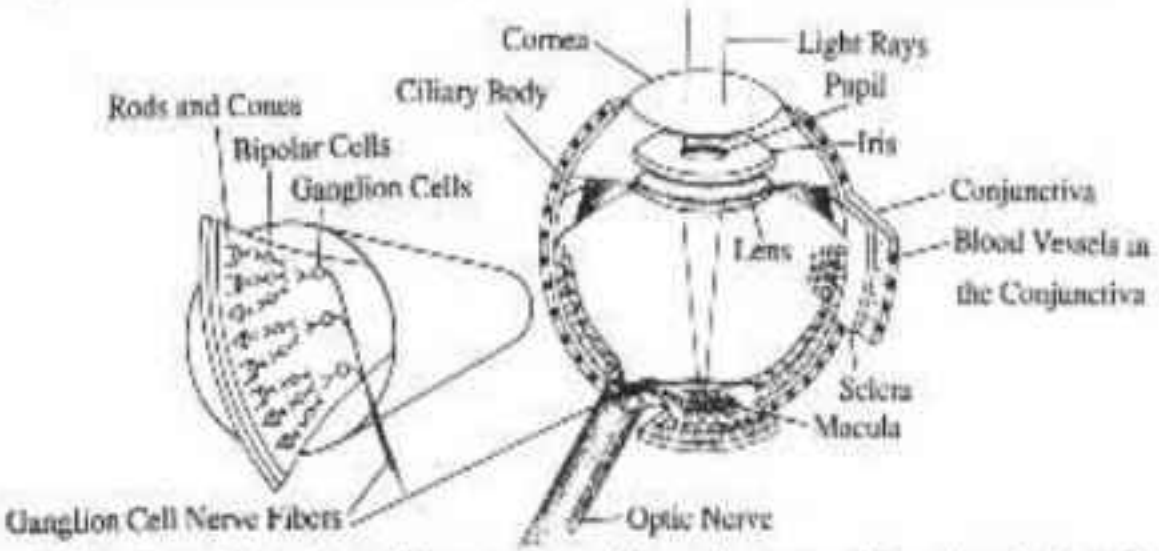
is called a central scotoma*. It may be due to an optic neuropathy, but may also be due to a macular lesion in the retina. Likewise, this:



*Scotoma: Any island of blindness (skotos = darkness) completely surrounded by normal vision.

is a paracentral* scotoma, indicative of either an optic neuropathy or a paramacular retinopathy. In practice, however, there are two uniocular field cuts which are so characteristic of an optic neuropathy that they can reliably be used to separate optic nerve from retinal lesions once you understand the anatomy of the retina and anterior optic nerve.

Light entering the eye strikes rods and cones resting on the floor of the retina. The rods and cones convert the light rays into electrical discharges which then travel back in the direction the light was coming from to synapse on an intermediate cell called the bipolar cell. This cell is situated at the end of a funnel, receiving synaptic discharges from perhaps ten or twenty nearby rods and cones (except in the macula where the ratio is 1:1). When enough rods and cones 'speak up' simultaneously, the bipolar cell discharges to the next cell, the ganglion cell, which stretches without synapsing all the way from the retina to the lateral geniculate body at the rear end of the thalamus.



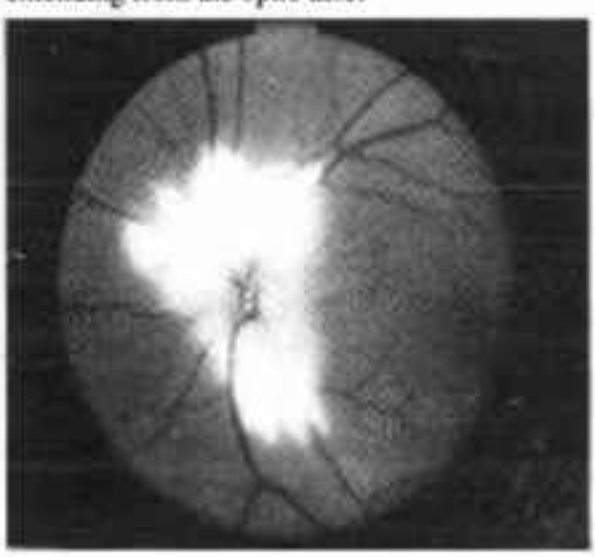
All the axons from the million or so ganglion cells stream along the retinal surface, arching around the macula toward the optic disc (tip of optic nerve) which, being devoid of rods and cones, corresponds to the visual blind spot*. These arching fibers—unmyelinated until they reach the optic nerve*—are known as the arcuate

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Paracentral: Para means 'next to'; peri means 'encircling.'

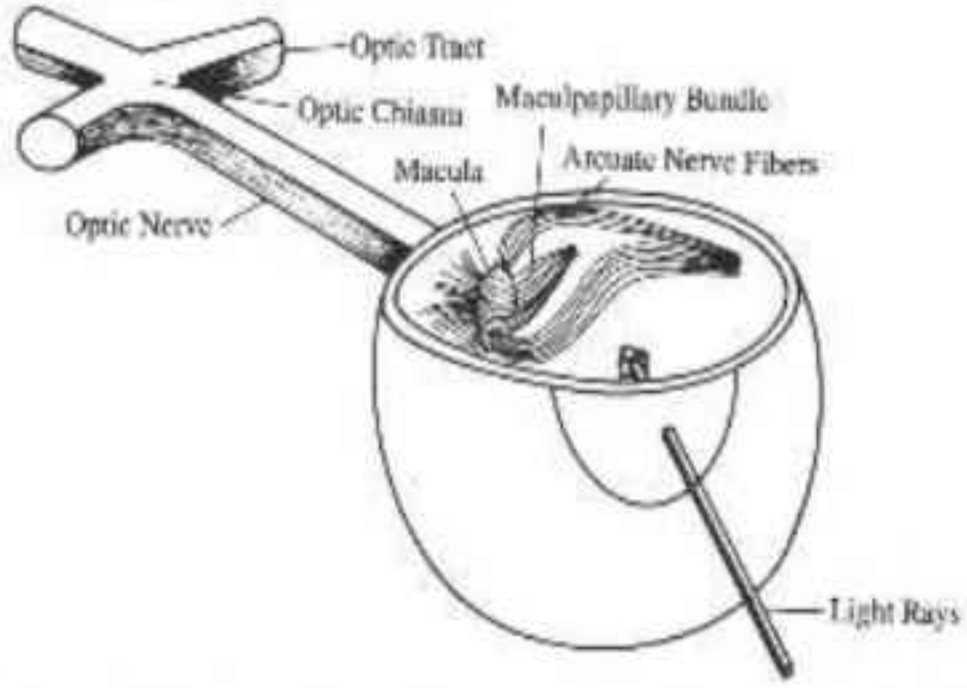
Blind Spot: Holding your thumb at full arm's length, you'll find the blind spot about six inches lateral to central fixation.

Optic Nerve: Occasionally, myelin extends from the optic nerve out onto the normally unmyelinated retina. These medullated (myelinated) nerve fibers appear as a swath of snow-white retina extending from the optic disc.

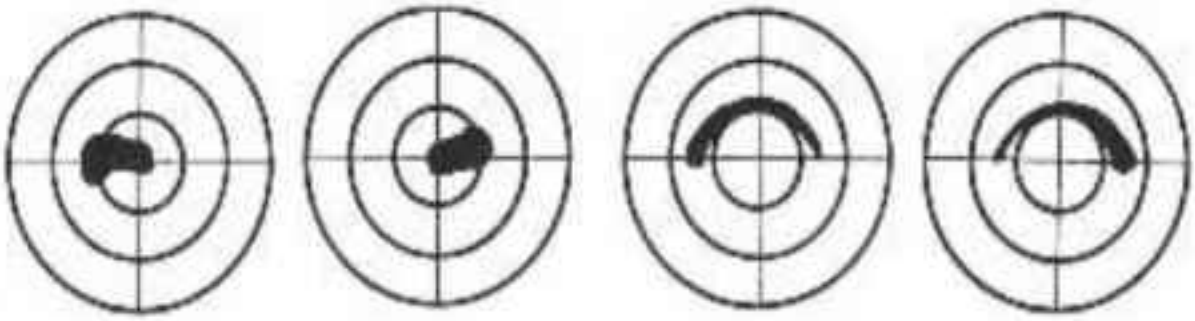




nerve fibers, and the layer of ganglion cell axons, the nerve fiber layer.[23] Ganglion cells situated above the retinal equator project their arcuate fibers north; those below the equator, south.[24] The thinnest, most densely packed axons are in the maculopapillary bundle* flowing straight from the macula to the disc across a small patch of intervening retina (picking up its axons, too).



As mentioned above, there are two visual fields characteristic of an optic neuropathy: the centrocecal scotoma and the arcuate scotoma.



Centrocecal Arcuate

Centrocecal Scotoma: A lesion on the temporal side of the optic nerve head interrupts the maculopapillary nerve bundle, producing a central scotoma that merges with the blind spot. A purely macular lesion would only produce a central scotoma, sparing the region between central fixation and the blind spot.[25]

Maculopapillary Bundle: The optic disc has two aliases: the papilla (as in papillitis or maculopapillary bundle) and the cecum (as in centrocecal scotoma – a central scotoma which merges with the blind spot).

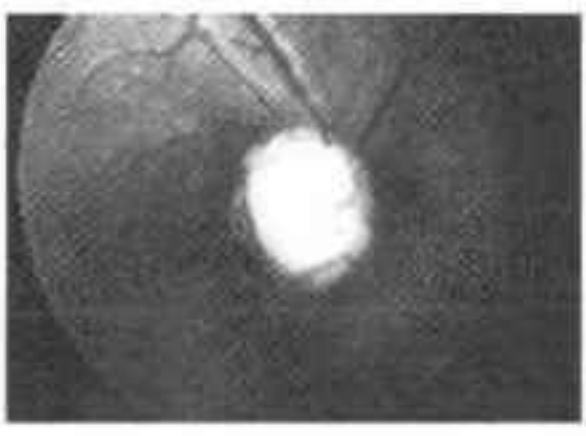
Arcuate Scotoma: Anatomically, this field cut corresponds to the arcuate nerve fibers—axons arching over and under the macula on their way to the optic disc. An optic nerve lesion picking off a splinter or wedge of these fibers produces a rainbow-shaped field cut which merges with the blind spot and respects the horizon. The lesion for this field cut is usually in the optic nerve (occasionally in the retina*, rarely in the chiasm[27]), and the most common causes are glaucoma*[30] (pressure on the optic nerve), multiple sclerosis[35] (demyelination* within the optic nerve), and ischemia of the optic nerve.[36]

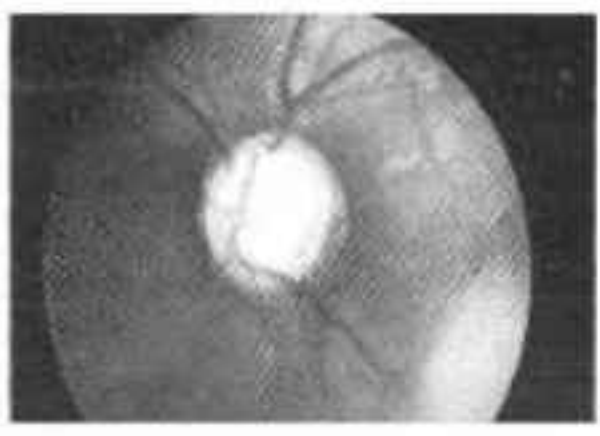
In the Retina: Retinal lesions damage patches of rods and cones, corresponding to punched-out scotomas. Only when retinal lesions expend superficially into the overlying nerve fiber layer do they produce arcuate scotomas. And even then, retinal arcuate scotomas differ from the arcuate scotomas of an optic neuropathy. In general, arcuate scotomas terminate at the site of the lesion, which, in the case of optic neuropathies, is the blind spot. Retinal arcuate scotomas stop at the retinal lesion, because axons downstream from the retinal lesion still have an unimpeded pathway to the optic disc.[26]

Glaucoma: A common eye disease in which intra-ocular pressure rises so high that retinal axons entering the optic disc are either suffocated or squeezed to death.[28] At first, slivers of the arcuate nerve fiber layer are picked off, but over months to years, entire swaths are damaged.[29] Fortunately, since the arcuate fibers arch around the macula, visual acuity is not affected until late.

The tip-off to glaucoma is not the arcuate field cut, which often escapes attention, but rather the appearance of the optic disc. Normally, in the center of the optic disc there is a small depression, called the optic cup, visible by its slightly more creamy yellow, less salmon color than the rest of the disc. You can also outline the cup by: 1) a tiny shadow along the edge of the cup where blood vessels dip in and out of the disc, and 2) small "circumlinear" arterioles skirting horizontally along the superior and inferior margins of the cup.

Elevated intraocular pressure (glaucoma) causes the optic cup to deepen, pale, and balloon out, eventually occupying 80–90% of the optic disc (instead of its usual 40–60%) and leaving a very thin rim of relatively normal (salmon colored) disc around the excessively pale cup. In primary optic neuropathies, optic disc pallor extends beyond the cup to the edge of the disc.[30] The edges of a deepening glaucomatous cup are precipitous, visible by the sharp angulation taken by blood vessels crossing the edge of the cup.[31] The glaucomatous cup is also vertically oval (where the arcuate nerve fibers enter the disc); a normal cup is round or horizontally oval.[32] Henschler and Oaher point out that glaucomatous cups often expand to include one or both circumlinear arterioles skirting along the perimeter of the cup.[33]



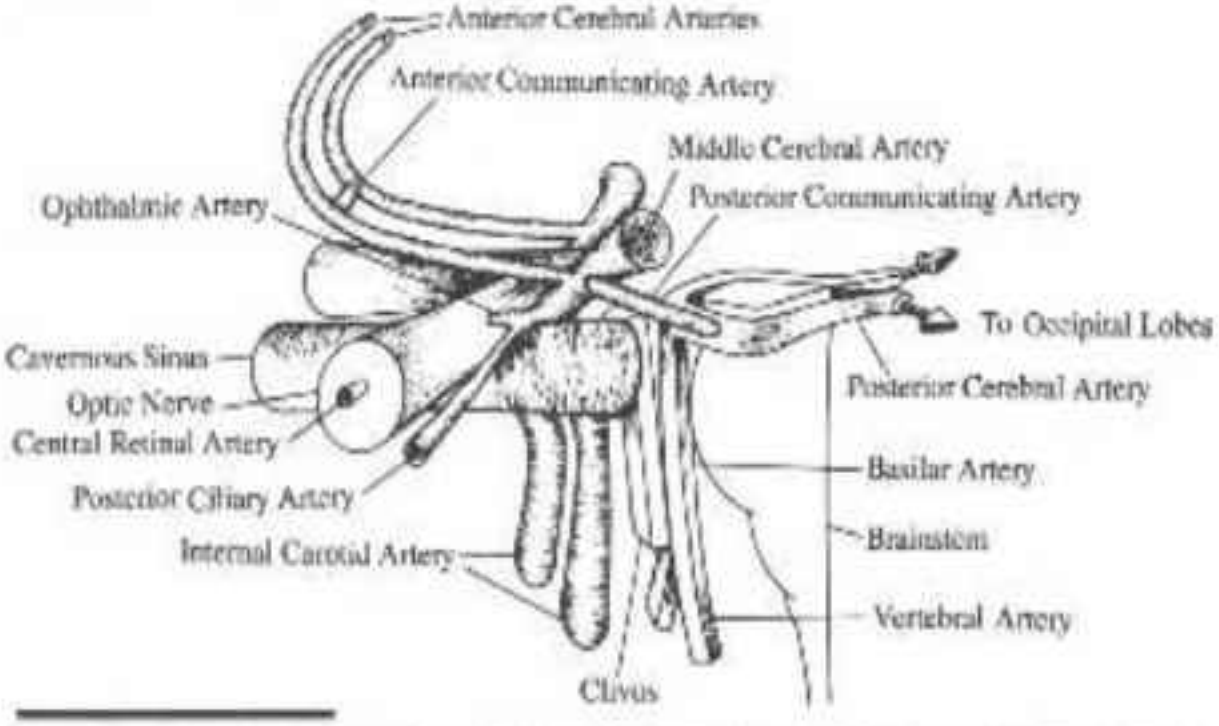


Acute glaucoma is terribly painful. The conjunctiva becomes injected (red), the cornea slightly hazy. The iris may even become paralyzed, making the pupil moderately dilated and unreactive to light. Locate an ophthalmologist quickly to lower such an acute rise in intraocular pressure.

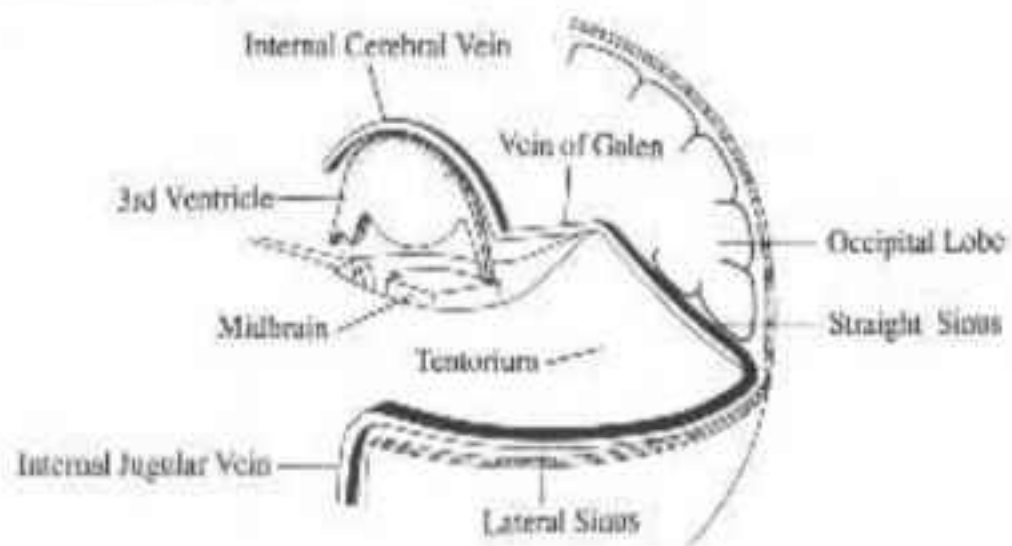
Demyelination: Though multiple sclerosis is supposed to be a purely demyelinating illness, the loss of *unmyelinated* arcuate nerves suggests that some axonal injury also occurs within the optic nerve.

Arcuate and centrocecal scotomas almost always signify optic nerve lesions. Another unilateral field cut, called an altitudinal field cut, may, like central scotomas, result from either optic nerve or retinal lesions. The term 'altitudinal' refers to the horizon separating the superior half of the retina from the inferior half. Altitudinal field cuts are almost always ischemic, usually involving the central retinal artery supplying the inner surface of the retina, and sometimes the posterior ciliary artery supplying the deeper layers of the optic disc*.

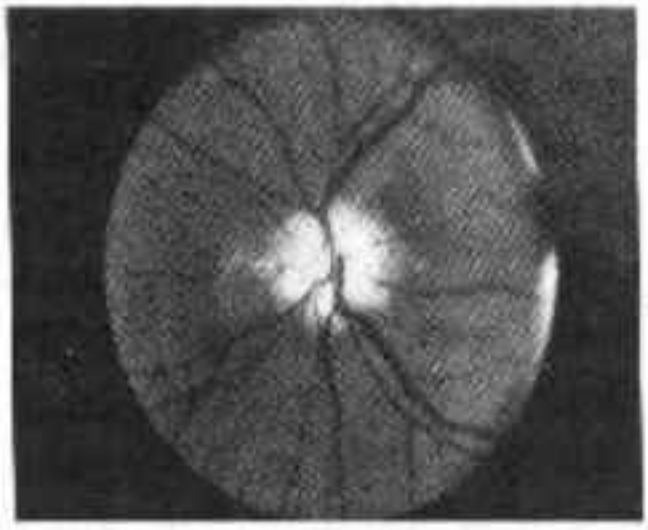
The arterial supply to the eye begins in the ophthalmic artery, the first major branch off the internal carotid artery. The ophthalmic artery gives off the central retinal artery and several posterior ciliary arteries, but only the central retinal artery punctures the optic nerve to reach the globe.[38] Just before emerging from the optic disc, the central retinal artery branches, its smaller branches supplying the *surface* of the disc (giving the disc its light-salmon tint[39]) and its larger branches supplying the superior and inferior retina up to, but not across, the horizon. These retinal arterioles travel under-cover of the nerve fiber layer.



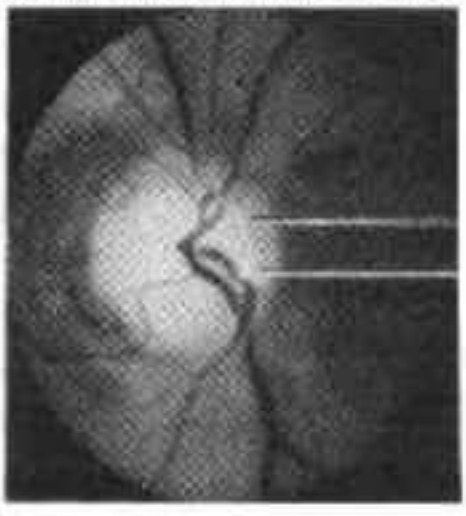
Deeper Layers of the Optic Disc: Bilateral inferior altitudinal field cuts have been reported in gunshot wounds to the occipital lobes above the calcarine fissure.[37] A bilateral *superior* altitudinal field cut from a bullet through the inferior occipital lobes is usually fatal, because the bullet also tears the straight sinus, a vital venous channel traveling along the superior ridge of the tentorium between the occipital lobes.

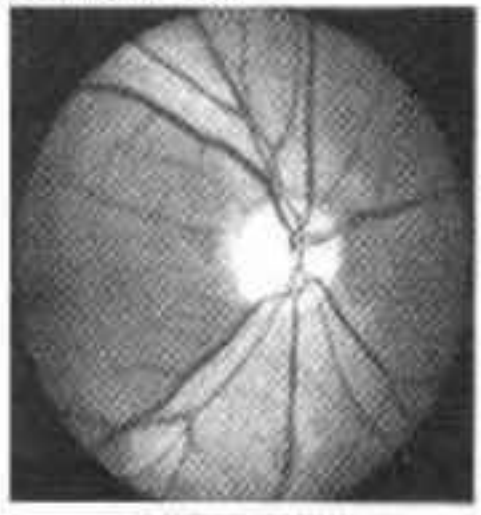


The posterior ciliary arteries, carrying 90% of the blood supply to the eye,[40] run alongside the optic nerve to the back of the globe where they supply the *deeper* layers of the optic disc.[41] The posterior ciliary arteries then scatter widely to supply the deep layers of the retina giving the retina its red color.[42] Sometimes the posterior ciliary circulation slips a small branch, the cilioretinal artery, onto the retinal surface to help supply the macula.[43] The cilioretinal artery appears as a cane-shaped arteriole hooking over the temporal side of the disc headed for the macula.



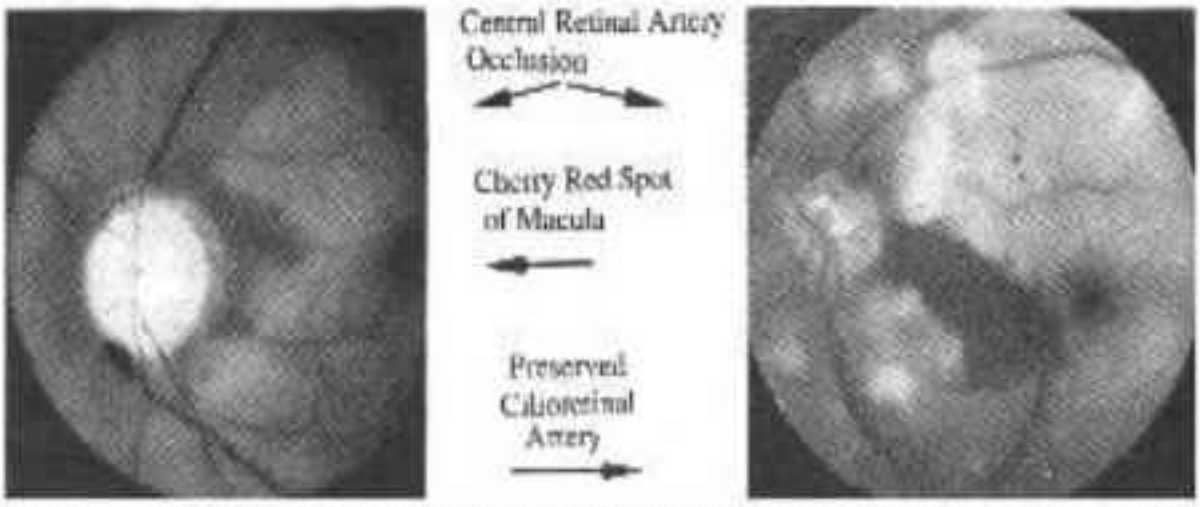
Ischemia of either the posterior ciliary *or* the central retinal artery can cause altitudinal field cuts *or*, if the ischemia is extensive enough, complete blindness.[44] Ophthalmoscopically, you should be able to distinguish the two arterial occlusions.[45] In central retinal artery obstruction you should see attenuated arterioles emerging from the optic disc, and—because the central retinal artery supplies the disc *surface*—a slightly pale disc (or a wedge of pale disc if only one branch of the central retinal artery occluded). If you're lucky, you may even see a refractile cholesterol embolus* in one of the branches of the central retinal artery. The infarcted nerve fiber layer becomes somewhat opaque, obscuring the underlying retina, as if you were looking at the retina through a thin sheet of ground glass. Later, as the swath of nerve fibers atrophies, the underlying retina and blood vessels become even more vibrant and distinct than usual. Compare these retinal vessels with ones in normal regions of the retina where a normal nerve fiber layer still overlies retinal arterioles.





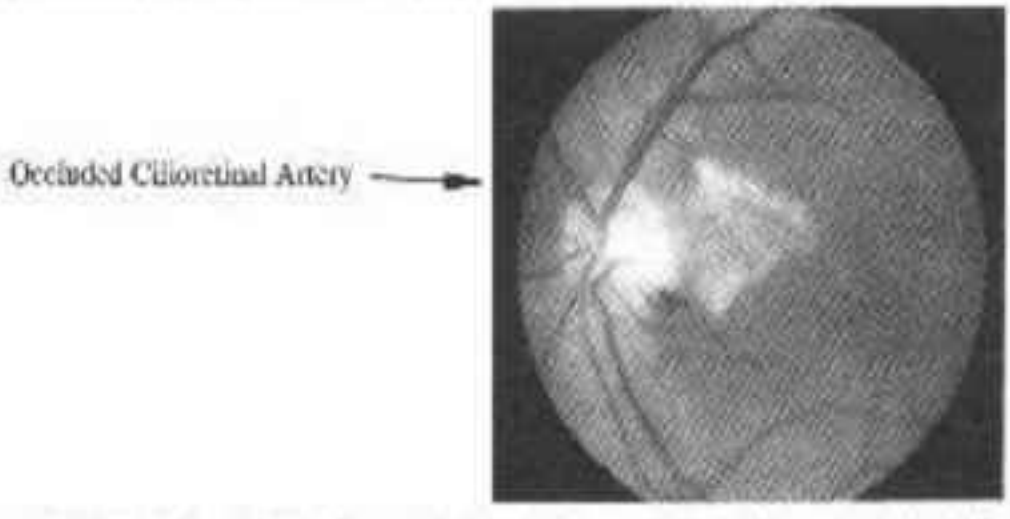
Refractile Cholesterol Emboli: Retinal emboli, which lodge far more frequently in the central retinal artery than they do in the posterior ciliary, are made up of cholesterol, platelets and fibrin, or calcium. Calcific emboli, which are particularly shiny (refractile), tend to embolize from the heart, cholesterol and platelet/fibrin emboli more from the carotid artery.[46]

In complete central retinal artery occlusion the entire retina may become obscured except for the fovea which, devoid of overlying axons, allows the deeper layers of the retina (supplied by the posterior ciliary artery) to shine through as a 'cherry-red spot.' Blindness may be avoided in central retinal artery occlusion if the patient is lucky enough to have a cilioretinal artery carrying independent blood from the posterior ciliary circulation to the macula[3,48]



Posterior ciliary artery ischemia is strikingly different from central retinal artery occlusion. The brunt of posterior ciliary ischemia is borne by the optic nerve head. Initially, the infarcted disc swells, mimicking papilledema even to the point of hemorrhages around the disc. Branches of the central retinal artery emerging from the disc retain their normal caliber. As the infarcted optic disc pales and the nerve fibers die, the fundus begins to resemble central retinal artery occlusion[3]. Visual acuity is affected early in posterior ciliary occlusion because of damage to the maculopapillary bundle entering the temporal side of the disc. In this case, posterior ciliary occlusion produces a central or paracentral scotoma. In other cases, a different sector of the disc may infarct, swell, and then atrophy. The resulting sectorial field cut (or arcuate field cut if the disc infarction is tiny enough) corresponds, quite naturally, to the focally infarcted disc.

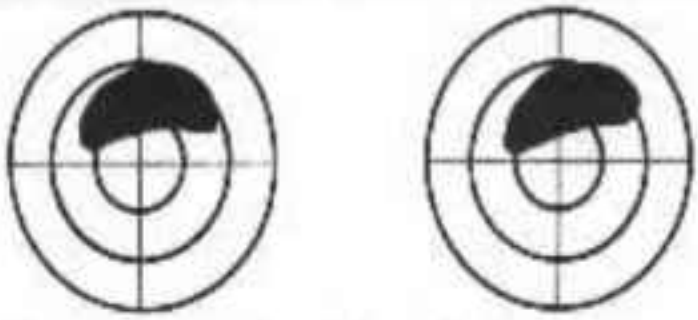
To the Macula: On the other edge of the sword, an isolated cilioretinal occlusion may destroy macular vision by infarcting the maculopapillary bundle.[47]



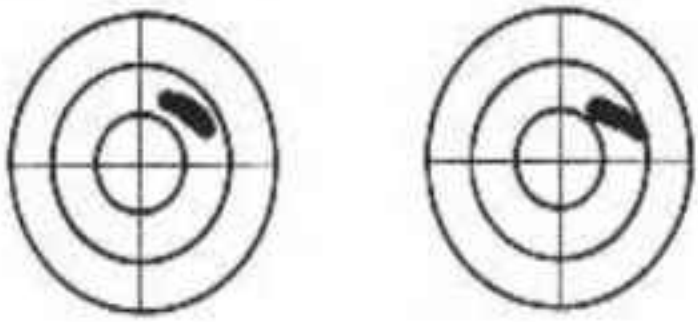
Resemble Central Retinal Artery Occlusion: Even though the posterior ciliary artery gives the retina its red color, the retina remains red in posterior ciliary artery occlusion. In general, only the short posterior ciliary arteries supplying the disc and immediately adjacent retina are severely affected, not those posterior ciliary branches supplying widespread areas of the deep retina.[49]

Bilateral Field Cuts—Prechiasmal

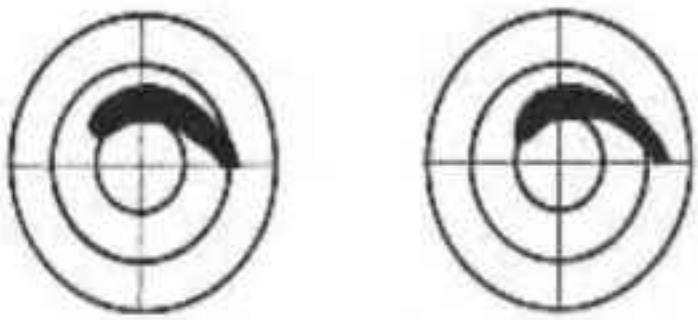
Though uniocular field cuts automatically place the lesion anterior to the chiasm; so do bilateral field cuts if they do not respect the vertical midline. That is, prechiasmal field cuts should come to the vertical midline and cross it without 'stepping off.'



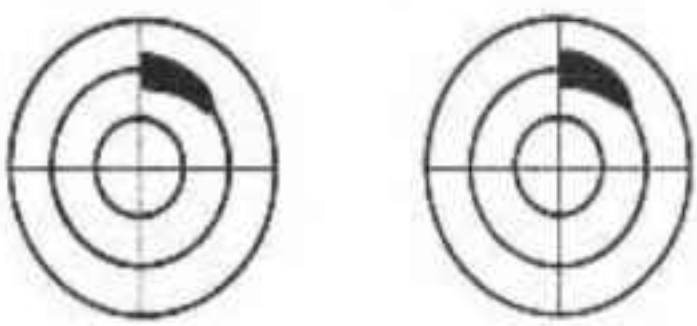
If the field cut doesn't come to the midline, like this:



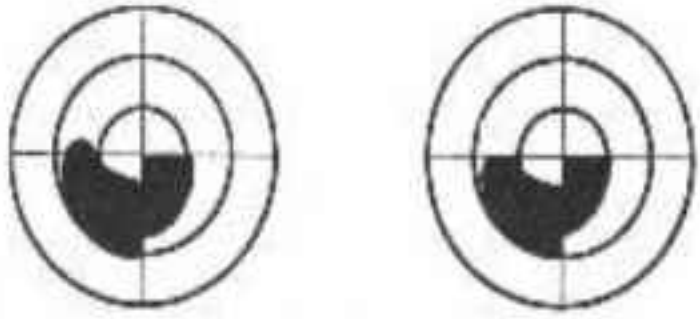
go back and use a smaller, dimmer target which will enlarge the field cut enough to bring it to the midline, like this:



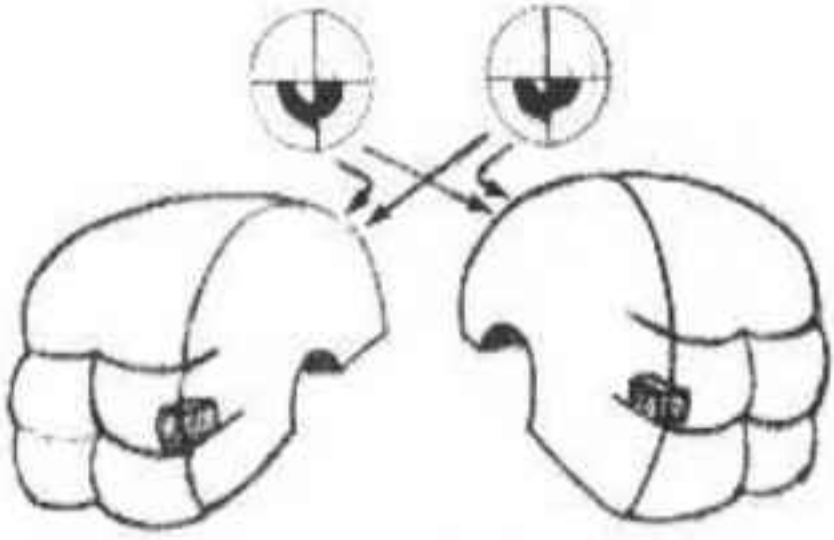
Even though this homonymous field cut looks retrochiasmal, it is prechiasmal because it doesn't respect the vertical. Instead of coming to the midline and stopping, this prechiasmal field cut crosses the vertical midline as if it never existed. To be intrachiasmal or retrochiasmal, the field cut must come to the vertical midline and stop:



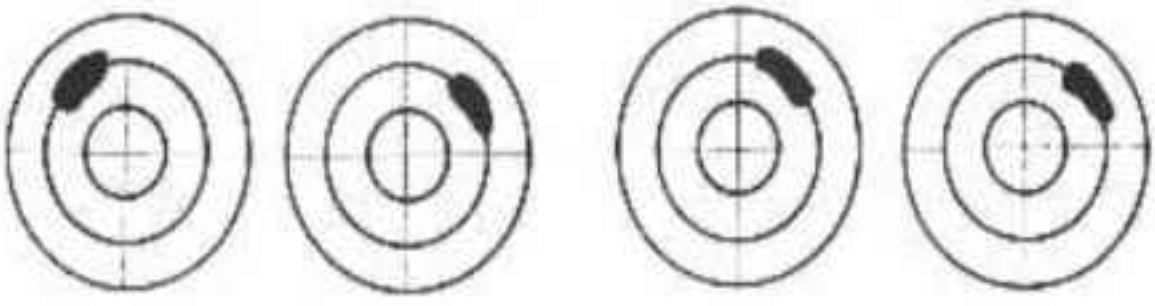
If an intra- or retrochiasmal field cut does cross past the midline, it must still respect the midline. That is, it must come to the vertical midline and 'step off' like this:



These look like bilateral, prechiasmal field cuts until you spot the step-off. These visual fields represent two separate inferior quadrantic hemianopsias due to two separate occipital lobe lesions, both superior to the calcarine fissure.[29]



If, with a smaller target, you can't get the field cut to come to the midline, then you can't be certain it's prechiasmal, but as with anything in medicine, begin with the obvious possibilities. For example, the field cut on the left should make you look in the chiasm and the one on the right should direct you behind the chiasm.



Where does this field cut point you?



Does the field cut respect the vertical? No, so it must be prechiasmal. This rather specific field cut is seen in retinitis pigmentosa, a degenerating illness of the retina, affecting rods early on (an early complaint is night blindness) and later, cones.[51] Because no rods reside in the macula, the field loss encircles the macula beginning (where rods are densest[52]) in the mid-periphery of the retina. The result is a doughnut of visual loss which later spreads centripetally and centrifugally, leaving a tiny island of relatively preserved macular (cone) vision.[53]

In summary, the characteristic features of a prechiasmal (retina or optic nerve) field cut are unilaterality, respect for the horizon, and no respect for the vertical. Respect for the horizon stems from the strict anatomy of both the nerve fiber layer and the arterial supply of the retina—neither ganglion cell axons nor retinal arterioles cross the horizon. Scotomas which respect the vertical are either chiasmal or retrochiasmal.

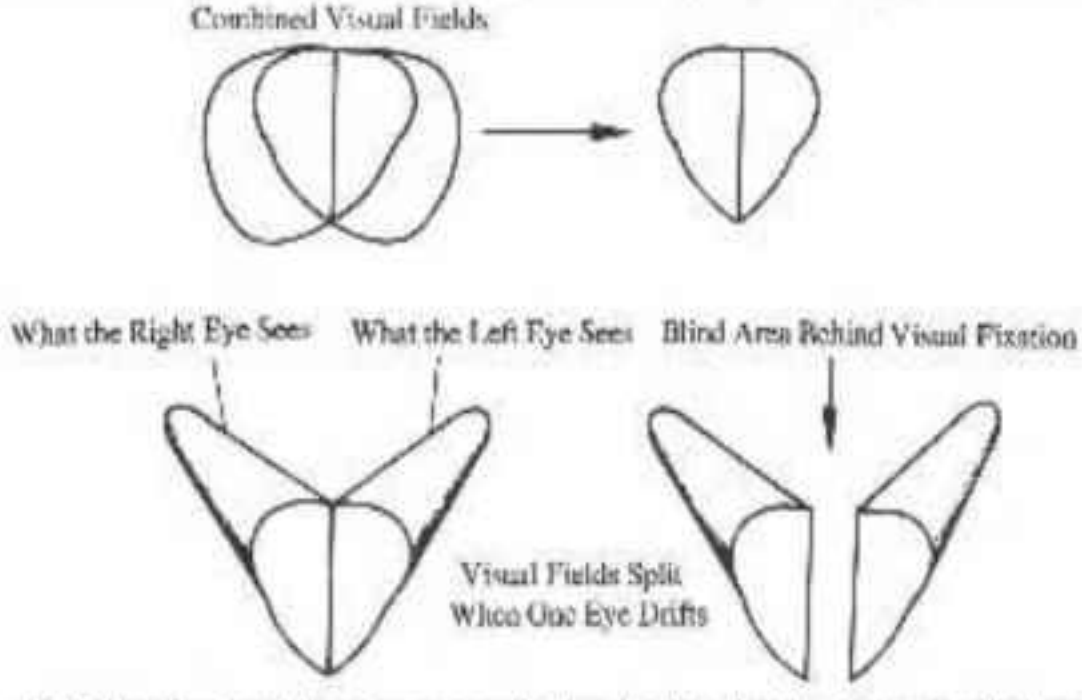
Chiasmal Field Cuts

To firm up the features of prechiasmal field cuts, we'll now contrast them with the visual fields of chiasmal and retrochiasmal lesions, even though these field cuts are outside the IInd cranial nerve.

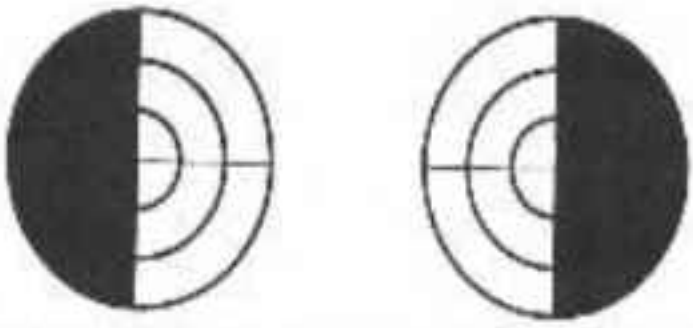
In the optic chiasm retinal axons from the temporal side of midline remain lateral, coursing into the ipsilateral occipital lobe, while retinal axons from the nasal side of midline cross in the chiasm to the contralateral occipital lobe. The midline, don't forget, is through the macula, not the optic disc.

A chiasmal field cut is a bitemporal hemianopia which respects the vertical*. The best example you could hope and pray for is this:

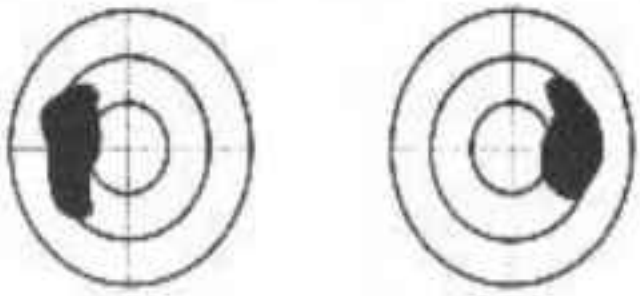
Respects the Vertical: Patients with very dense bitemporal hemianopias may come up with two curious problems. 1) They can't thread a needle. When focusing on the thread, they can't see the needle held behind the thread, because they're blind to anything directly beyond their fixation point.



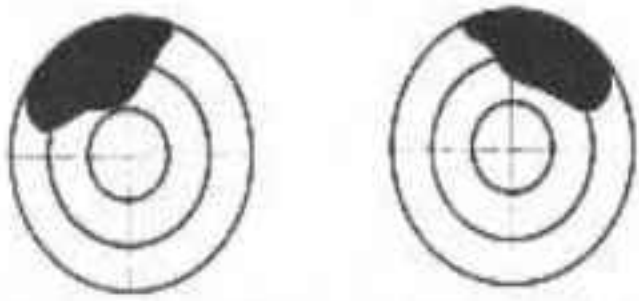
And 2) the visual world may become vertically spliced. As long their eyes are yoked, everything's all right. But if one eye should drift because of an old exophoria, their visual world splits apart.[54] (Exophoria is a latent weakness of the medial rectus muscle that becomes evident only when the patient covers the eye—i.e., fixation prevents the eye from fixating laterally. *Exotropia* is persistent weakness of the medial rectus muscle, even when both eyes are uncovered. Esophoria and esotropia refer to weakness of the lateral rectus muscle, so that the eye floats inward.)



Most of the time, though, you'll have to settle for something like this:

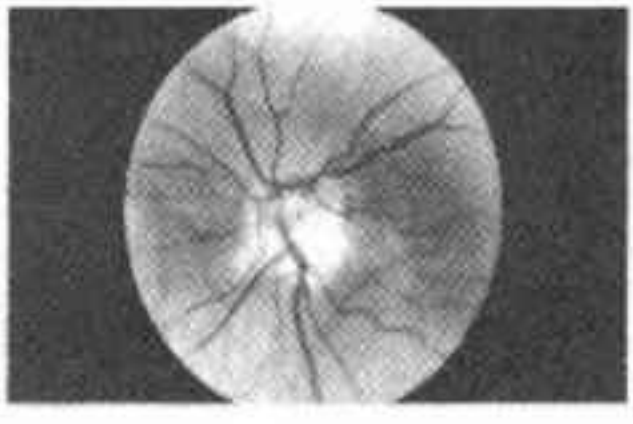


As mentioned previously, you can bring this field cut closer to the midline by using a tiny target, especially a tiny red target. As you move a red target from the temporal field toward the midline, the patient will detect a sudden improvement in vibrancy as the red target crosses the midline. Don't settle for anything less than strict respect for the vertical midline. A field cut that crosses the vertical without stopping or stepping off is not due to a chiasmal lesion. For example:



is not a chiasmal lesion. It might represent bilateral retinal detachments*, or tilted discs, for starters. The tilted disc is a normal anatomic variant; by plugging into the eye at an oblique angle, the optic nerve head appears tilted (oval) through the ophthalmoscope. This aberrant anatomy produces a superior temporal field cut, unbeknownst to the patient, since he's had it all his life.[35]

Tilted Disc



*Retinal Detachment: The retina peels off from its scleral base, usually beginning at a point near the periphery. Lasers can weld the retina back down.

Remember that for chiasmal and prechiasmal diseases, you can stay comfortably close to the vertical midline*. Have the patient compare the clarity of your hands, add up your fingers, or compare color vibrancy, all of which are more rewarding than trying to decide when the patient can see your wiggling finger as you move it in from the distant periphery.[61] Besides, a moving target, especially a wiggling one, is so strong a stimulus that only very dense peripheral field cuts will be detected; more subtle, 'relative', field cuts will go undetected. When you do want to test the peripheral fields, use the same technique as you did for the central 30 degrees: hand clarity, finger addition, and red washout.

The anatomic reason for the bitemporal field loss is, of course, that nasal retinal axons cross in the chiasm. What's surprising about chiasmal lesions is that despite the small size of the chiasm, the crossing fibers are almost invariably interrupted long before the uncrossed fibers, and often without any clinical involvement of the uncrossed fibers at all. This is doubly surprising when you look at the size of lesions producing the bitemporal hemianopia. Commonly a huge pituitary tumor has grown up out of the pituitary fossa and compressed the entire optic chiasm. Despite this bulky insult, only the crossing fibers are affected (or affected way out of proportion to the uncrossed fibers), probably because the bitemporal hemianopia is not due so much to direct axonal compression as it is to *arterial* compression. The crossing fibers receive their main blood supply underneath the chiasm from the internal carotid, posterior communicating, and posterior cerebral arteries encircling the base of the brain. As pituitary tumors and craniopharyngiomas* (the two most common causes of chiasmal field cuts) extend upward, they interrupt the blood supply to the crossing fibers, but spare the *descending* blood supply to the uncrossed fibers coming from the two superiorly placed anterior cerebral arteries*.[62]

Crossing of nasal retinal fibers in the chiasm is not plain and simple. Inferior nasal fibers (receiving impulses from the superior temporal field) dip briefly into the *contralateral* optic nerve for a millimeter or two before entering the chiasm. This brief detour is called Wilbrand's knee. Clinically, this means that whenever you uncover a monocular field cut, especially a central, centrocecal, or paracentral one, you also

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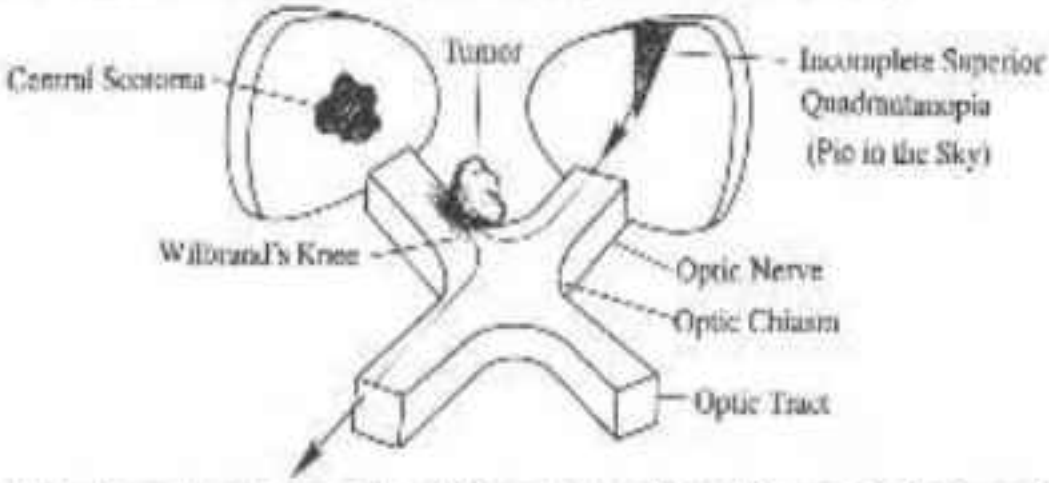
Vertical Midline: Visual field testing for chiasmal lesions can be done by concentrating on the 30 degrees surrounding central fixation.[54] Macular fibers are spread throughout the optic chiasm,[55] and therefore, lesions almost anywhere in the chiasm may affect macular or paramacular vision.[56] In fact, chiasmal lesions may occasionally produce bilateral central scotomas simulating bilateral optic neuropathies.[58]

For suspected retrochiasmal lesions you will have to extend your visual field testing outside the central 30 degrees, because macular fibers in the occipital lobe are no longer spread out; instead, macular fibers are funneled to the tips of the occipital lobes, allowing partial occipital lobe lesions to spare macular and paramacular fields.[59]

Craniopharyngioma: A tumor arising from embryonic pituitary stalk cells which were trapped during fetal development in the parasellar area. Craniopharyngiomas, which become symptomatic by compressing the hypothalamus, pituitary gland, and optic chiasm, are usually calcified and can, therefore, frequently be suspected on a plain skull xray by the presence of calcium above the sella turcica (sella=saddle, turcica=Turkish).

Anterior Cerebral Arteries: Not everyone agrees that bitemporal field cuts from chiasmal compression have a vascular pathogenesis. O'Connell believes that crossing chiasmal fibers are normally stretched tauter than the lateral, uncrossed ones. Tumors compressing the chiasm preferentially damage the already-stretched, crossing fibers.[62]

need to carefully look at the *other* eye; a seemingly trivial field cut in the superior temporal field of the other eye automatically localizes the lesion proximally in the contralateral optic nerve (the one with the central, centrocecal, or paracentral scotoma). The proximal optic nerve lesion has nipped Wilbrand's knee, producing a "junctional" scotoma (junction between the optic nerve and chiasm).[64]



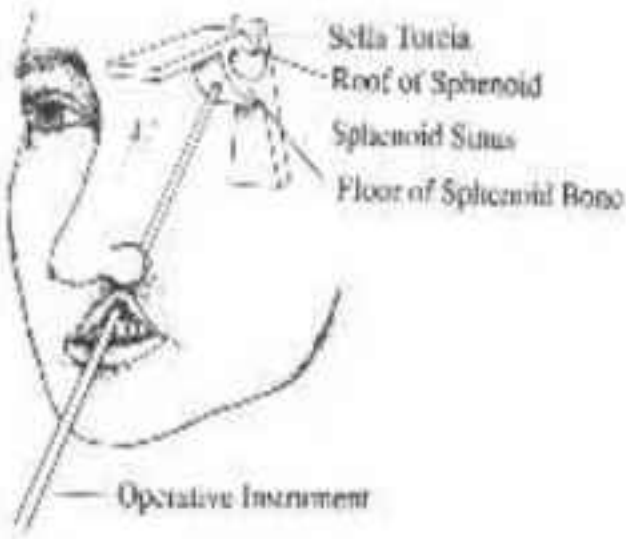
A lot of small structures lie within an inch of the chiasm. Looking up from the chiasm, you're gazing at the hypothalamus. Just above that, directly in the midline, is the 3rd ventricle curving downward to straddle the chiasm. The anterior notch of the third ventricle is the optic recess; the one right behind it is the infundibular recess. Once in a while, an enlarging 3rd ventricle will stomp on the chiasm, causing a chiasmal field cut (bitemporal hemianopia).[65] Underneath the optic chiasm, a full centimeter away, is the pituitary fossa, or sella turcica, which houses the bean-sized pituitary gland sprouting its stalk up behind the chiasm to the cloudy reaches of the hypothalamus alongside the anterior 3rd ventricle. The bony lip in front of the sella is the tuberculum* sella; in back, the dorsum sella. The small bony wings extending from the tuberculum sella are the anterior clinoids*, those off the dorsum sella, the posterior (or dorsal) clinoids. The dorsum sella forms the top end of the clivus, while the floor of the pituitary fossa forms the roof of the sphenoid sinus, an air-filled midline cavity*. On either side of the pituitary gland surges venous blood inside the

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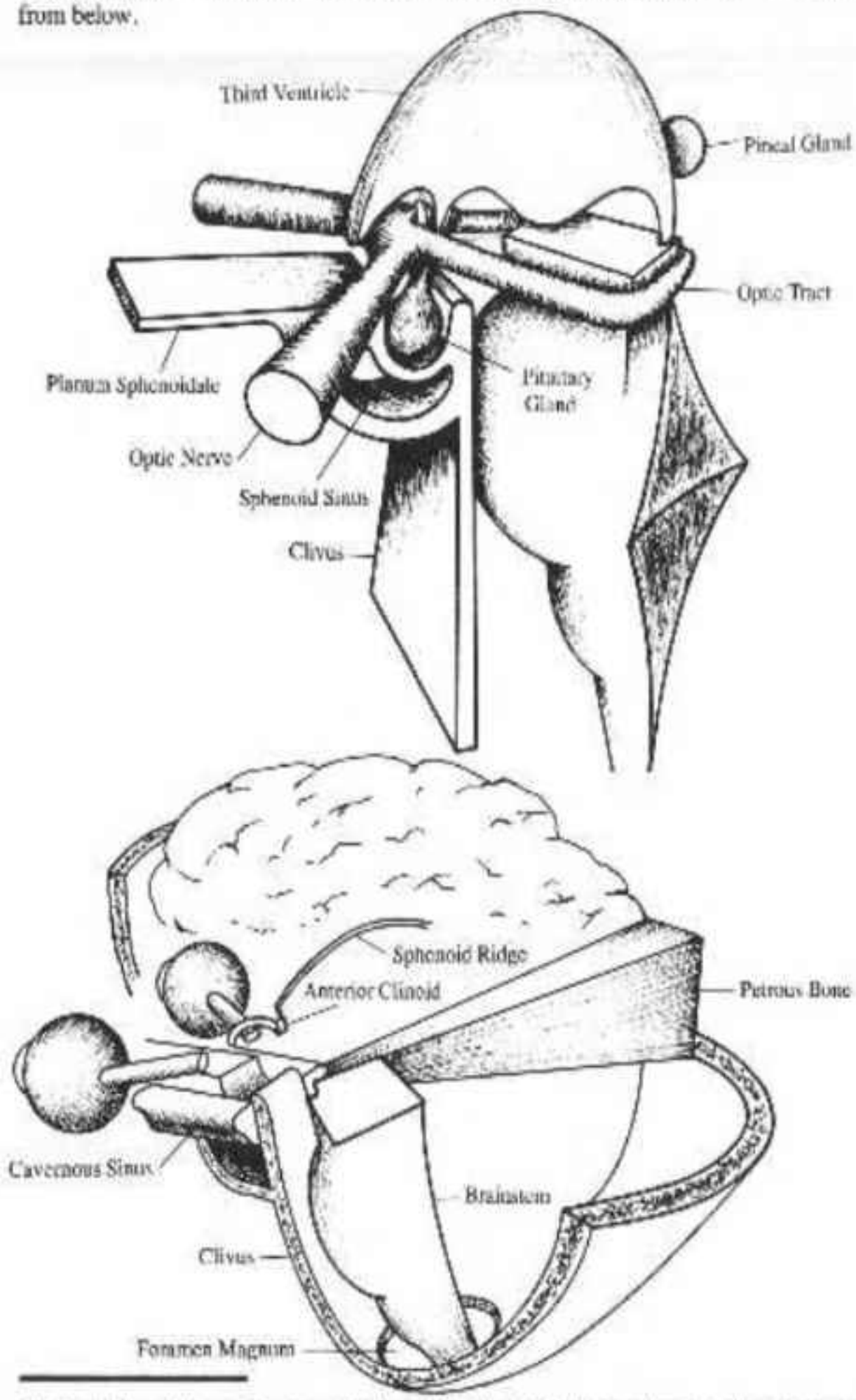
Tuberculum: Means nubbin.

Clinoid: From Greek, meaning bed-shaped.

Midline Cavity: By drilling a hole through both the floor and roof of the sphenoid sinus, neurosurgeons can often remove pituitary tumors through the nose without having to open the skull and lift the "hood" (frontal lobes).



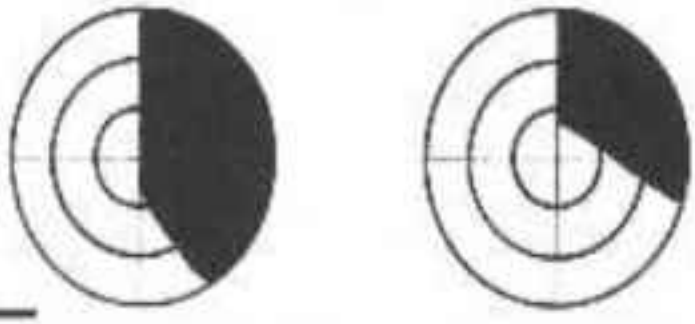
cavernous sinus. Within the lumen and wall of the cavernous sinus lie cranial nerves III, IV, VI and $V^{1\&}$ as well as the carotid artery which at this point penetrates the skull from below.



V^1: The fifth cranial nerve has three divisions: V^1, V^2, and V^3. The first division, the opothalmic, travels the whole length of the cavernous sinus.

Retrochiasmal Field Cuts

The third type of visual field cut is the homonymous hemianopia. Prechiasmal lesions, you recall, produce unilateral and bilateral field cuts that do not respect the vertical. Intrachiasmal lesions produce bitemporal hemianopias. Retrochiasmal lesions cause complete or incomplete homonymous hemianopias*—field cuts in the right (or left) half of the visual world of both eyes. Again, the field cuts must respect the vertical midline*, but they do not have to match—one can be larger than the other. In general, though, the more congruous (exactly like each other) the field cut in each eye, the more occipital the lesion, as the widely scattered optic radiations in the deep parietal and temporal lobes converge on the occipital striate cortex*. Conversely, the more incongruous the field cuts, the more anterior the lesion. The most incongruous homonymous hemianopias occur with optic tract and lateral geniculate lesions*.[66] So,

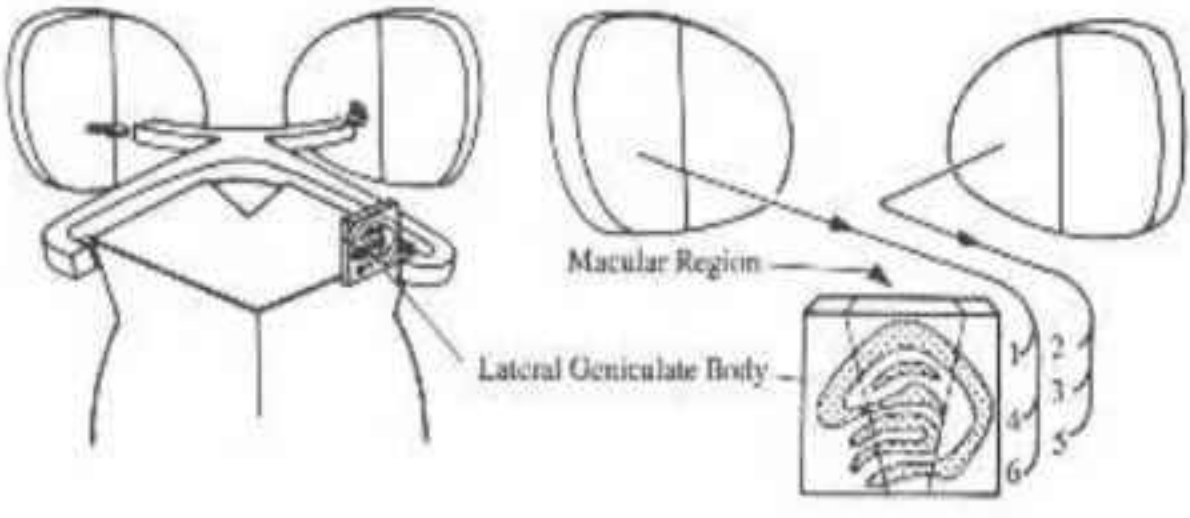


Complete or Incomplete Homonymous Hemianopias: Complete versus incomplete field cuts are not the same as dense versus relative field cuts. An incomplete visual field cut occupies only part of a quadrant or hemifield. A relative field cut may be complete or incomplete, but is only detectable by using more subtle techniques like finger counting.

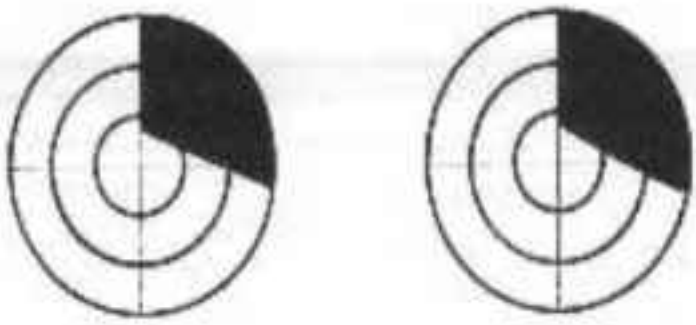
Vertical Midline: It's reportable when bilateral occipital lobe strokes meet at the vertical midline without a step-off, producing a field cut that looks prechiasmal.[65]

Striate Cortex: Striate refers to a thin strip (or striatum) of white matter within the calcarine cortex, the cortical region that receives all the optic radiations from the lateral geniculate body. Don't confuse striate cortex with corpus striatum—the caudate and putamen taken together.

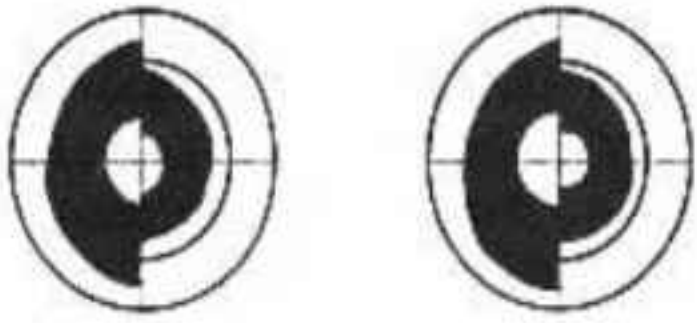
Lateral Geniculate Lesions: The right lateral geniculate body is the first synaptic stopover for all retinal ganglion axons serving the left visual field. Fibers from the contralateral eye synapse in layers 6, 4, and 1 of the lateral geniculate body; those from the ipsilateral eye in layers 5, 3, and 2. Macular fibers dominate the central core of each lateral geniculate body which explains why geniculate lesions favor the macular region (incongruously).[67]



is more anterior than:



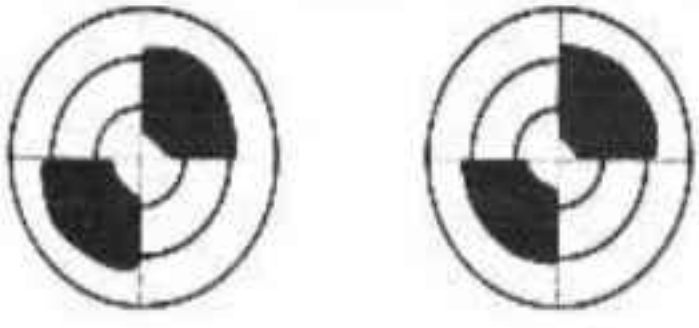
What's this?:

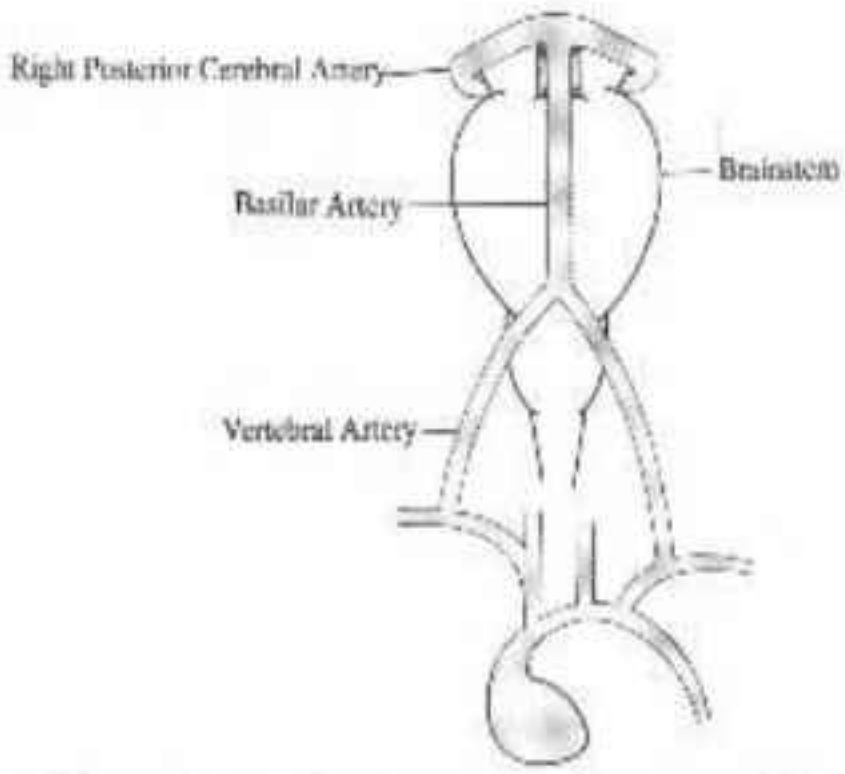


Each homonymous field has a 'step-off'—each respects the midline. If you saw the right homonymous field cut alone, you'd say the patient had a left retrochiasmal lesion. And if you saw the left homonymous field cut alone, you'd say he had a right retrochiasmal lesion. Together, he must have bilateral retrochiasmal lesions, the most common cause of which is bilateral strokes of the occipital lobes*.[10]

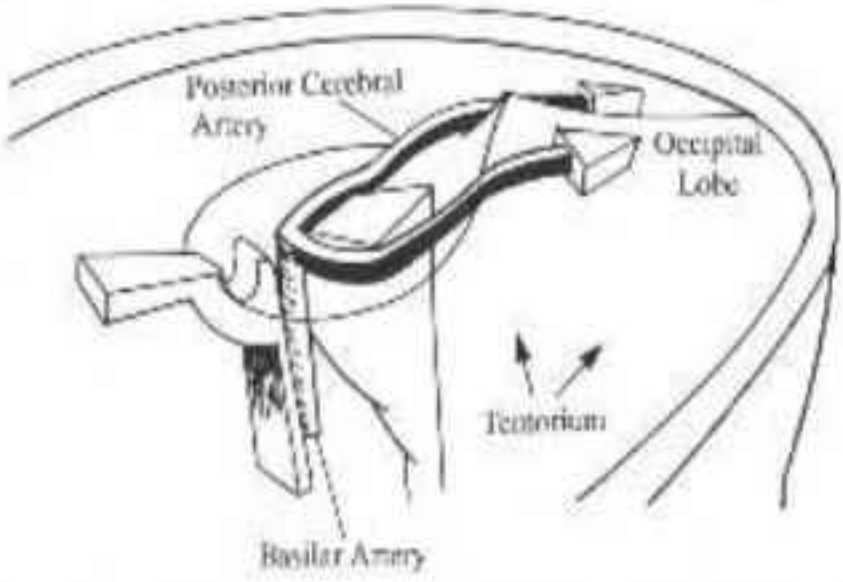
This situation occurs more frequently than you'd expect, because it only takes a single vascular occlusion (of the basilar artery) to infarct both occipital lobes. The occipital lobes and the medial temporal lobes are the only parts of the cerebral hemispheres supplied by the basilar, or posterior, circulation. The *main* job of the basilar, however, is to supply the most important two inches of the body—the brainstem. To do this, the basilar artery has been assured a reliable blood supply from two separate vertebral arteries. These two major pipes, each of which alone is fully capable of supplying the basilar, originate at the subclavian artery and join in front of the lower pons to form the basilar.

Occipital Lobes: The same reasoning localizes this checkerboard field cut to both occipital lobes:[10]

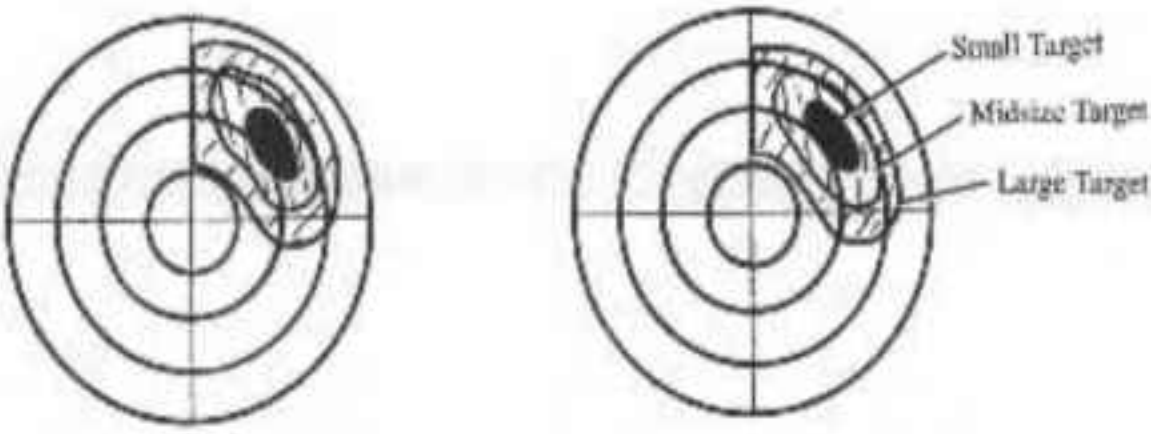




After asceoding the brainstem, the basilar artery divides in front of the midbrain into two posterior cerebral arteries which wrap around the midbrain, slip up over the free edge of the tentorium, and toddle back to supply the occipital lobes. *Bilateral* occipital lobe infarctions occur because impaired circulation anywhere along the basilar artery, from whatever cause, jeopardizes these tenuous terminal twigs reaching deep into the occipital lobes. (Regardless of where you step on the hose, water stops flowing out the end.) Occasionally, one of the posterior cerebral arteries is caught sneaking over the free tentorial edge by a herniating temporal lobe (chapter 22). Following recovery, the patient may be left with a homonymous hemianopia.[71]

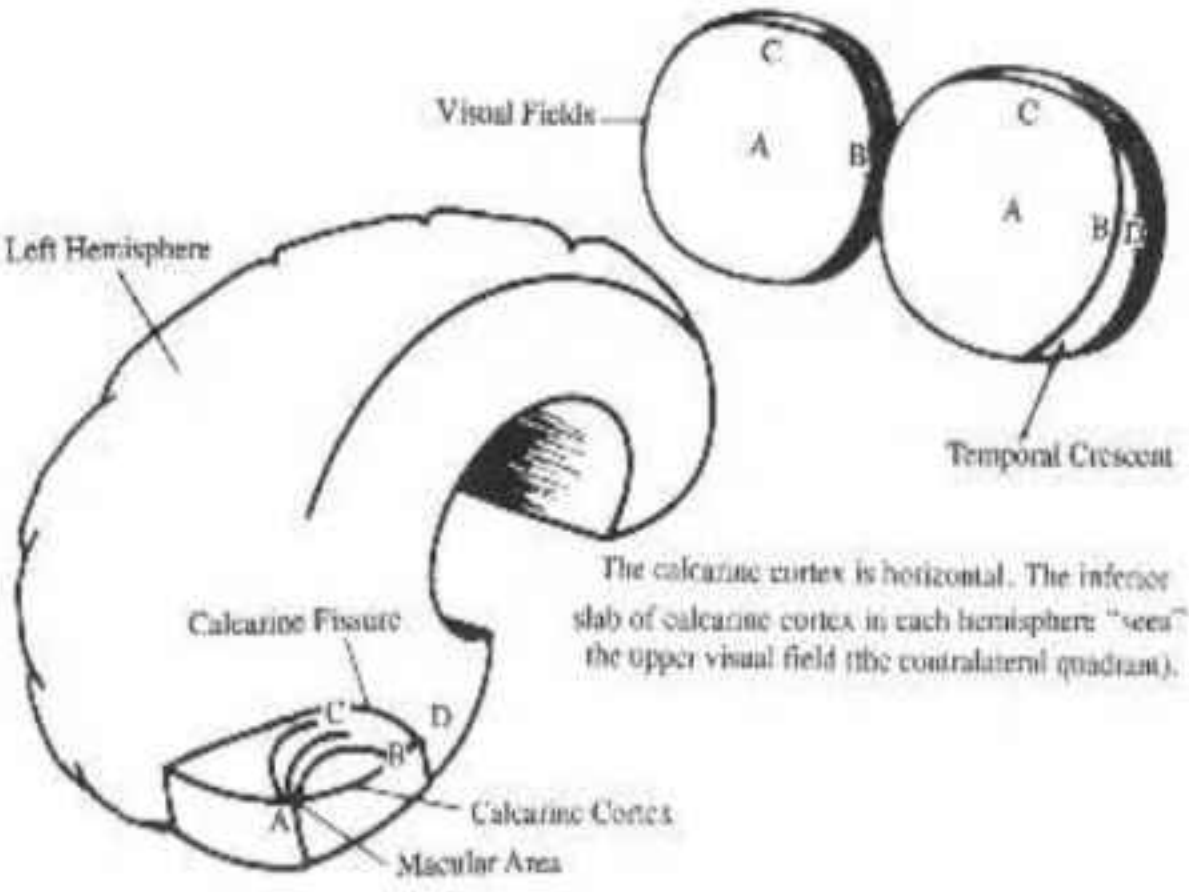


The slope of the border surrounding a retrochiasmal field cut may help distinguish an old stroke from a tumor. If the margins of the field cut remain crisp regardless of the target size, called a precipitous slope, the etiology of the field cut must be one that produces sharp borders, like an old stroke. If, on the other hand, a gradually smaller target gradually enlarges the field cut ('sloping margins'), then strands of tumor cells are likely infiltrating the edges of the lesion, or else edema is present around a recent stroke.



Because macular fibers terminate at the very tip of the occipital lobes, a small lesion at both occipital tips (like a blow to the occiput) can produce bilateral central scotomas. And because the macular area in each occipital lobe has a second, independent blood supply from the anterior cerebral artery (occasionally from the middle cerebral), bilateral posterior cerebral occlusions may produce widespread blindness that spares macular vision in both eyes.[72] For this reason, large dense homonymous hemianopias that spare central (macular) vision are usually attributed to occipital lobe infarctions*.

Finally, there is one area of each eye's visual field not seen by the other eye: the temporal crescent. Lateral geniculate fibers supplying the temporal crescent synapse anteriorly along the calcarine fissure.[74] An occipital lobe lesion which spares the anterior calcarine fissure would therefore produce the following visual field:



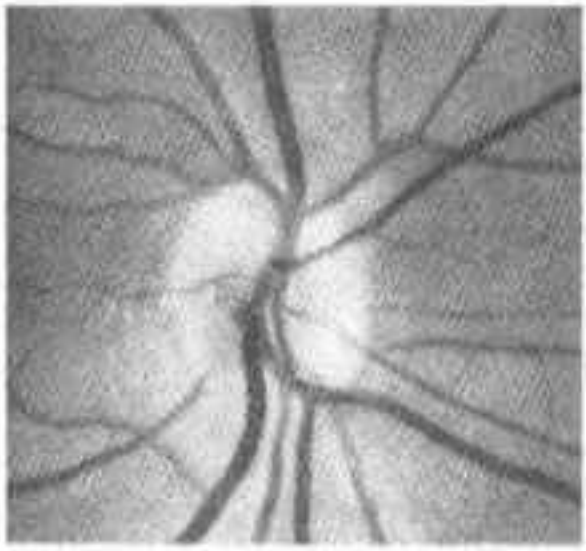
The calcarine cortex is horizontal. The inferior slab of calcarine cortex in each hemisphere "sees" the upper visual field (the contralateral quadrant).

Occipital Lobe Infarctions: The other likely explanation for macular sparing with unilateral occipital lobe lesions is that each macula is *fully* represented in both occipital lobes.[73]

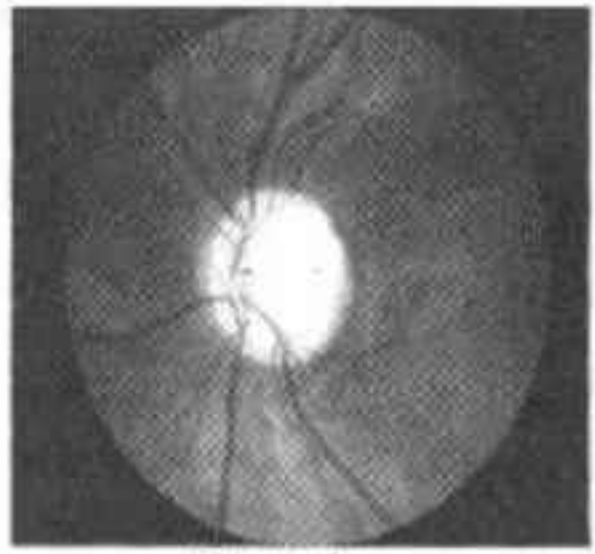
Optic Disc and Retina

So far we've established the following signs of optic nerve dysfunction, or more accurately, prechiasmal dysfunction: unrefractable visual impairment, diminished color discrimination, Marcus Gunn pupil, and visual field cuts which are either unilateral, do not respect the vertical midline, or have a horizontal (altitudinal) margin. The final clue to optic nerve dysfunction is direct observation of the optic nerve head itself, the optic disc.

The single most clinically useful characteristic of the disc is its color: normally a creamy yellow with a light-salmon hint. The creamy yellow color is most evident on the temporal side of the disc where maculopapillary fibers storm the disc as a concentrated bundle of axons. The salmon hint is from tiny capillaries on the disc surface feeding all those axons. If the axons die off, the disc loses both its yellow and salmon colors, as if the capillaries had no reason to be there any more*. An atrophic disc turns chalk-white or dirty-gray.



Normal



Optic Atrophy

No Nerve Fiber Layer Overlying the Retina

True papilledema* and optic disc swelling do the opposite of optic atrophy: they dilate the disc's capillaries, turning the disc an angry, fiery red*. At times you can actually distinguish individual dilated capillaries on the disc surface. The formerly glassy-smooth disc surface becomes rough and red, resembling red steel wool.

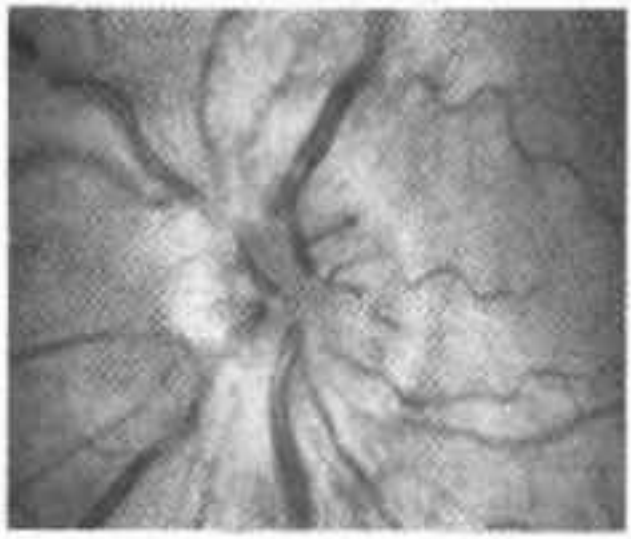
Any More: Actually, optic pallor is caused more by axonal loss than capillary loss. The number of capillaries on an atrophic disc is, surprisingly, only slightly diminished.[77] The atrophic disc's white appearance is probably a reflection of the underlying support structure of the disc as well as all the astrocytes (CNS 'fibroblasts') replacing the dead axons.

True Papilledema: Strictly speaking, papilledema refers only to optic disc swelling due to raised intracranial pressure. Optic disc swelling due to intrinsic optic neuropathies (like optic neuritis, ischemic optic neuropathy, or optic nerve tumors) is simply called optic disc swelling.

Fiery Red: High intracerebral pressure does dilate disc capillaries (papilledema), but only indirectly (i.e., not by directly obstructing the central retinal vein). High intracerebral pressure obstructs the normal flow of axoplasm bound for the optic nerve within the nerve fiber layer. As a result, the 'constipated' ganglion cell axons become swollen and edematous. According to Hayreh, it is really optic disc edema that obstructs veins and capillaries on the disc, not direct compression of the central retinal vein by high intracerebral pressure.[78]

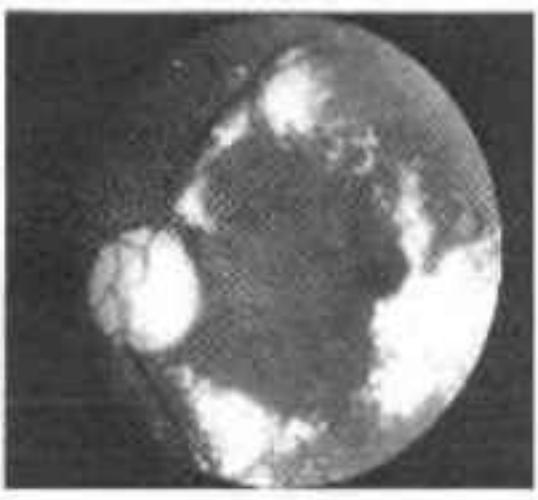
The second important sign of optic disc swelling is obscuration of vessels crossing the margin of the disc.[77] To get underneath the nerve fiber layer, branches of the central retinal artery and central retinal vein normally pass through a thin, transparent nerve fiber layer at the disc edge. In optic disc swelling, these vessels must dive through a jungle of heaped-up and opacified nerve fibers* trying to enter the disc. Using your green ophthalmoscope light to help visualize the nerve fiber layer,[79] look for coarsening of the arcuate striations sweeping into the disc between 10 and 1 o'clock, and 5 and 8 o'clock in the right eye; between 11 and 2 o'clock, and 4 and 7 o'clock in the left eye*.[80]

Marked Papilledema
Hyperemia
Swollen Veins
Coarsening of the Nerve Fiber Layer
Obscuration of Vessels Crossing the Disc Edge
Tortuous Veins

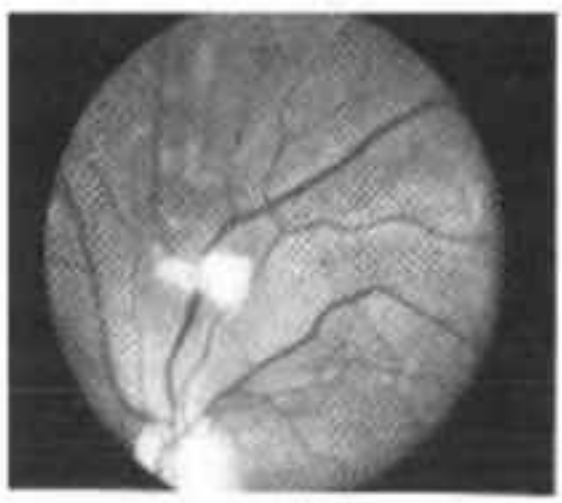


Opacified Nerve Fibers: Opacification of ganglion cell axons probably results from the obstruction of axoplasmic flow carrying important nutrients to the neurons' terminal boutons in the lateral geniculate body.

Soft exudates represent small, localized infarctions of the nerve fiber layer. Hard exudates result from serum lipids leaking into the retina through damaged capillaries. Soft and hard exudates are rarely seen in true papilledema.[78]



Hard Exudates: Leakage of Lipid (Note Smooth Edges)



Soft Exudates: Nerve Fiber Layer Infarction (Note Fuzzy Edges)

In the Left Eye: Even with the green filter, it's difficult to discern the very delicate axons within the maculopapillary bundle entering the temporal side of the disc.

A third important finding in papilledema is venous engorgement and tortuosity. To accommodate all the extra venous blood backed up onto the retina, retinal veins dilate and then lengthen by becoming tortuous. In marked papilledema, the blood in the retinal veins also becomes darker*.

Other features of papilledema are loss of venous pulsations, hemorrhages around the disc, and retinal wrinkling. Venous pulsations are a little difficult to see at first, but look for them in the center of the disc where retinal veins dive into the optic nerve. At this point the veins can be seen tangentially and venous pulsations are easier to see*. The presence of venous pulsations means that the spinal fluid pressure is almost certainly normal, but the converse—the absence of venous pulsations—does not necessarily mean that the spinal fluid pressure is high, because many normal people do not have venous pulsations.[1] The disappearance of venous pulsations, however, does suggest that the intracranial pressure has risen above normal.



Retinal hemorrhages from whatever cause occur primarily in two locations: superficially along the nerve fiber layer, or deep among the rods, cones, and bipolar cells. You can distinguish the two locations by the shape of the hemorrhage. A small amount of blood dissecting between the axons of the nerve fiber layer is shaped like a splinter or, if the hemorrhage is larger, a torch flame. Blood dissecting upward from the deep retina between the vertical columns of rods, cones, and bipolar cells looks,

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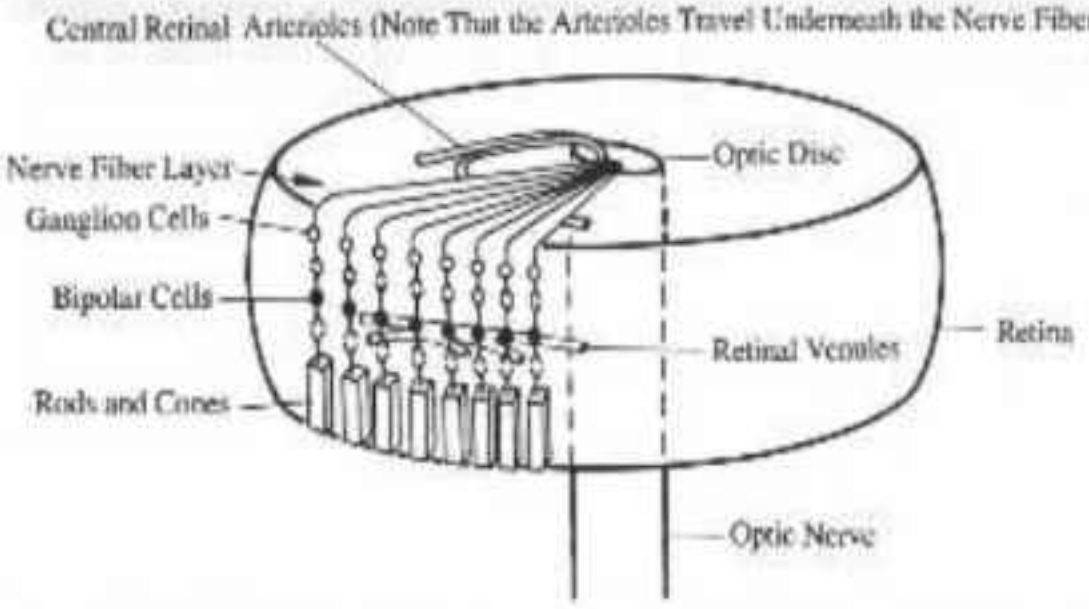
Becomes Darker: The color of arteries and veins depends on the amount of oxygen in the blood—the more oxygen, the redder; the less oxygen, the more burgundy-colored. In marked papilledema, retinal venous blood, unable to drain out of the retina at its usual pace, becomes sluggish and stagnant. The extra loitering allows oxygen to leak into surrounding tissues, turning the veins a dark burgundy color.

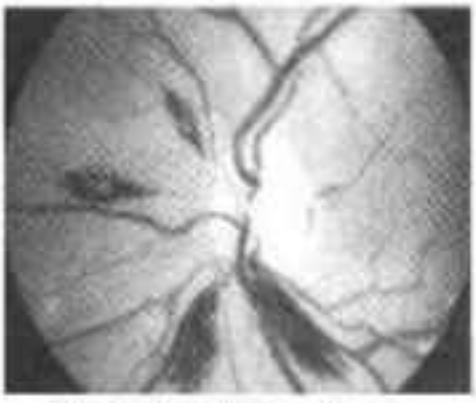
Easier to See: Normally, in the rest of the body, it's arteries that pulsate, not veins. In the eye the veins pulsate because the vitreous humor compresses them with each systolic heart beat. Each pulse of arterial blood raises intraocular pressure above venous pressure (compressing the veins) unless, as in papilledema, venous pressure is already elevated because of elevated intracranial pressure.

Retinal arterioles do not pulsate because only arteries pulsate, not arterioles, and arterioles are what you see in the retina.

Retinal arterioles can be made to pulsate if you press on the eyeball hard enough to raise the intraocular pressure above the diastolic blood pressure. With each diastole, intraocular pressure will then collapse the retinal arterioles (which you see as pulsations). If you press even harder on the eyeball, the arteriolar pulsations will cease altogether when the intraocular pressure reaches the level of the systolic blood pressure. By measuring the intraocular pressure at the time the arteriolar pulsations cease, you are indirectly measuring the systolic blood pressure in the ophthalmic artery. A low ophthalmic artery pressure suggests stenosis of the internal carotid artery. This useful test is called oculoplethysmography.

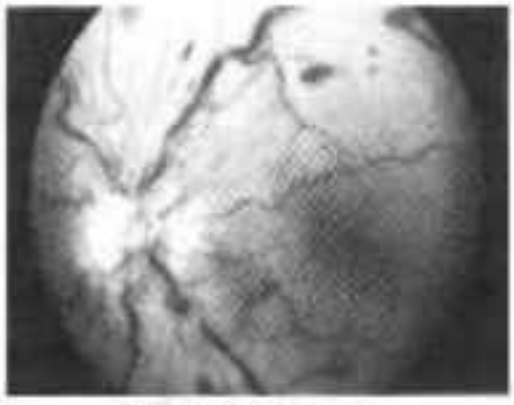
end-on, like a dot or blot[4]. Larger hemorrhages amidst the deep retina resemble splotches of ketchup, or smooth-edged lakes called subhyaloid hemorrhages. Splinter, flame, and subhyaloid (but not dot and blot) hemorrhages may result from any sudden increase in intracranial pressure, like a subarachnoid or intracerebral hemorrhage.[54]





Roth Spot

Flamed-Shaped Hemorrhages in the Nerve Fiber Layer

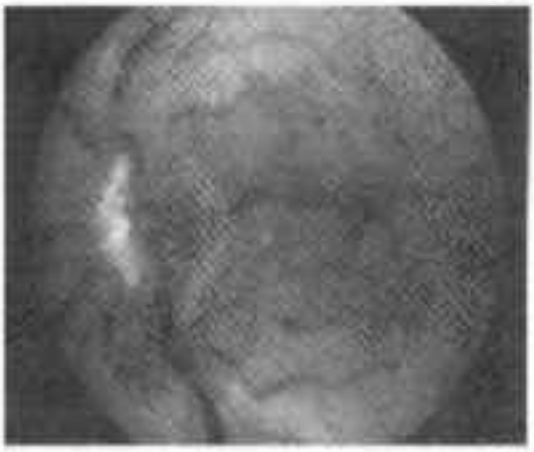


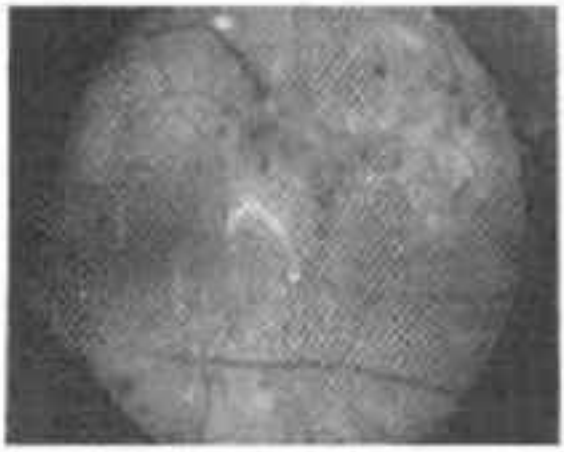
Splinter Hemorrhages

Dot or Blot: Small dot and blot hemorrhages are most commonly seen in diabetic retinopathy. Tiny, fragile aneurysms form on diabetic capillaries lying in the deep retinal layers.[42]

Dot and blot hemorrhages may also be seen in "venous stasis retinopathy," a relatively rare condition caused by chronic retinal ischemia, usually resulting from a severely stenotic ipsilateral carotid artery.[57]

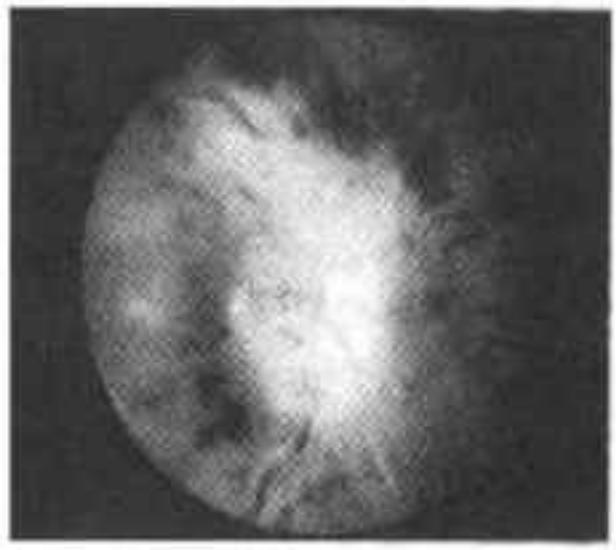
Dot and Blot Hemorrhages





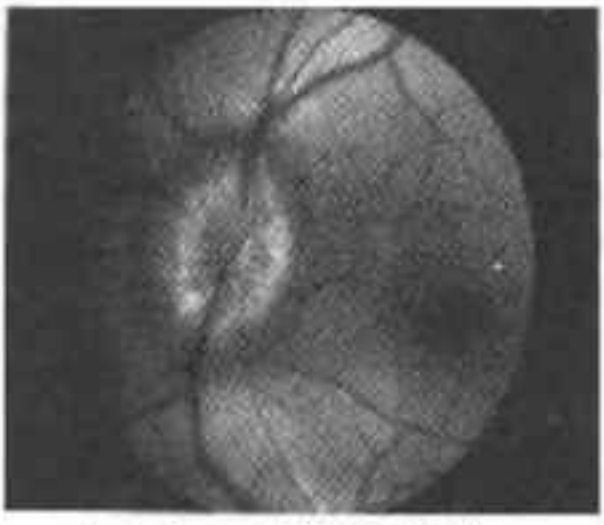


Subhyaloid Hemorrhage



Marked Papilledema with Hemorrhages and Obliteration of Blood Vessels Crossing the Disc Margin

Retinal wrinkling, a sign of more chronic papilledema, is visible on the temporal side of the disc as a series of parallel, curved ripples. Elevated venous pressure forces edema back into the deep retina, buckling the retina like water under linoleum. If enough edema accumulates, a puddle of fluid may lift up an entire section of retina. Extension of such edema out to the macula produces symptoms of blurred vision or prominent afterimages*.



Papilledema with Retinal Wrinkling



Optic Disc Swelling Due to Papillophlebitis

In certain cases of unilateral retinal edema, prominent optic disc swelling with engorged, non-pulsatile veins may distract you from seeing the margin of edema under the retina. Despite the disc abnormalities, the patient only complains of mildly blurred vision or afterimages—no headaches, seizures, confusion, incoordination, or weakness. Generally seen in young people, this benign condition, called papillophlebitis*, is due to idiopathic venous occlusion within the optic nerve. Fortunately, blood

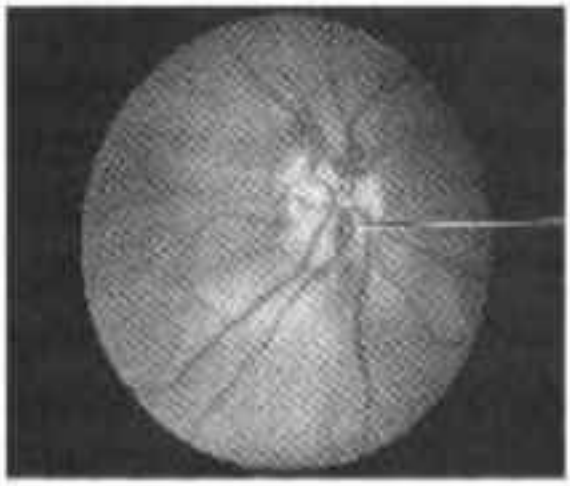
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Afterimages: The persistence of an image after looking away from it, as when you look at a bright light bulb.

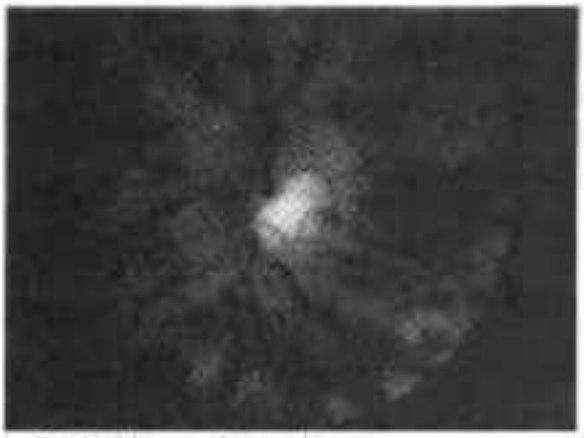
Papillophlebitis: Phlebos is a vein (Greek).

manages to find alternative routes out of the eye, avoiding frank venous infarction of the retina and nerve fiber layer*.[87]

More gradual obstruction of retinal venous drainage by, for example, a slow growing sphenoid wing* meningioma or optic nerve sheath meningioma allows time for new veins to develop on the disc surface, enabling blood to shunt around the obstructed central retinal vein. Retinal venous blood tunnels through the disc via one or two massively dilated capillaries, called 'optociliary shunt vessels,' into the patent ciliary circulation.[88]



Infarction of the Retina and Nerve Fiber Layer: Venous infarctions in the eye are strikingly bloody.[85] (So are many venous infarctions of the brain.[86])

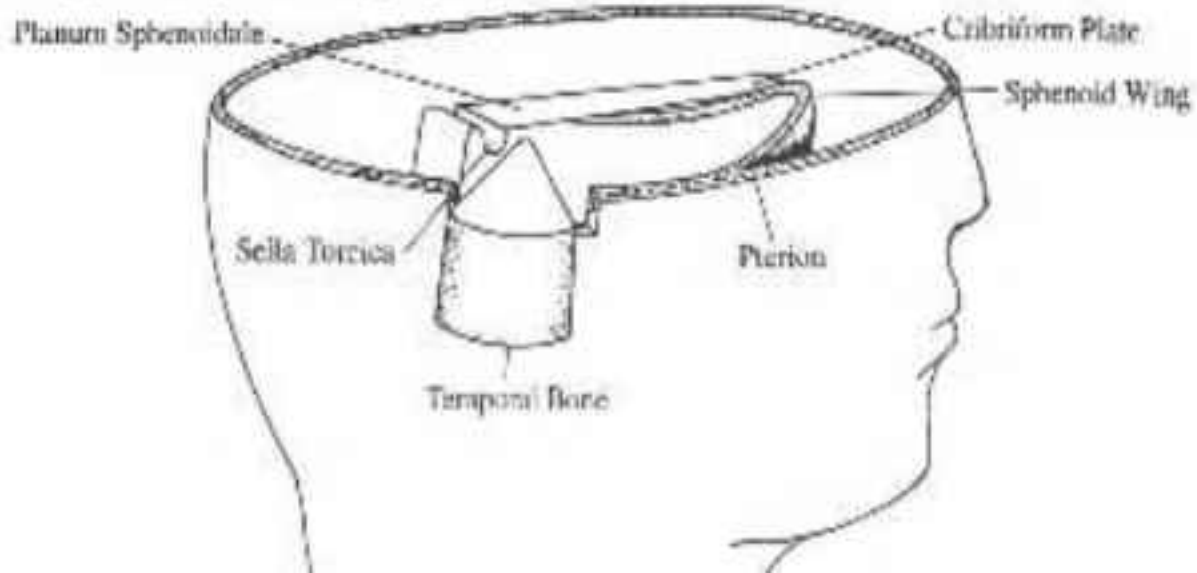


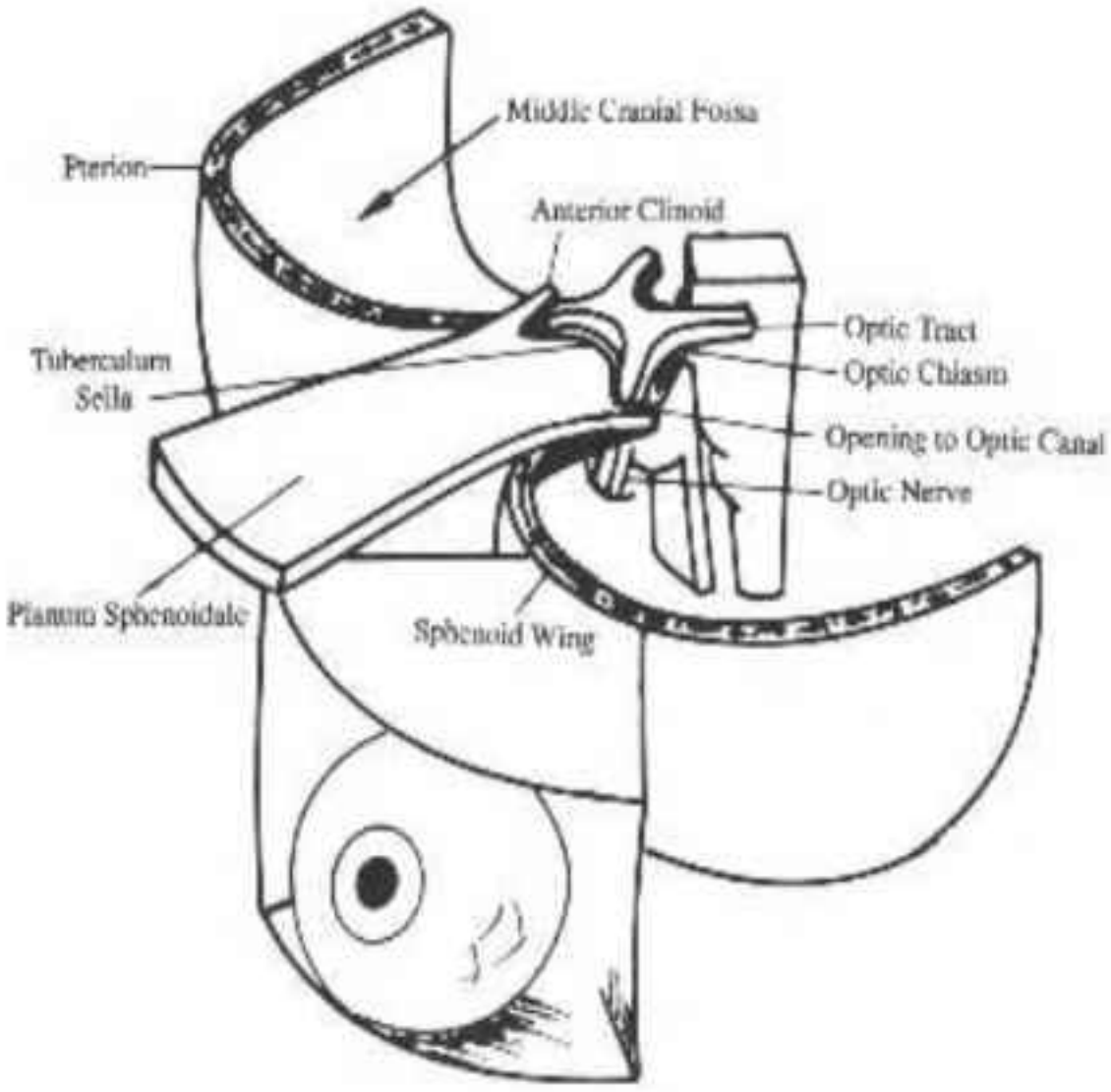
Retinal hemorrhages due to Central Retinal Vein Occlusion



Retinal Hemorrhages due to Venous Occlusion

Sphenoid Wing: The bony ridge of the sphenoid bone (sphenos = wedge), the bone which forms the posterior orbital wall. The lateral part of the sphenoid wing is called the pterion. Meningiomas arising from the sphenoid wing frequently compress the optic nerve.





Chronic papilledema, regardless of its cause, is unhealthy for the optic nerve.[89] After months of papilledema axons in the optic nerve begin to die, producing unrefractable diminution of visual acuity, red washout, Marcus Gunn pupil, and disc pallor. For reasons still unclear, optic nerve axons controlling the inferior nasal visual field tend to die first, so be sensitive to this area when following a patient with chronic papilledema.[90] Another typical pattern of visual loss from chronic papilledema is concentric (generalized) constriction of the visual field. Urgent intervention may be needed when a patient with papilledema complains of transient (typically seconds) visual obscuration or brief periods of frank blindness. These symptoms may herald permanent blindness within days to months[91] (not everyone agrees[92]).

Papilledema vs Optic Disc Swelling

Though papilledema is pathognomonic of optic nerve dysfunction, papilledema is not pathognomonic of primary optic nerve damage (an optic neuropathy). That is, papilledema is only a presenting sign; the primary pathology—the pathology causing the presenting sign—may actually be in the brain, far removed from the optic nerve. For example, marked hypertension may cause disc swelling either by infracting and swelling the optic disc,[93] or by raising intracranial pressure and preventing axoplasmic flow out of the retinal nerve fiber layer (true papilledema).

So how do you distinguish optic disc swelling caused by primary optic neuropathies—like ischemic optic neuropathy, optic neuritis, and optic nerve gliomas—from that caused by raised intracranial pressure? First of all, mere edema of the optic nerve doesn't impair transmission, so until chronic atrophy sets in, papilledema causes no loss of visual acuity, no loss of color discrimination, and no effect on the visual fields except for an enlarged blind spot corresponding to the enlarged disc.[94] Intrinsic optic nerve lesions that swell the disc, besides being unilateral (usually), cause early scotomas, early Marcus Gunn*, and early loss of visual acuity and color discrimination.[96] In addition, ocular pain and photophobia suggest an inflammatory optic neuropathy like optic neuritis*.

The combination of papilledema in one eye and optic atrophy in the other is called the Foster Kennedy syndrome. Classically, this happens when an olfactory groove meningioma or sphenoid wing meningioma compresses one optic nerve (atrophy), while raising the intracranial pressure enough to produce papilledema in the other eye.[98] Actually, the Foster Kennedy syndrome is more commonly due to optic disc ischemia. *Acute* optic disc ischemia causes the disc to swell and then atrophy. The Foster Kennedy syndrome occurs when the *other* optic nerve head suddenly swells from an acute ischemic insult (the first eye having already undergone optic disc atrophy).[99]

To distinguish ischemic Foster Kennedy from that due to tumors, check for signs of a true optic neuropathy in the eye with the swollen disc head. Poor visual acuity, red washout, central field loss, and unrefractable visual impairment should point immediately to ischemia, because true papilledema from increased intracranial pressure won't affect optic nerve function until late.[100]

In all this discussion of the ophthalmoscopic appearance of papilledema, I have not mentioned the most commonly looked-for sign: blurring of the disc margin, an acceptable sign, but frequently not very useful. When you most need to know if there is papilledema—for example, a drunk in the emergency room rolling around on the stretcher—how are you going to focus on the disc margin? But simply seeing that yellow sun (disc) roll across the red sky (retina) tells you there is no capillary dilation on the disc, and hence, no papilledema. Moreover, when you need to know if papilledema is worsening, it's easier to tell if a particular arteriole or vein crossing the disc margin is becoming more obscured than it is to judge the amount of blurring at the disc margin. Some doctors also focus the ophthalmoscope on the highest point of the disc and then on the retina to decide if the disc is swollen. The difference in diopters is a quantitative measurement of the papilledema.

The other reason it's difficult to use disc blurring to judge the presence of papilledema is that some normal people have blurred disc margins due to drusen: small, round, refractile bodies that form in the optic nerve and slowly work their way to the

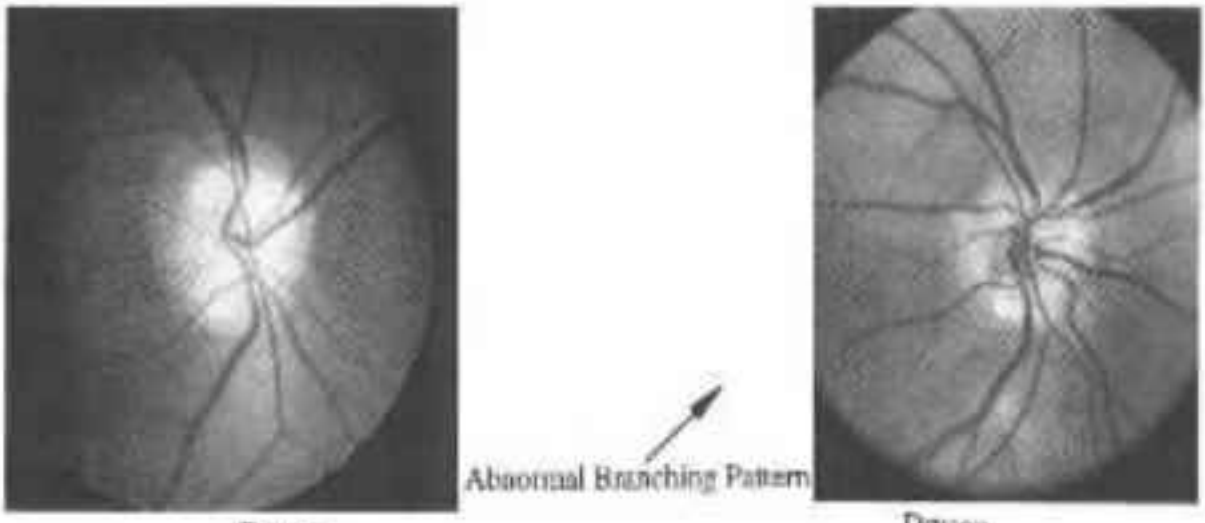
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Early Marcus Gunn: In fact, if you're sure the patient has an optic neuropathy, but can't find the Marcus Gunn pupil, look carefully for an occult optic neuropathy in the other eye. Marcus Gunn only detects a *relative* afferent pupillary defect; it'll miss symmetrical optic neuropathies.[35]

Optic Neuritis: Optic neuritis may herald multiple sclerosis by months or years.[97] It would be important to predict which patients with acute optic neuritis will later develop multiple sclerosis, because medication might someday be able to prevent the recurrent bouts of demyelination.

Retrobulbar neuritis is a term used to describe the same acute, usually painful loss of central vision as in optic neuritis, but with a normal appearing disc. The site of inflammation is assumed to be in the optic nerve, well behind the disc.

disc surface.[101] These tiny luminous pearls commonly obliterate the optic cup, blur the disc margin, and enlarge the blind spot as in papilledema.[102] However, in this condition, called pseudopapilledema, the veins are not engorged, tortuous, or dark, and the arterioles crossing the disc margin do not become obscured, because they do not have to penetrate heaped-up bundles of swollen nerve fibers as they do in true papilledema.



Sometimes drusen do cause nerve fiber bundle defects by interrupting a bundle of arcuate fibers.[103] Rarely, drusen may even cause small hemorrhages around the disc.[104] The little critters are easiest to see when you suspect them. So, if someone with obscured disc margins is sitting there without even a complaint of a headache, think of drusen*. Then look carefully for a small, white pearl (or chunky piece of rock candy) peeking out from behind the disc edge. Decide if the vessels crossing the disc margins are obscured (they shouldn't be), and then concentrate on the arterioles emerging from the optic disc. The branching pattern is congenitally anomalous: too many branches are seen too close to the center of the disc. Since drusen run in families, check the parents. If you're still unsure, fluorescein angiography (by an ophthalmologist) may help. In papilledema and optic neuritis intravenous fluorescein, a relatively harmless dye,[105] leaks out of the swollen capillaries and stains the disc surface. So if there's no leakage, there's no papilledema or optic neuritis. In addition, fluorescein makes the drusen stand out.

A few shortcuts and technical hints may minimize exasperation when first learning to use the ophthalmoscope. If the patient keeps moving his eye, have him lie supine; he'll be better able to keep his eye still for you. Approach the eye with a dim ophthalmoscope light to prevent the pupil from constricting before you can spot the disc. If everything looks blurred through the ophthalmoscope, have the patient blink or, if the patient is comatose, pull the eyelid over the cornea; a dry cornea won't transmit light well. When looking through the ophthalmoscope, place the back of your long finger on the patient's cheek so that when the patient's head moves, your ophthalmoscope follows, allowing you to maintain visual contact with the disc. And get that ophthalmoscope as close as you can to the patient's cornea; your foreheads should almost be touching, as if you were viewing a construction site with your eye up against the knot hole.

Drusen: Though drusen are usually buried in both optic nerves, in their slow (years) sojourn to the disc surface, drusen usually present unilaterally, or at least asymmetrically.

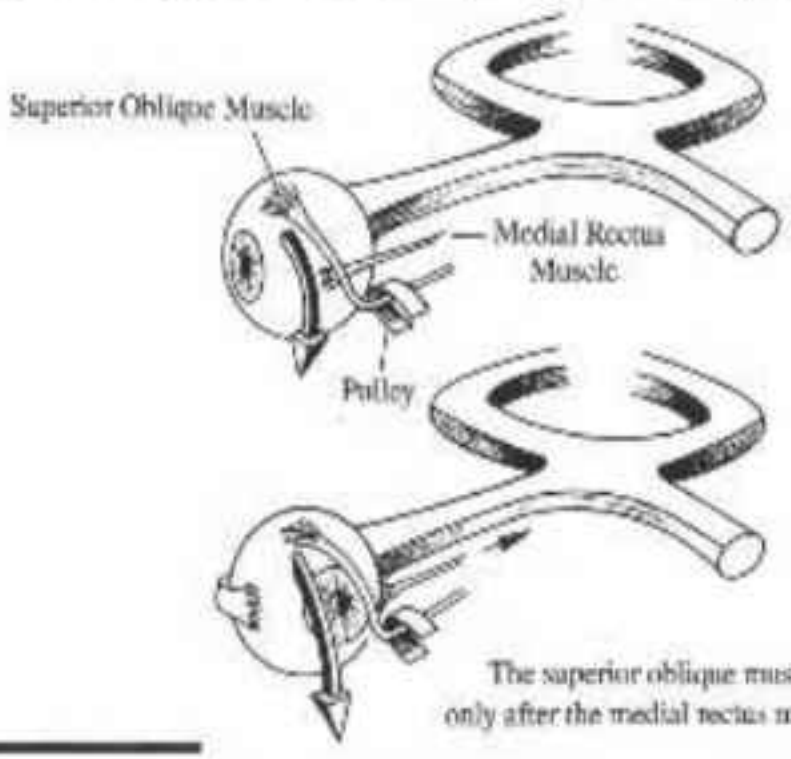
III, IV, AND VI: OCULOMOTOR, TROCHLEAR, AND ABDUCENS NERVES

Extrinsic Eye Muscles

Continuing with the cranial nerves, the IIIrd cranial nerve (the oculomotor) is one of three nerves that move the eye, the other two being the IVth (trochlear*) and the VIth (abducens*). The four eye muscles innervated* by the oculomotor nerve are the superior rectus*, inferior rectus, medial rectus, and inferior oblique. The lateral rectus muscle is handled by the abducens (VIth) nerve, and the superior oblique muscle by the trochlear (IVth) nerve.

The rectus muscles move the eye medially, laterally, up, and down, which seems like enough mobility—why the superior and inferior obliques? Mother Nature originally designed our orbits* to face somewhat laterally. Following suit, she anchored the four rectus muscles at the very back of the orbit. Problems arose when the eyeballs were inserted, because the eyeballs had to face forward. This meant that the superior and inferior rectus muscles were only effective when the eye abducted (looked laterally). When the eye adducted (looked medially), the superior and inferior rectus muscles lost their mechanical advantage.

The superior and inferior oblique muscles solved the problem of how to pull the adducted eye up and down. The superior and inferior obliques skirt along the medial side of the orbit, slip through a little pulley, and insert *across* the eyeball. When the eye adducts, the superior oblique is in an ideal position to pull the eye downward, the inferior oblique ready and set to pull the eye upward.[106] So reading a book, descending stairs, and looking to God with pathos, all require the obliques' cooperation.



The superior oblique muscle pulls the eye down only after the medial rectus muscle adducts the eye.

Trochlear: Means pulley, for reasons you'll see in a minute.

Abducens: Drawing away (i.e., toward the lateral).

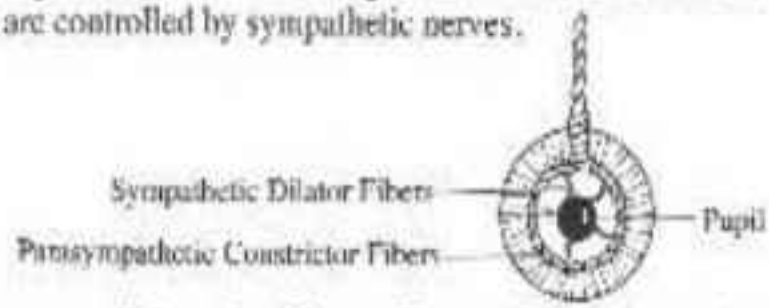
Innervated: A muscle with a nerve attached to it. Denervated means the nerve has separated from the muscle.

Rectus: Straight.

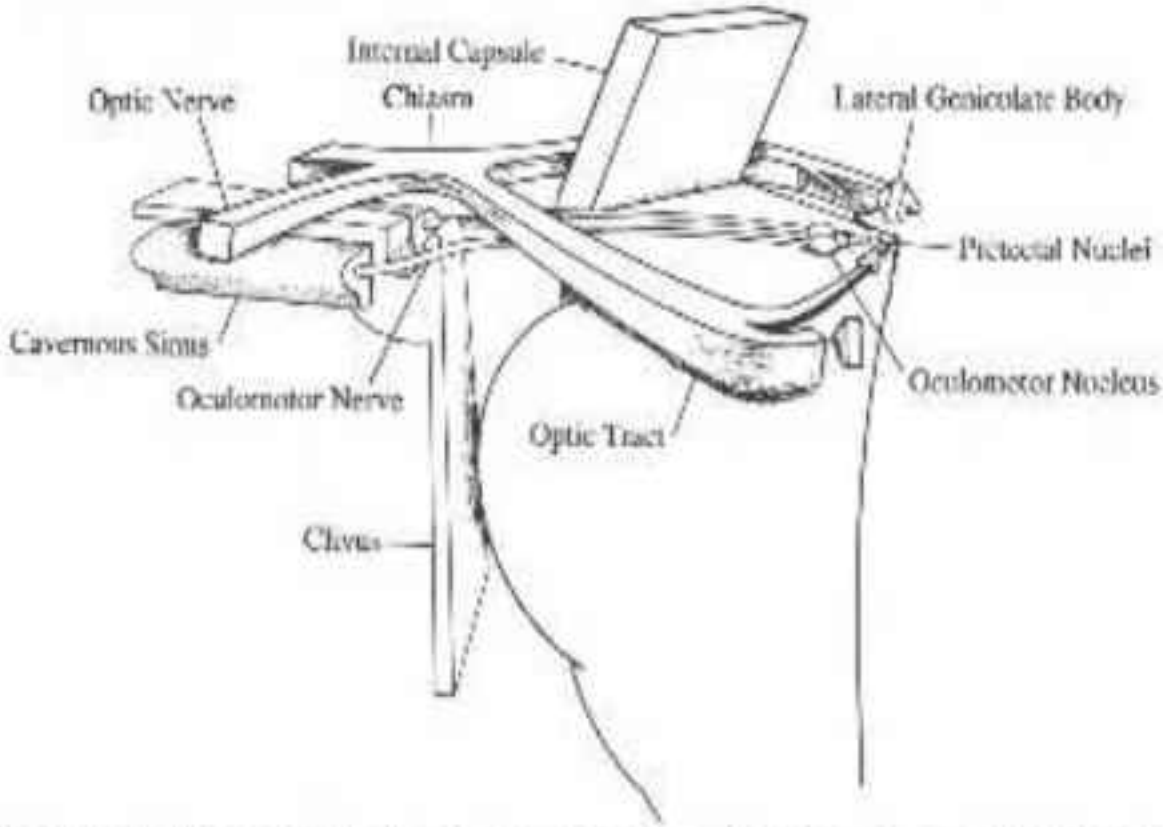
Orbit: The bony socket around the eyeball.

Intrinsic Eye Muscles

The six muscles just discussed are the extrinsic eye muscles. The intrinsic eye muscles, located in the iris, open and close the pupil in response to light and emotions or when focusing on near objects. Pupillary constrictor fibers run circumferentially around the iris, closing it like a noose. Pupillary dilator fibers are arranged radially, like wheel spokes, to pull the iris open. The constrictor fibers are controlled by parasympathetic nerves traveling within the oculomotor nerve. The pupillary dilator fibers are controlled by sympathetic nerves.



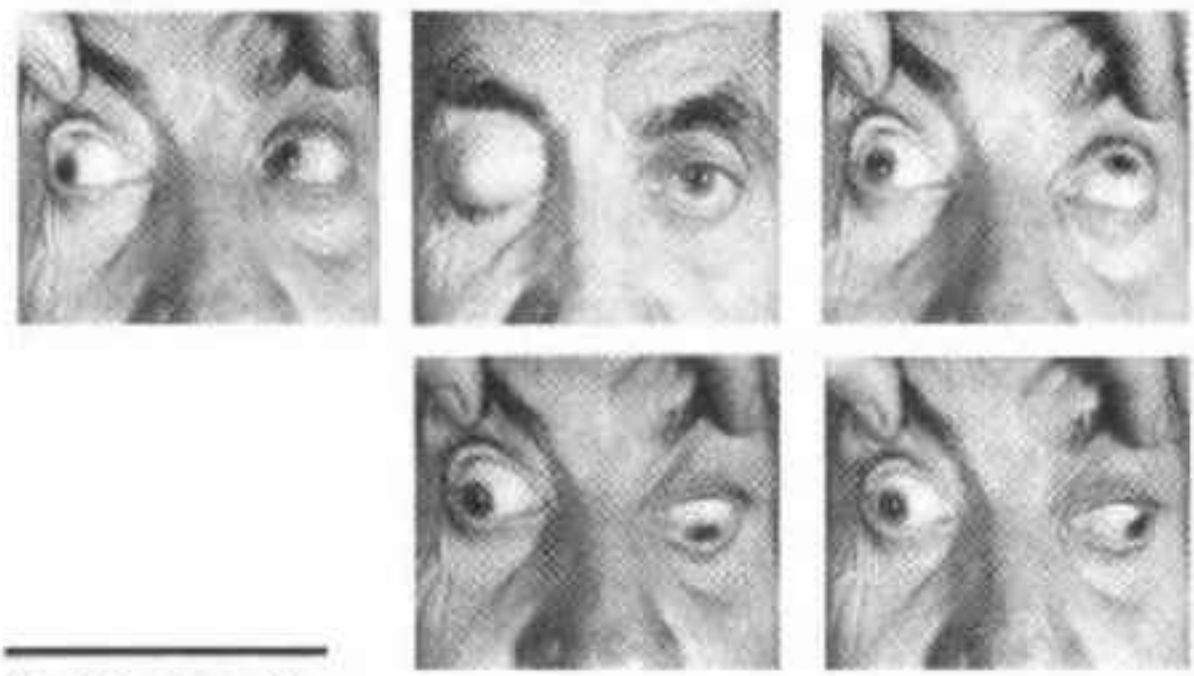
As you recall from the Marcus Gunn reflex, light reaches the oculomotor nucleus via a slip of light-bearing fibers that depart the optic tract just as the optic tract is about to plug into the lateral geniculate body. From the pretectal nuclei, light signals are routed to the Edinger Westphal nucleus, and then out the midbrain along parasympathetic fibers within the oculomotor nerves.



The pupils also constrict when the eyes converge. Whenever you want to inspect something close-up, the oculomotor nerves need to perform three separate motions which together are called the accommodation reflex: they need to converge the eyes, constrict the pupils, and round up the lenses for proper focusing. The stimulus for the accommodation reflex begins in the occipital lobes where the macular regions in each occipital lobe receive slightly different images. Instructions are immediately sent to the midbrain convergence center to adduct the eyes, and simultaneously to the Edinger Westphal nucleus. Parasympathetic fibers traveling within each oculomotor nerve then constrict the iris and stimulate the ciliary body to round up the lens. The smaller pupils improve resolution (like looking through a pinhole), and the adjusted lenses focus the image on the retina.

The oculomotor nerve also innervates levator palpebrae superioris, the muscle which opens the eyelid. The oculomotor is indeed a busy nerve, what with the extrinsics (medial rectus, superior rectus, inferior rectus, inferior oblique), the intrinsics (pupillary constrictors), and the lid elevator (levator palpebrae superiorus) to worry about.

If you cut the oculomotor nerve, where would the eye be? What would the pupil look like? You can't tell until you lift the eyelid (the levator is paralyzed). When you do, you'll find the eyeball abducted (normal abducens nerve), unable to look up, down, or in, and a dilated fixed* pupil—a complete IIIrd nerve palsy. Some patients have only ophthalmoplegia* (including ptosis*) with a normal, reactive pupil. This dissociation of eye movement from pupillary constriction has an anatomic basis. The parasympathetic fibers run together along the superior and medial perimeter of the oculomotor nerve.[107] A compressive lesion, like an aneurysm, selectively injures these peripherally placed parasympathetic fibers, producing a dilated pupil with ptosis and ophthalmoplegia. The interior of the oculomotor nerve, containing the axons that control eye movements and eyelid elevation, is supplied by small arterial twigs that poke *into* the nerve. Thrombosis of one of these twigs, as in diabetes, selectively damages the motor axons and hence, a 'pupil sparing ophthalmoplegia'*.



Fixed: Unreactive to light.

Ophthalmoplegia: Ophthalmos is eye in Greek; plegia means a blow or stroke, as if struck down, i.e., paralyzed. Paresis means weakness, anything short of complete paralysis.

Ptosis: Means to fall, in this case to droop.

Pupil Sparing Ophthalmoplegia: Sudden hemorrhage from an aneurysm of the posterior communicating artery (chapter 31) commonly injures the bypassing oculomotor nerve. The fixed pupil and painful eye can sometimes be mistaken for acute glaucoma, another painful pupil-fixing condition. Glaucoma, however, won't cause ophthalmoplegia.

There *have* been a few, exceptional cases of pupil-sparing ophthalmoparesis (but not ophthalmo*plegia*) caused by aneurysms,[108] and conversely, oculomotor paresis with a fixed pupil due to diabetes.[109] Moreover, the rule that oculomotor nerve compression dilates and fixes the pupil holds mainly for *proximal* extra-axial lesions. Compressive lesions in the cavernous sinus tend to mimic ischemic lesions by causing pupil-sparing ophthalmoplegia, presumably because the parasympathetics in the cavernous sinus do not occupy the same vulnerable position in the distal oculomotor nerve that they do in the proximal oculomotor nerve.[110]

Horner's Syndrome

For reasons not immediately obvious, Mother Nature designed two muscles to keep the eyelid open. You'd think, that's great: if levator palpebrae superioris fails, there's a back-up muscle. Unfortunately, the second muscle, called Mueller's muscle, is only a dinky little squirt, innervated by the sympathetic nerves, and capable of giving only a tiny tug on the eyelid*. This is the second time we've run across the sympathetics which, along with the parasympathetics, comprise the autonomic nervous system*. The autonomic nervous system is just that: an entire nervous system unto itself, devoted to handling the silent day-to-day affairs of the body too mundane (or too important) for the cortex to worry about, like pupillary constriction and dilation, salivation, gut movement, sweating, squeezing the bladder, speeding up and slowing the heart, maintaining the blood pressure, and getting an erection.

Whenever the sympathetics to Mueller's muscle are injured, the upper eyelid droops and the lower one elevates, both ever so slightly. You can detect subtle ptosis by looking at how close the upper eyelid skirts over the pupil. Normally, there is a small gap between the eyelid and the pupil (not the iris); sympathetic ptosis narrows this gap, often allowing the eyelid to cover part of the pupil. Look at the upper eyelid, at the distance between its bottom edge (where the eyelashes insert) and the first eyelid crease. Widening of this narrow stretch is a sensitive measurement of ptosis. In addition to ptosis, the pupils become smaller because the sympathetics normally dilate the pupil. With the sympathetics knocked out, unopposed parasympathetics (traveling in the IIIrd nerve) can now constrict the pupil slightly more. This combination of miosis* and mild ptosis is called a Horner's syndrome*.

Tiny Tug on the Eyelid: Perhaps Mueller's muscle was invented to pull the eyelids back for a more unobstructed view during imminent danger or battle? Or to scare prey into submission, or to scare off predators?

Autonomic Nervous System: The autonomic nervous system is divided into two, frequently opposing, divisions: sympathetics and parasympathetics. The sympathetics prepare you for fight or flight by heightening vigilance, dilating the pupils (to see better in the dark), widening the eyes, speeding up the heart rate, raising the blood pressure, tightening your sphincters, and diverting blood from the skin to the internal organs. The parasympathetics govern more relaxed activities like salivation, lacrimation, urination, and defecation (the 'SLUD' reaction), as well as constricting the pupils, slowing the heart, dilating the bronchial tubes, and promoting the production of gastric and pancreatic digestive enzymes.

What is curious about the sympathetics and parasympathetics is their strict anatomic separation. The parasympathetics exit the central nervous system by way of the brainstem and sacral spinal cord, while the sympathetics exit only from the thoracic and lumbar spinal cord. Moreover, the first sympathetic synapse outside the spinal cord occurs in a chain of ganglia ('the chain gang') close to the cord, while the parasympathetics travel far out into the periphery before synapsing in their ganglia (the ciliary, sphenopalatine, otic, submandibular, celiac, and mesenteric ganglia). With widely separated ganglia at distant sites, the parasympathetics can exercise more selective, local control. Conversely, by having their ganglia more intimately connected, the sympathetic fibers tend to act more in unison.

Miosis: A pupil slightly smaller than the contralateral one. Anisocoria simply means that the pupils are of unequal size.

Horner's Syndrome: Dr. Horner was a Swiss ophthalmologist in the mid-1800's.



Horner's Syndrome



Horner's Syndrome

Anatomy

How do the oculomotor, trochlear, abducens, and sympathetic nerves get to the eyeball? First, recall that the brainstem is made up of the midbrain, pons, and medulla. The IIIrd and IVth nerve nuclei* abut each other in the midbrain; the VIth nerve nucleus lies far away in the lower half of the pons. The midbrain sits behind (and a little higher than) the pituitary. Just lateral to the pituitary is the cavernous sinus draining blood back from the frontal lobe, the eye, and the face (which is why you should not pick facial pimples—bugs get into the cavernous sinus*).

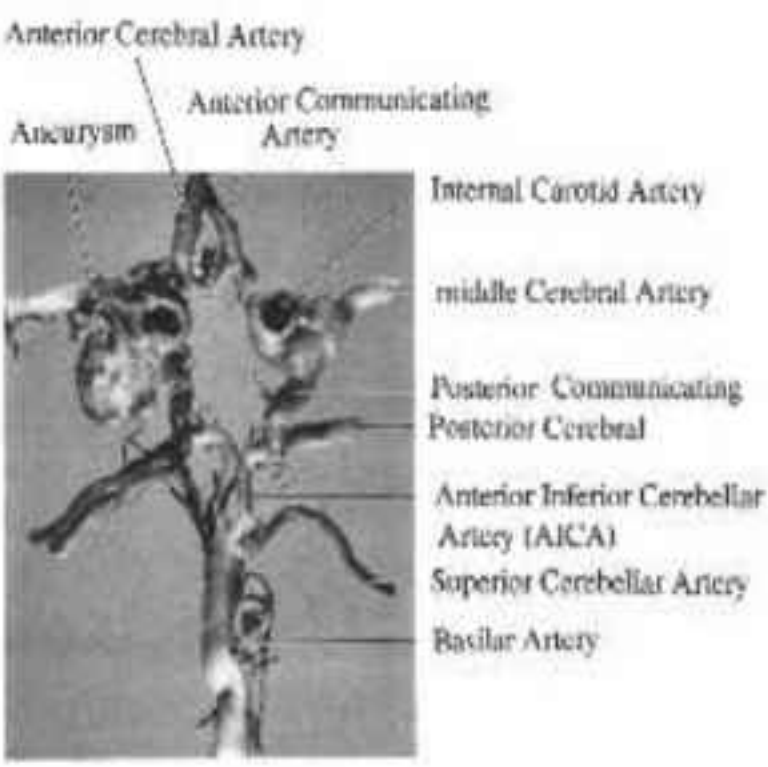
The oculomotor nerve leaves the midbrain ventrally, crosses under the posterior communicating artery*, penetrates the cavernous sinus, travels upstream (against the

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Nuclei: A brainstem nucleus refers to a collection of cell bodies for one cranial nerve.

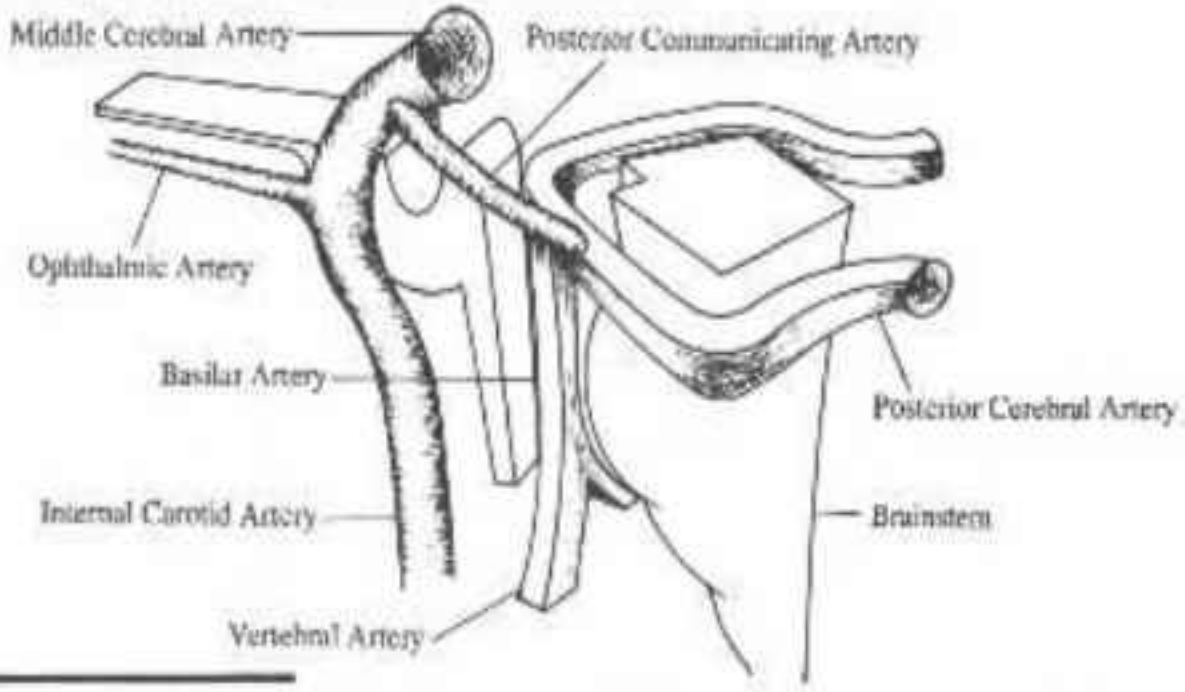
Cavernous Sinus: For this reason, the central facial area draining into the cavernous sinus is known as the 'Triangle of Death.'

Posterior Communicating Artery: This is where aneurysms of the posterior communicating artery characteristically cause oculomotor nerve palsy.[11]

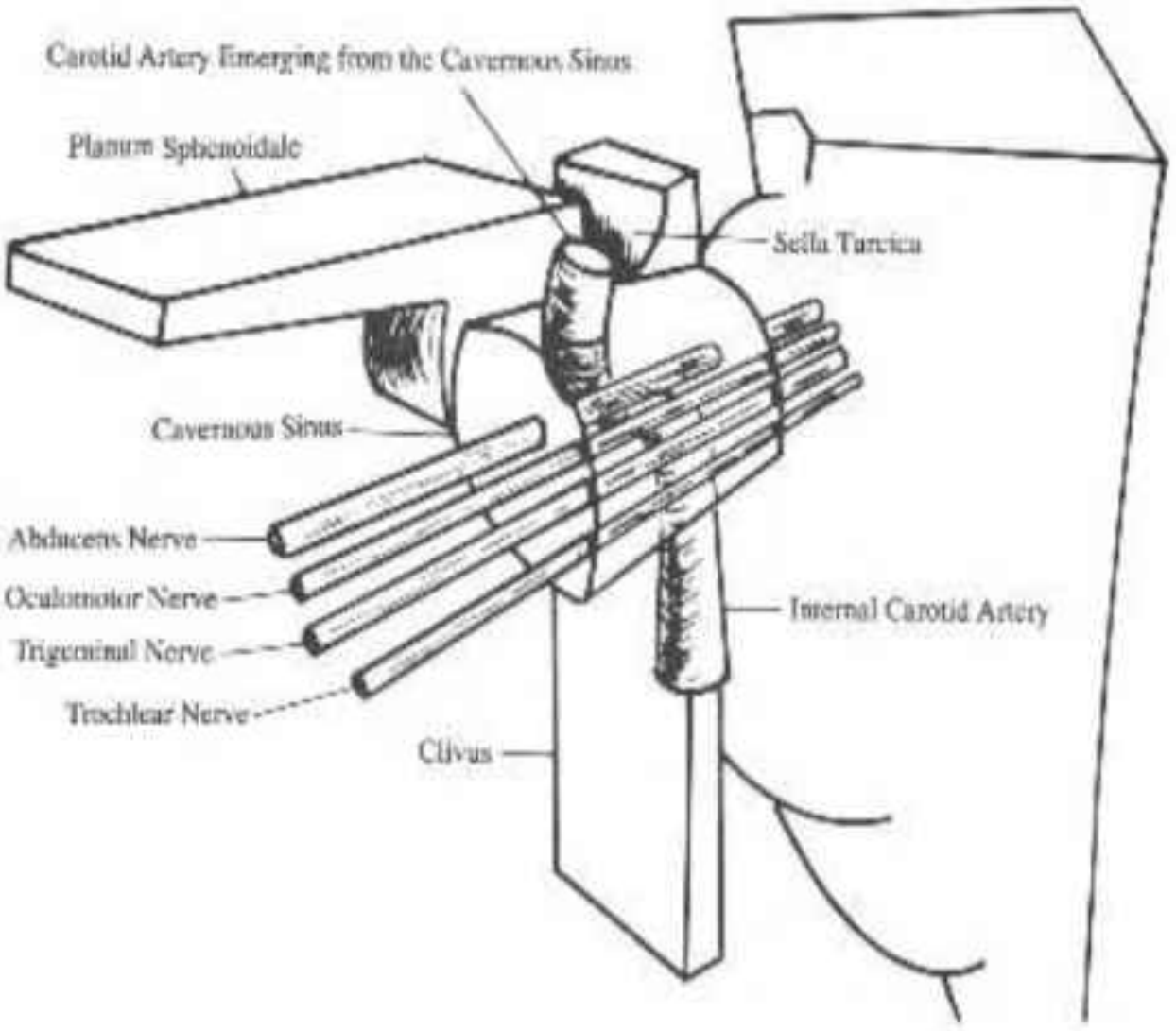


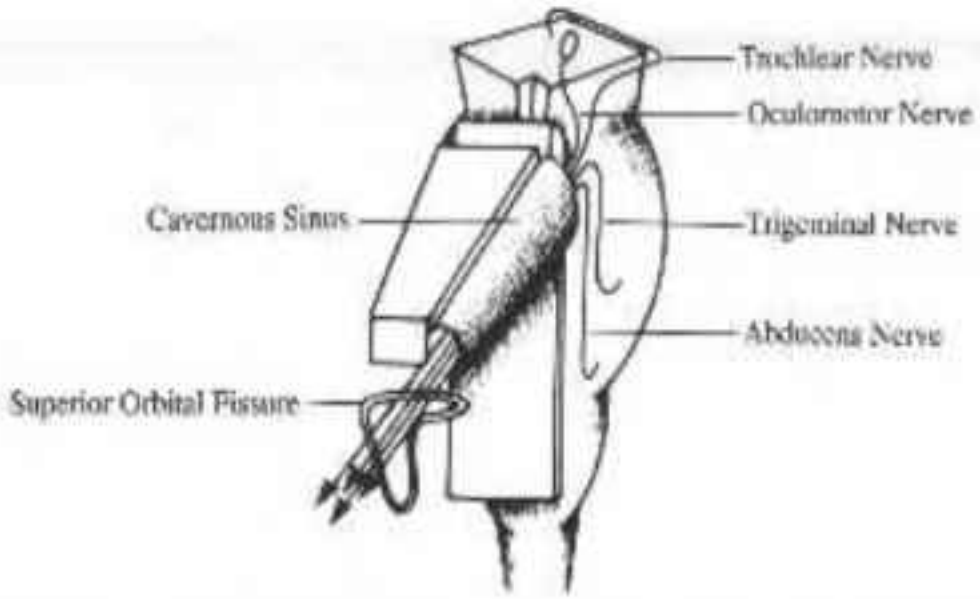


flow of venous blood*), and exits the cavernous sinus anteriorly through a bony archway, the superior orbital fissure, into the orbit.



Against the Flow of Venous Blood: Actually, the IIIrd nerve does not—nor does the IVth, VIth, or V—come into direct contact with venous blood in the cavernous sinus. These cranial nerves are embedded within various layers of the lateral wall of the cavernous sinus.[12] In fact, the cavernous sinus is probably not even a single channel but rather a collection of interconnecting veins.[13] The term cavernous refers to the sinus' resemblance to the trabeculated interior of the penis: the corpus cavernosum. (Trabeculated is like the interior of a sponge).

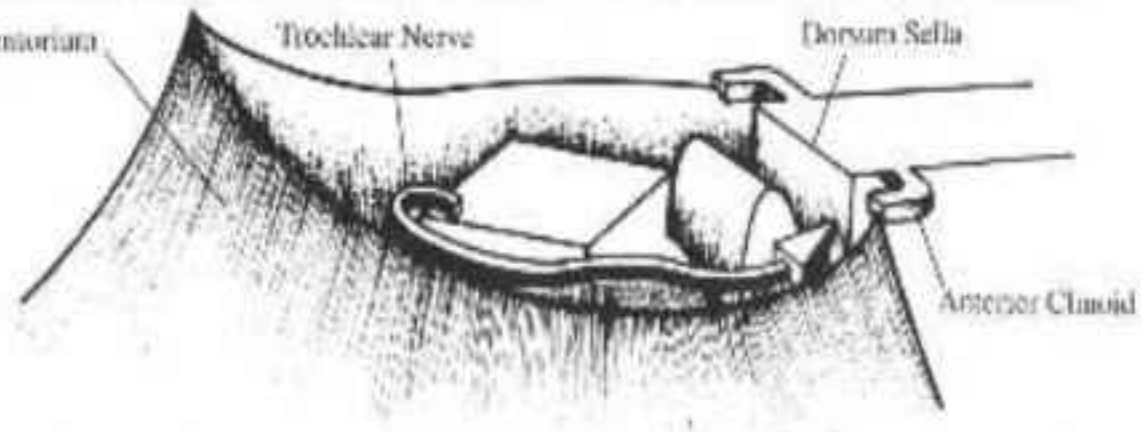




The trochlear nerve leaves its midbrain mooring dorsally, wraps around the contralateral side of the brainstem[8] and, like the oculomotor, enters the cavernous sinus and passes through the superior orbital fissure to the orbit.

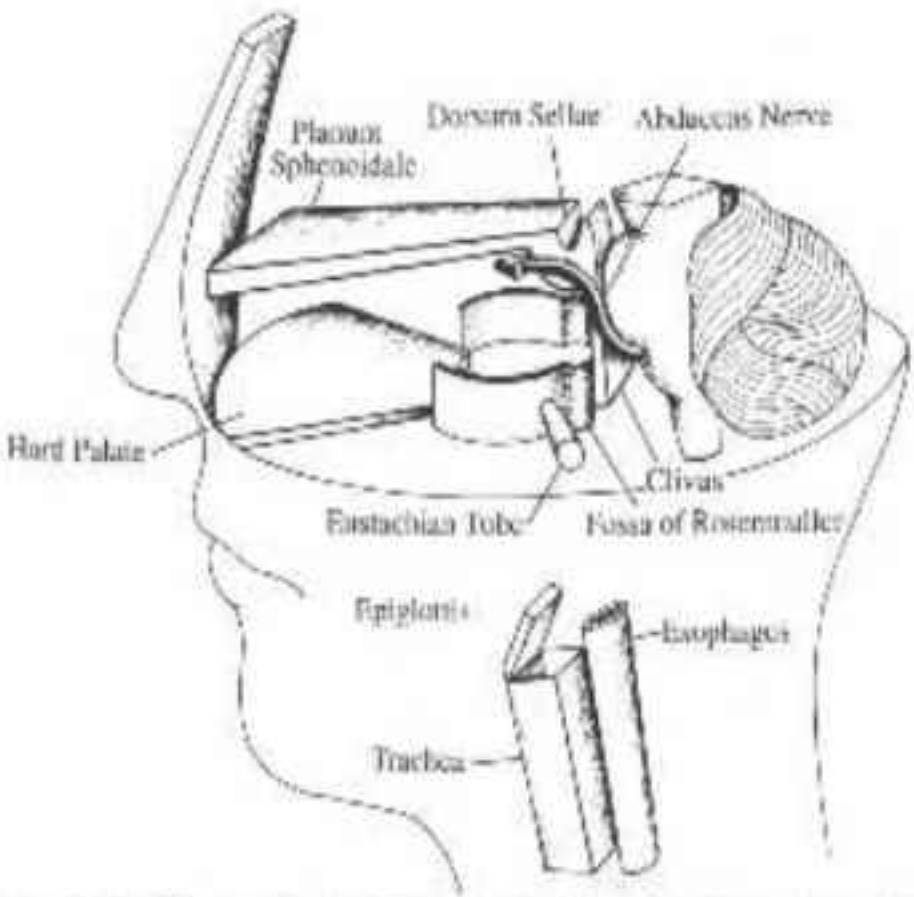
The abducens leaves the lower pons ventrally, but since the pons is up against the clivus, the abducens must first climb the clivus, skirting medial to the temporal bone[9], to reach the cavernous sinus. The abducens nerve travels within the lateral wall of the cavernous sinus, paralleling the oculomotor, trochlear, and ophthalmic division of the trigeminal nerve through the superior orbital fissure into the orbit.

Contralateral Side of the Brainstem: As it wraps around the midbrain, the trochlear nerve is particularly vulnerable to a judo chop by the free edge of the tentorium which is also reaching around the midbrain to attach to the anterior clinoids.[116] *If trivial* head trauma causes IVth (or IIIrd or VIth) nerve palsy, suspect a tumor somewhere near the upper brainstem or cavernous sinus.[115]



Medial to the Temporal Bone: In its ascent up the lateral aspects of the clivus, the VIth nerve lies exposed to nasopharyngeal carcinoma, a malignant tumor that usually begins within the fossa of Rosenmuller and obstructs the adjacent Eustacian tube. (The obstructed Eustacian tube causes partial hearing loss by backing up serous fluid into the middle ear, called serous otitis media.) As the tumor infiltrates the nasopharynx, it compresses the cranial nerves bound for the cavernous sinus.[118]

In skirting by the medial temporal bone the VIth nerve is also vulnerable to any inflammation within the temporal bone. A VIth nerve palsy due to inflammation within the temporal bone is known as Gradenigo's syndrome.



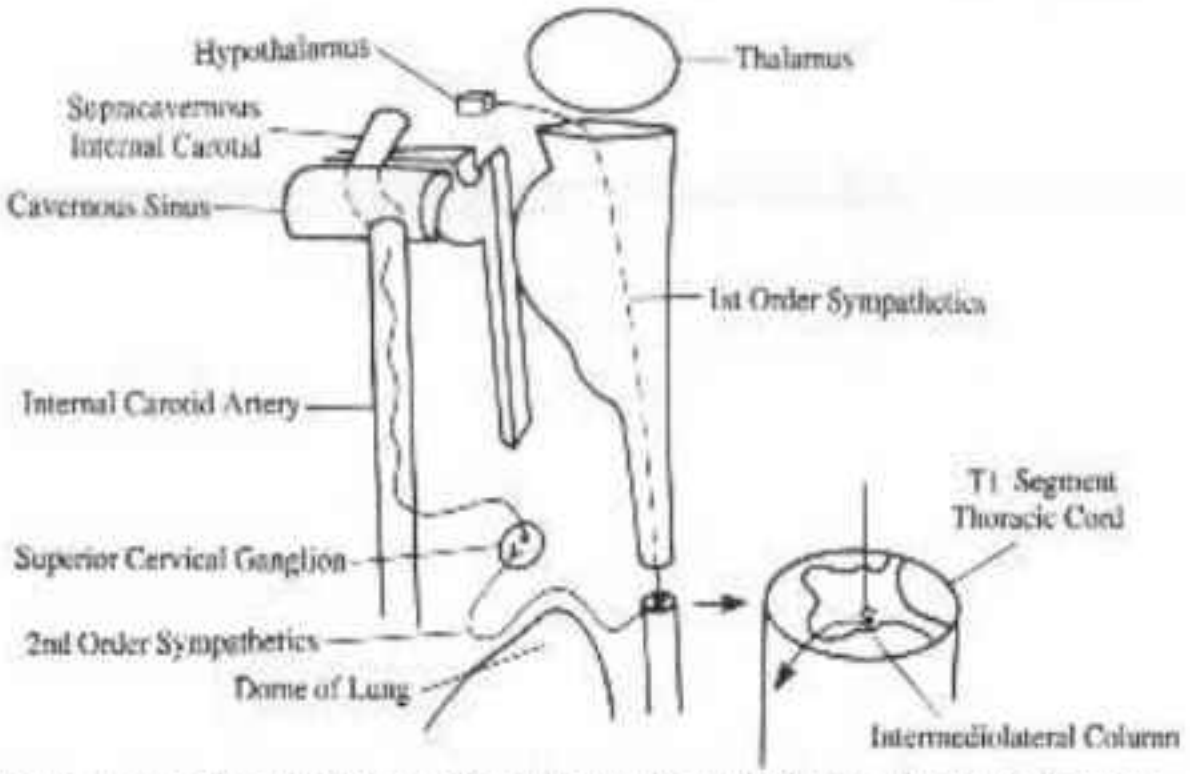
Sympathetic fibers get to the eye through a circuitous route, beginning in the hypothalamus and descending through the midbrain, lateral pons, and lateral medulla. In the lateral medulla, the sympathetic tract travels next to the descending tract of V and the ascending spinothalamic tract carrying pain and temperature upward from the opposite side of the body.

Interestingly enough, it's not until the sympathetics reach the thoracic spinal cord at T1–2 that they first synapse. Only then do the sympathetics exit the central nervous system. This first sympathetic synapse occurs in a column of thoracic cord gray matter midway between the dorsal and ventral horns, called the intermediolateral cell column. From here, second order sympathetics exit the upper thoracic cord and slip over the dome of the lung* to synapse in the superior cervical ganglion situated deep in the neck.

Dome of the Lung: While slipping over the dome of the lung, second order sympathetics are vulnerable to entrapment by lung tumors in the apex of the lung, called Pancoast's tumor (apical lung cancer and an ipsilateral Horner's).[117] This tumor behooves you to separate a second order from a third order Horner's syndrome, a task most easily done chemically.

The first step is to prove that a miotic pupil is due to sympathetic interruption and not simply to congenital anisocoria. This is typically done by dimming the lights[118] or by dripping 5% cocaine into the eyes; both of these will dilate a normally innervated pupil. The pupil that doesn't dilate (or doesn't dilate as briskly as its partner) has an interruption in one of the three sympathetic neurons.

Now drip hydroxyamphetamine into the abnormal eye. This drug selectively grooves the third order neuron to dilate the pupil. If the pupil fails to dilate, the Horner's must be due to a third order sympathetic lesion. If the pupil does dilate (meaning that the third order sympathetic is still connected to the pupillary dilator muscle), then the interruption must be in either the first or second order neuron. Unfortunately, there are a fair number of false negatives with hydroxyamphetamine, so you cannot completely rule out a first or second order lesion if the hydroxyamphetamine test is negative.[119] So far, there are no eye drops that can distinguish a first order from a second order Horner's.[120]



From the superior cervical ganglion, third order sympathetics piggyback the common carotid and then the internal carotid artery into the skull, after which the sympathetics depart the carotid to make their way through the cavernous sinus to the eyeball. Some of the sympathetics ascending the common carotid artery follow the external carotid artery onto the face to stimulate the facial sweat glands. If the sympathetics to the eye are interrupted after the external carotid departs the common carotid, only ptosis and miosis result. A more proximal interruption produces the full blown triad of Horner's syndrome: ptosis, miosis, and ipsilateral facial anhidrosis*.

Sympathetic nerves within the internal carotid adventitia* can also be damaged by illnesses affecting the internal carotid artery, like internal carotid artery dissection or occlusion. Since carotid dissection or occlusion may also infarct the ipsilateral hemisphere,[122] the cause of an acute hemiparesis and a simultaneous contralateral Horner's is often internal carotid artery occlusion or dissection*.[123]

Another instance of carotid artery damage to the sympathetics is Raeder's paratrigeminal neuralgia*,[126] a migraine headache with a transient Horner's syndrome. Presumably, the Horner's develops when the internal or common carotid artery dilates (a proposed mechanism of migraine pain). Along with pain fibers in the arterial wall are stretched the sympathetics snaking up through the adventitia.

Anhidrosis: No sweating. Sympathetic lesions above the carotid bifurcation may cause anhidrosis of a small patch of the forehead, the only part of the face not supplied by those sympathetics traveling with the external carotid artery.[121]

Adventitia: The outer wall of an artery.

Occlusion or Dissection: Conceivably a Horner's and contralateral hemiparesis could also be due to infarction of half the medulla, but such a stroke would require the simultaneous occlusion of two separate arteries supplying the medulla—the medial and lateral branches of the vertebral artery (chapter 31). Vertebral artery occlusion rarely infarcts the medial medulla, probably because of collateral twigs to the medial medulla from the basilar artery.

Paratrigeminal Neuralgia: Originally, Raeder's paratrigeminal syndrome indicated a Horner's syndrome with involvement of the Vth (trigeminal) nerve.[124]

Even more than Raeder's paratrigeminal neuralgia are migraine patients who suffer parasympathetic blockade during their headache, which you see as a dilated pupil.[125]

Extrinsic Eye Muscle Examination

Testing the IIIrd, IVth, and VIth cranial nerves entails looking at the extrinsic and intrinsic eye muscles: slow and fast (pursuit and saccadic) eye movements, ptosis, and pupillary reaction. You can conveniently look for nystagmus[8] at this point too, even though nystagmus is usually due to brainstem, cerebellar, or labyrinthine (inner ear) pathology.

Smooth Pursuit

Ask the patient to follow a target left, right, up, and down. The eyeballs should move like smooth ball bearings in well-oiled sockets. These smooth pursuit movements should not be interrupted by sudden, short, back-and-forth shivers (fixation instability indicative of cerebellar dysfunction[127]), or by ratchet-like stops and starts (usually cerebellar or extrapyramidal*[129]).

Ophthalmoparesis

As the patient pursues left and right, watch the 3 o'clock and 9 o'clock edge of the iris; make sure each iris touches the corner of the eyelid ('buries the eye').





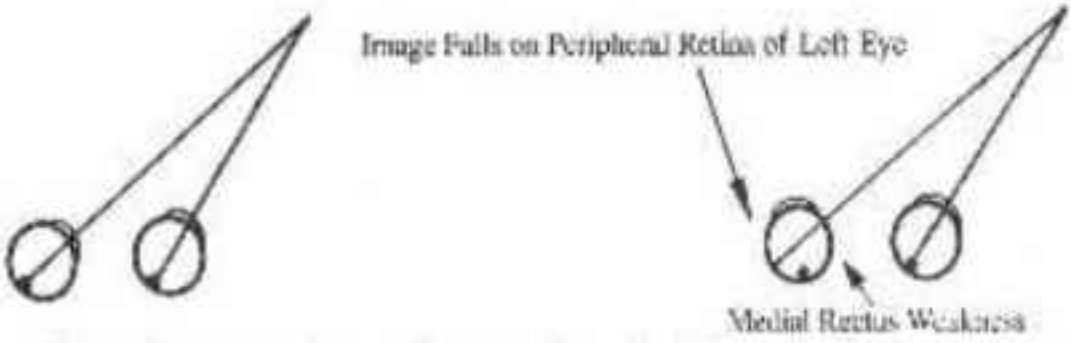
If there's a question in your mind about one eye not moving fully, ask the patient if he sees one or two targets. If he sees two objects, the direction in which the targets are most separated is the direction of action of the weak muscle. You now have to determine if the weak muscle is in the left or right eye. Look at the reflections of a flashlight or window on the patient's pupil. Since the reflections should be at exactly the same spot in each eye, you can tell which eye is not pulled over enough just by looking at the reflections.

Nystagmus: Rhythmic jerking of the eyes. From the Greek: to drowse, referring to the head jerk on nodding off to sleep in the sitting position.

Cerebellar or Extrapyramidal: Ratchety pursuit to just *one* side suggests a disturbance in the cerebral hemisphere ipsilateral to the weak pursuit. (In general, the left hemisphere pursues targets to the left, the right hemisphere to the right.[128])

To be sure, alternately cover and uncover the suspicious eye while instructing the patient to keep looking at the target. If the suspicious eye is indeed weak, when it is covered (the good eye still looking at the target), the weak eye, not having a target to focus on, will float away from the weak muscle. Now when you now remove the cover, the weak eye, suddenly caught sneaking off stage by the spotlight, scurries back to stage center. The direction of this corrective step signals the weak muscle. The cover-uncover test also helps assure you that the muscle is weak when the patient says he sees two images. If there was no corrective movement when you uncovered the suspicious eye, then the eye did not float away from fixation, and therefore no eye muscle weakness. The target does not have to be too far from central fixation to demonstrate this, perhaps halfway from extreme lateral (or up or down) gaze. Remember that a weak muscle does not mean a weak nerve; it may be the muscle itself that's weak and, in fact, unless there is simultaneous weakness of up, down, and medial movements, it is hard to call IIIrd nerve dysfunction.

Another effective way to elucidate ophthalmoparesis is the red filter test in which a red filter is placed over one eye. The image which appears further out in the periphery is coming from the weak eye. So if the patient tells you the furthest out image is red, the eye behind the red filter is the weak one. The reason for this is that the image strikes the macula of the good eye (because it's looking at the target), but the peripheral retina of the bad eye which naturally interprets the image to be in its peripheral visual field. A variant of this test is to alternately cover and uncover one eye as you ask "which image is being cut off?" The image further out in the peripheral visual field points to the weak eye.



Sometimes the eye won't move because the eyeball is mechanically restricted by an intraorbital mass, or because one of the eye muscles is bound down or shortened by scar tissue. These situations are easily ruled out by an ophthalmologist who simply tugs on the eyeball ('forced ductions') to check that it is free to move in all directions.[130] If there's resistance, the ophthalmoplegia must be due to a mechanical limitation of eye movement, not paralysis of an eye muscle. An interesting example of this is Duane's syndrome: congenital lateral rectus weakness due to absence of the VIth nerve.[131] The lateral rectus muscle is, instead, partially innervated by the IIIrd nerve. As a result, when the eye looks medially, the co-contracting lateral and medial rectus muscles pull the eyeball inward. Look for narrowing of the palpebral fissure (ptosis of the upper eyelid and upside-down ptosis of the lower eyelid) as the eye sinks into the orbit on adduction; you may have to look at the eye from the side to detect this inward movement.

Once in a while you'll encounter strange eyelid or pupillary movements indicative of prior oculomotor nerve damage. These phenomenona, called misdirection, stem from an initial injury to the IIIrd nerve, followed by misdirected regrowth of the axons into the wrong IIIrd nerve muscles. For example, axons which used to supply the

inferior rectus may end up innervating levator palpebrae superiorus. This aberrant regeneration becomes apparent when the patient looks down. Instead of following the eyeball, the eyelid elevates. Pupillary constriction on adduction is another common example of misdirected reinnervation following a IIIrd nerve injury[6,134]

Synkinesis Following Recovery from Oculomotor Injury



Eyelid Elevates on Adduction

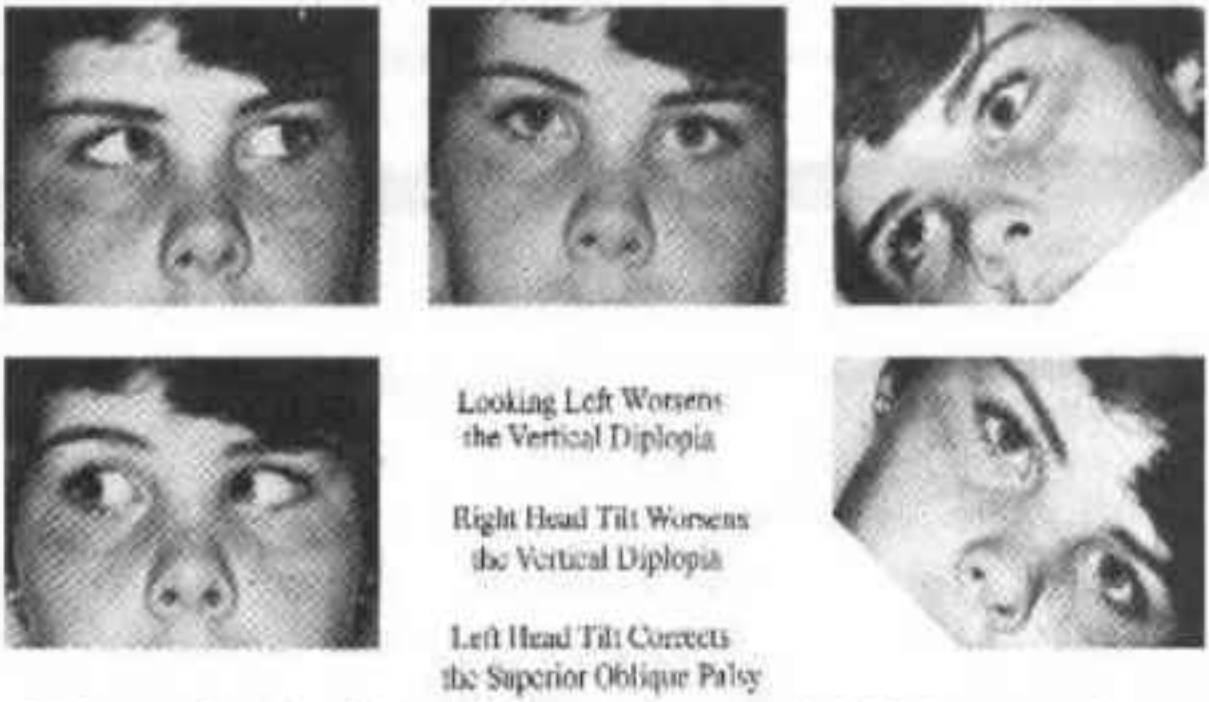
Trochlear nerve paralysis allows the eye to float upward at rest. Suppose the right trochlear nerve is out. Without the superior oblique to pull it down and in, the right eye floats upward. Unfortunately, when you see the elevated right eye, you don't know which eye is abnormal. Is one of the depressors of the right eye weak—the right superior oblique or the inferior rectus—or is one of the elevators of the left eye weak—the left inferior oblique or the superior rectus? You can be pretty sure the right superior oblique is weak if the patient can't look down and in with the right eye (the field of maximal separation), but to be absolutely sure, go through a few simple steps.[135]

First ask the patient to look left. If the diplopia worsens on left gaze, then either the left superior rectus or right superior oblique is weak, because both these muscles work primarily when the eyes are looking left. Now ask the patient to put his right ear on his right shoulder. The right IVth nerve normally would rotate his right eye clockwise (from your viewpoint), pulling the eye down and in. Without a IVth nerve, tilting the head like this will produce maximal separation*. Finally, ask the patient to put his left ear on his left shoulder. The left superior oblique rotates the left eye counterclockwise and the right inferior oblique rotates the right eye counterclockwise. No weakness of these two muscles, so no double vision. In other words, a patient with a right IVth nerve palsy will walk into your office with a left head tilt ('you tilt away to get away from the diplopia').

IIIrd Nerve Injury: Lepore and Glaser propose that misdirection takes place, not in a peripheral site, but in a *central* site—the oculomotor nucleus.[132]

Primary regeneration (without a history of previous oculomotor nerve injury) is likely due to a slowly enlarging mass compressing the oculomotor nerve.[122]

Maximal Separation: Whenever we tilt our heads, the eyes rotate slightly in the opposite direction (counter rotate) to help keep the retinal image upright.[136] The superior and inferior oblique muscles counter-rotate (intort and extort) the eyes. Without a superior oblique, the eyes separate even further when the head tilts, apparently because the superior rectus muscle (also a weak intorter of the eye) tries to intort the eye when the head tilts, and ends up elevating the eye further.



Looking Left Worsens the Vertical Diplopia

Right Head Tilt Worsens the Vertical Diplopia

Left Head Tilt Corrects the Superior Oblique Palsy

This rotary function of the trochlear nerve becomes clinically important when you want to test the IVth nerve in the face of a IIIrd nerve palsy—i.e., when the IIIrd nerve can't pull the eye medial for the IVth nerve to then pull the eye downward. To examine the IVth nerve in this circumstance, concentrate on a single conjunctival blood vessel and see if the right eye rotates clockwise (counterclockwise for the left eye) when you ask the patient to look down and in.

Saccadic Eye Movements

Saccades* are tested by having the patient glance back and forth between two targets held about a foot apart. A patient who consistently overshoots the target and zeroes in with one or two small, ricocheting corrections (ocular dysmetria)—somewhat like an intention tremor—is likely to be suffering from cerebellar dysfunction.[137] So is the patient whose eyes briefly flutter back and forth after he glances at a target ("flutter dysmetria").

Slow saccades, so slow that the eyes seem to glide to their target, are commonly seen in Huntington's chorea,[138] olivopontocerebellar degeneration*,[140] and Fisher's syndrome*.[142] Purely cerebellar lesions do not slow saccadic velocity.[143] Hypometric saccades (saccadic undershoot) are ones that take two or three skips to reach the target. Consistent undershooting to one side suggests a mild gaze paresis to that side (next chapter); undershooting to both sides, like ratchery pursuit, is of little localizing value since it is seen in both cerebellar and basal ganglia diseases.[144] Though a bedside examination of fast and slow eye movements is often accurate enough for clinical localization, eye movement recordings using infrared detectors give a far more accurate depiction of abnormal saccades.

Saccades: From the French 'sacher,' to pull—a term that compares the medial and lateral rectus muscles to bridle reins.

Olivopontocerebellar Degeneration: A hereditary progressive degeneration of the pons, cerebellum, and olivary nucleus in the medulla. Over the years, patients develop spastic ataxia (pyramidal and cerebellar dysfunction) with prominent brainstem signs.[139]

Fisher's Syndrome: A self-limited illness of sudden ataxia, ophthalmoplegia (including the pupils), and areflexia. Thought to be due to demyelination of peripheral and cranial nerves.[141]

Intrinsic Eye Muscle Examination

So much for eye movements. Ptosis we have mentioned—look at how close the eyelid comes to the pupil. Pupillary reaction is also fairly easy. If the pupils react, fine. Moreover, if the pupils react well to light, accommodation will almost certainly be normal, too. In fact, it's so rare for any disease to impair pupillary constriction to accommodation without also impairing pupillary constriction to light,[145] that there's almost no need to check the accommodation reflex unless the pupils are either very sluggish or unreactive to light*.

If the pupils don't react to light, the anatomic differential diagnosis includes the afferent limb (retina, optic nerves, optic tracts) and the efferent limb of the light reflex (the pretectum, Edinger Westphal nucleus, parasympathetic fibers in the oculomotor nerves, and the pupillary constrictor muscle in the iris). The afferent limb can be ruled out by checking for unrefractable visual impairment, red washout, visual field loss, and pale discs. (Marcus Gunn may be absent if the optic nerves are equally affected.)

On the efferent side, each anatomic site has an etiologic differential diagnosis. The most common etiologies for an impaired light reflex include:

Midbrain	*Parasympathetics*	*Muscle*
Tertiary Syphilis	Adie's syndrome	Trauma
Parinaud's syndrome	Oculomotor nerves	Atropine eye drops
	Fisher's syndrome	
	Botulism	

Midbrain

Look at the size of the pupils. If they're small and somewhat irregular in outline, have the patient look at his thumb which you hold about six inches from his face. If the pupils now constrict, i.e., accommodate to near vision, you've found an Argyll Robertson* pupil, almost always a sign of (treated or untreated) tertiary syphilis* or diabetes. The well-worn mnemonic for remembering the Argyll Robertson pupil is that it's like an old prostitute who accommodates but doesn't react (so they say).

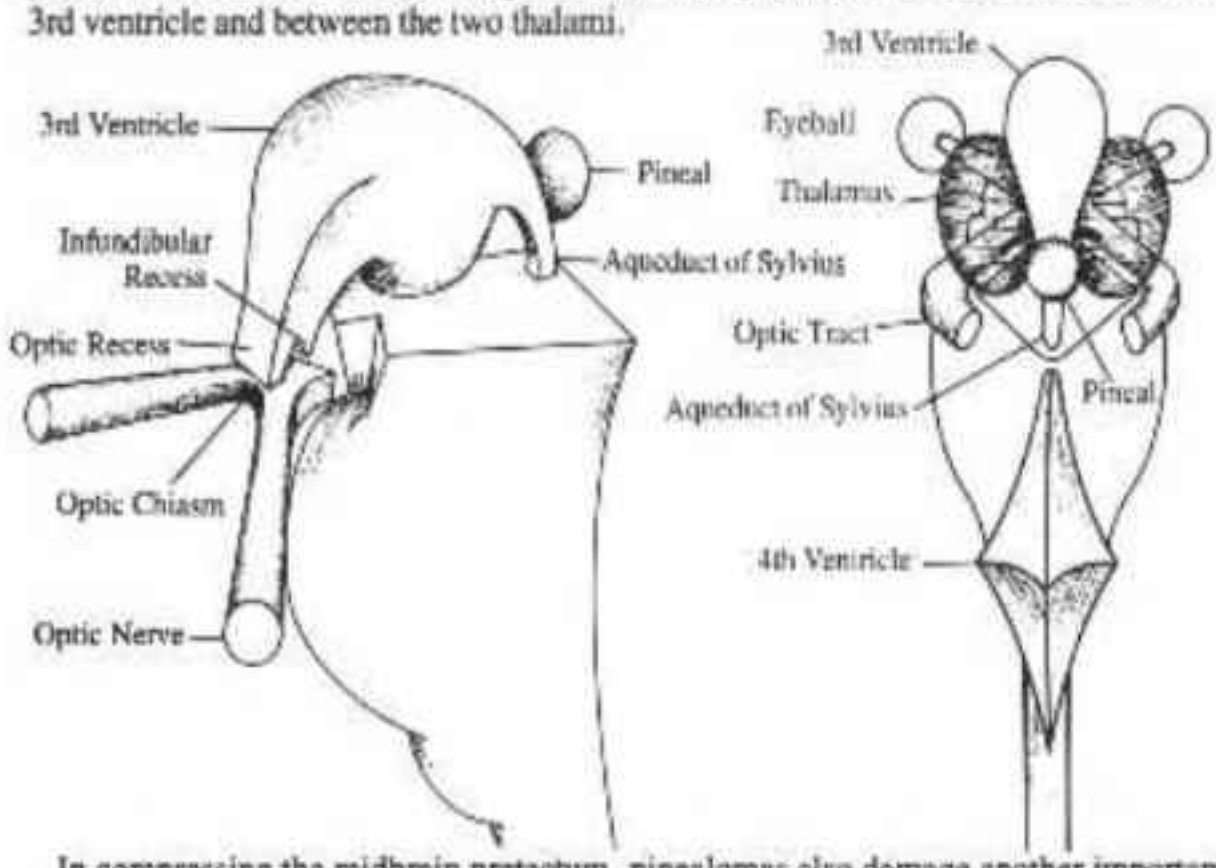
The anatomic explanation for the Argyll Robertson pupil in syphilis is uncertain. Most believe the lesion to be in the dorsal midbrain where the slip of fibers from the optic tract tells the IIIrd nerve nucleus to constrict the pupil. A lesion there would spare the more ventrally placed accommodation fibers descending from the occipital lobes.

Unreactive to Light: Diphtheria and the Fisher variant of Guillain Barre are two rare examples in which loss of accommodation may occur before loss of the pupillary reflex.

Argyll Robertson: Scottish ophthalmologist of the late 19th century.

Tertiary Syphilis: Syphilis attacks in three stages.[146] The first stage is a genital ulcer which heals by itself. Months to years later, a rash appears on the body, often associated with an arteritis in the brain or other internal organ. The third stage, tertiary syphilis (Winston Churchill's father succumbed to this disease), occurs years later in the form of progressive dementia, personality changes (characteristically delusions of grandeur), Argyll Robertson pupils, hearing loss, severe proprioceptive loss in the legs, and 'lightning' pains in the legs (Tabes Dorsalis). The take home message about syphilis is: don't be reassured because the ulcer on your penis or labia disappeared.

The small, irregular Argyll Robertson pupil is only one example of light-near dissociation (better pupil constriction to accommodation than to light). Any lesion that injures the midbrain pretectum (where light intensity is received), but spares the tegmentum (where accommodation instructions are received), can produce light-near dissociation. Such a characteristic, but fortunately uncommon, lesion is the pinealoma, a tumor of the pineal gland suspended just above the midbrain behind the 3rd ventricle and between the two thalami.



In compressing the midbrain pretectum, pinealomas also damage another important midbrain structure—the upgaze center. The constellation of dorsal midbrain signs: inability to look up and bilateral light-near dissociation with medium-sized pupils (not small and irregular like Argyll-Robertson pupils) is called Parinaud's syndrome.[147] Another cause of Parinaud's syndrome is a dilated 3rd ventricle compressing the dorsal midbrain. In fact, when ventricular shunts are inserted for hydrocephalus, inability to look up fully is an early sign that the shunt is malfunctioning.[148]

Parasympathetics

Adie's* pupil, which is usually unilateral, is another example of light-near dissociation. The pathology takes place in the parasympathetic nerves, 90% of which innervate the ciliary body; the remaining 10% innervate the iris sphincter. When these parasympathetic nerves are damaged (by a virus?), the pupil becomes dilated and fixed to both light and accommodation until reinnervation occurs. When recovery begins, reinnervation occurs randomly, which means that 90% of the iris sphincter becomes reinnervated by nerves that should have gone to the ciliary body. This mismatch translates into light-near dissociation, because 90% of parasympathetic instructions to constrict the pupil never make it to the iris, being dissipated instead in the ciliary body.[149]

Parinaud: French ophthalmologist of the late 1800's.

Adie's: Dr. Adie was a British neurologist in the early 20th century.

To confirm the denervated Adie's pupil, capitalize on the fact that a denervated muscle becomes supersensitive to acetylcholine. A few drops of dilute (.125%) pilocarpine* will constrict an Adie's pupil, but not a normal one. Denervation supersensitivity persists even after the iris is reinnervated, because the reinnervation is imperfect.[150]

When parasympathetic innervation is first lost in Adie's syndrome, the pupil is relatively large, but with time and reinnervation the pupil constricts into the 2mm range, a size that—with the light-near dissociation—makes an old Adie's resemble an Argyll-Robertson pupil.

An ophthalmologist can directly observe the denervated segments of the iris with a slit lamp, an apparatus that views the eye through a narrow band of light. With the slit lamp he can see the denervated (paralyzed) segments dragged into constriction by the neighboring segments which do constrict, a phenomenon called segmental palsy.[151] Because the normal segments must drag the paralyzed segments, pupillary constriction and redilation may take a whole minute or more, hence 'tonic' pupils.

For still unexplained reasons, Adie's pupil is associated with hypoactive or absent deep tendon reflexes in the arms and legs (occasionally in the arms or legs alone).[152]

If the pupils are large and completely unreactive to light, look carefully for any weakness of the superior, inferior, or medial rectus muscles to suggest incomplete IIIrd nerve lesions. If you find weakness of eye movements in all directions, look again for slowed saccades and cerebellar ataxia to suggest Fisher's syndrome, a self-limited illness of cranial and peripheral nerves.

If the patient with unreactive pupils is totally paralyzed on a respirator, look for botulism (chapter 26).

Muscle

Sometimes, after eye trauma, the pupil doesn't work because of local damage to the pupillary constrictor fibers.

Anticholingeric eye drops, like atropine*, block the parasympathetic neurotransmitter, acetylcholine, and allow the unopposed sympathetics to dilate the pupil.

Nystagmus

Nystagmus is one of those signs in neurology (the Hoffmann reflex is another) which causes an initial flurry of excitement that subsides as you try to use it to localize the lesion. The issue is almost always whether the nystagmus is due to labyrinthine or brainstem/cerebellar pathology; is the nystagmus 'peripheral' or 'central'?

Pilocarpine: A drug which mimics acetylcholine, the chemical released by parasympathetic nerve endings in the iris. Any drug which mimics the parasympathetic nervous system is a parasympathomimetic. A drug which opposes the parasympathetic nervous system is a parasympatholytic. (Sympathomimetics and sympatholytics mimic and oppose the sympathetic nervous system.)

Atropine: Another name for atropine is belladonna, meaning 'Beautiful Lady' (because her pupils are large).

Vertical Nystagmus

First of all, upbeat or downbeat nystagmus is almost always of central origin, representing disrupted connections between the cerebellum and brainstem. Theoretically, upbeat or downbeat nystagmus could be due to a pure brainstem or pure cerebellar lesion, but in practice the lesion often involves both, as, for example, a cerebellar mass pressing against the brainstem. Downbeat nystamus—especially downbeat nystagmus in the primary position (looking straight ahead)—is usually due to a combined disturbance of the lower brainstem and adjacent cerebellar flocculus*, like Arnold Chiari malformation*.[151] Upbeat nystagmus in the primary position implicates the brainstem, its connections to the cerebellar vermis, or occasionally the vermis alone.[155]

Horizontal Nystagmus

For me, any horzontal nystagmus coarse enough to be seen ten feet away is almost always of central origin. Unfortunately, the converse (fine nystagmus is peripheral nystagmus) isn't necessarily true. In fact, fine cerebellar nystagmus can resemble vestibular nystagmus. Each labyrinth normally 'pushes' the eyes away from it. Maximal nystagmus is therefore evoked when the eyes look away from the weak labyrinth, in which case, the eyes drift back toward midline and jerk laterally. The cerebellum helps maintain eccentric gaze (gaze off to one side); when the patient looks to the side of a cerebellar lesion, the eyes also drift back toward midline and jerk laterally.[156] So, when you see nystagmus on lateral gaze (eyes jerking laterally), you must decide if the patient has an ipsilateral cerebellar lesion or a contralateral vestibular lesion.

When nystagmus is so fine that I have to get within a foot to see it, I rely on the following points: 1) Central lesions allow the eyes to jerk in different directions when gazing in different directions; peripheral nystagmus jerks in the same direction, regardless of where the eyes gaze. 2) Mixed horizontal and vertical, or horizontal and rotary, nystagmus is probubly peripheral; the two axes of nystagmus suggest a disturbance of two semicircular canals. 3) If the patient can stop his nystagmus by fixating on the target, the nystagmus is also likely peripheral. 4) If the nystagmus is only elicited by tilting the head, repeated attempts to elicit the nystagmus quickly fail with peripheral nystagmus.[157]

Fortunately, horizontal nystagmus alone is rarely a pivotal sign. You can usually rely on the presence of cerebellar or brainstem signs to confirm central nystagmus, and sometimes on the presence of tinnitus and hearing loss to confirm peripheral nystagmus.

Pendular Nystagmus

One of the coarsest forms of nystagmus is pendular nystagmus—a continuous, rapid, horizontal, to and fro wiggling of the eyes, even when looking straight ahead. You can't *imagine* how the person is able to see with his eyes in constant motion, but if the nystagmus is congenital and the target is stationary, everything looks just fine, thank you. The visual acuity may not be normal, but the patients don't complain about what you'd expect them to complain about—oscillopsia: a jiggling world.[158]

Flocculus: The phylogenetically ancient part of the cerebellum, located near the posterior vermis, intimately connected to the vestibular nuclei.

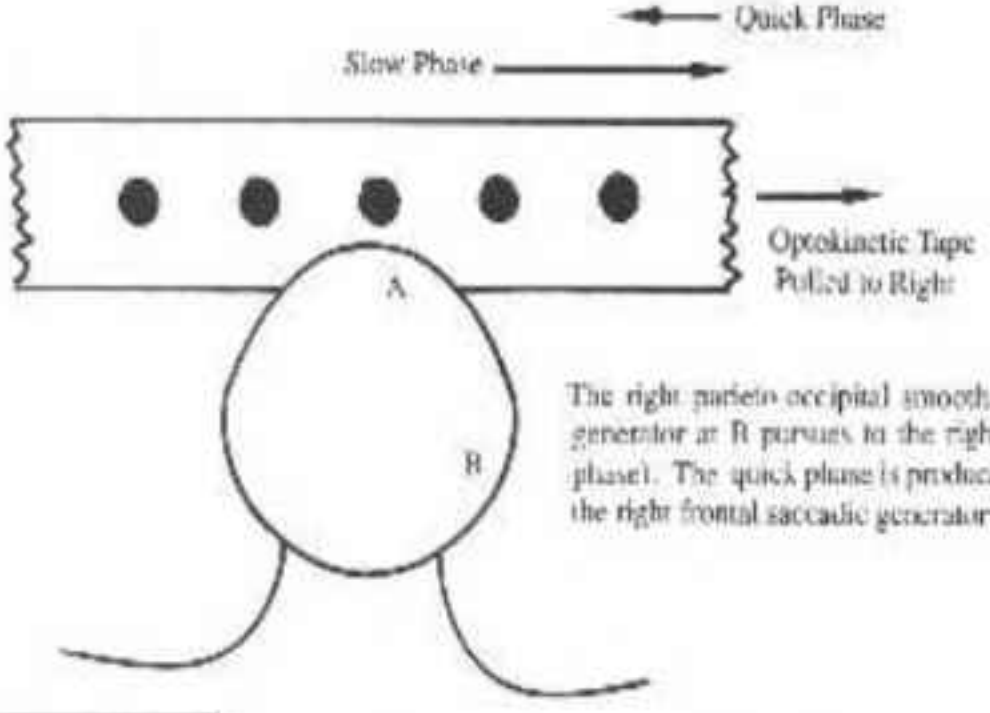
Arnold Chiari Malformation: A congenital malformation of the posterior fossa: the medulla, 4th ventricle, and cerebellar tonsils are wedged into the foramen magnum.[155]

Patients with *acquired* pendular nystagmus, however, usually do complain of oscillopsia. Acquired pendular nystmus may result from an afferent defect or an efferent one. An afferent example occurs (rarely) in coal miners confined to dark environs for long periods. Their eyes adapt to the long periods of poor illumination with a searching (pendular) nystagmus which, presumably, improves resolution by moving the target back and forth across the macula. Efferent pendular nystagmus is speculated to result from small midbrain lesions, perhaps involving the cerebellar outflow tracts from the dentate nucleus.[159]

Optokinetic Nystagmus

Optokinetic nystagmus is an interesting test used mostly to confirm parieto-occipital lesions. When the optokinetic tape* is pulled from the patient's left to his right, the right parieto-occipital lobe tracks the target to the right (smooth pursuit).[160] The eyes saccade left to track each newly arriving target*. In right parieto-occipital lesions, smooth pursuit to the right is lost, which you see as absent optokinetic nystagmus to the right.

Clinically, optokinetic nystagmus is helpful in deciding whether a homonymous hemianopia is due to a stroke or a brain tumor.[161] Since the smooth pursuit generator is in the parieto-occipital cortex, outside the posterior cerebral artery blood supply to the occipital lobes, occipital strokes do not impair optokinetic nystagmus. However, tumors, which *do* cross vascular boundaries, will interrupt the smooth pursuit generator when the tumor extends beyond the confines of the posterior cerebral artery*.[162]



The right parieto-occipital smooth pursuit generator at B pursues to the right (slow phase). The quick phase is produced by the right frontal saccadic generator at A.

Optokinetic Tape: A *tape* of repetitive targets pulled across the patient's visual field. The patient follows each target briefly and then refixates on the next arriving target, like watching a freight train go by.

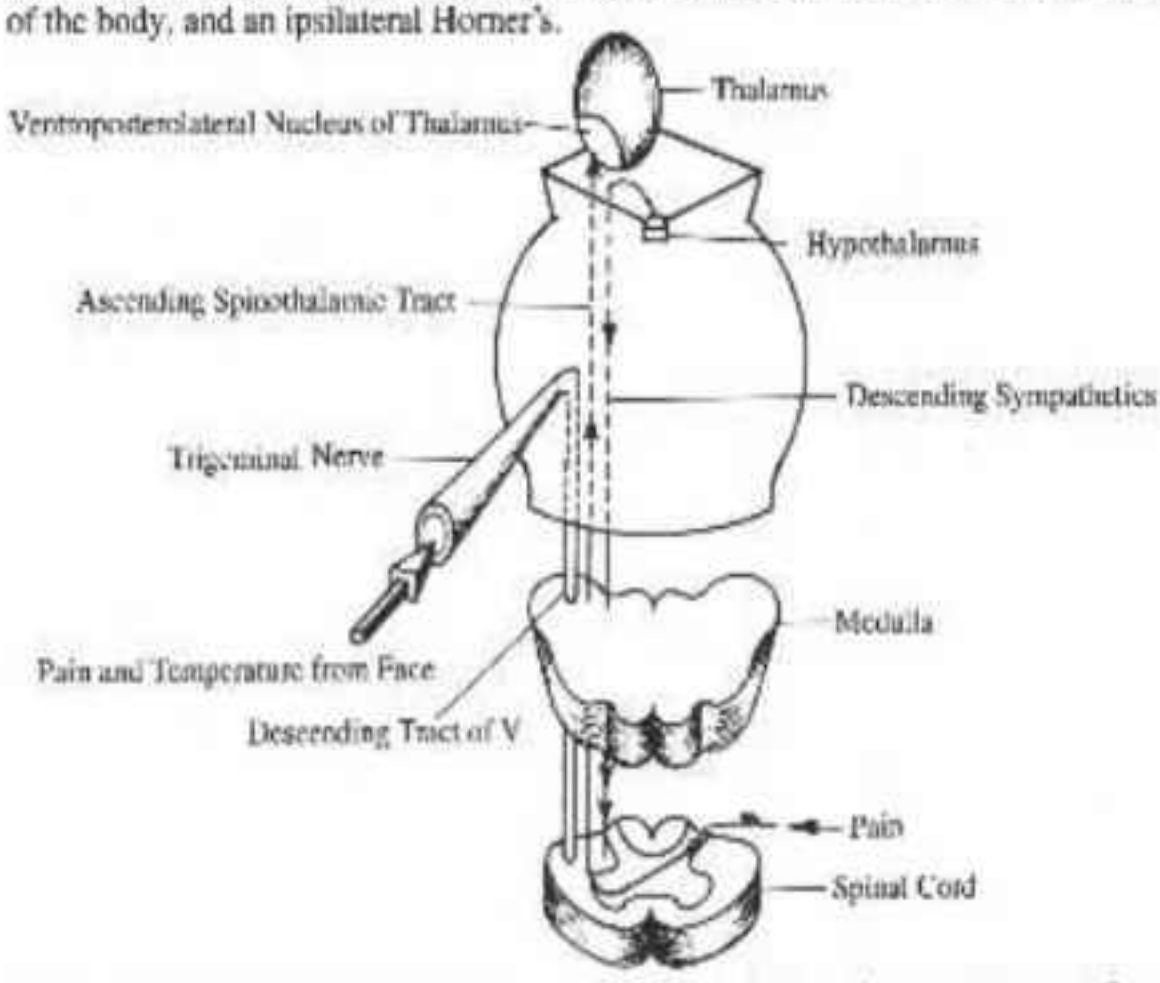
Newly Arriving Target: It's not clear what structure—frontal lobe, occipital lobe, or brainstem—tells the eyes to *jut* back to the next arriving target.

Posterior Cerebral Artery: Surprisingly, in patients with brain tumors optokinetic nystagmus is better preserved when the tape is pulled into the *blind* visual field. The intact parieto-occipital smooth pursuit generator (contralateral to the lesion) pulls the eyes into the hemianopic field, a feat that the damaged generator cannot mirror.

V: TRIGEMINAL NERVE

Anatomy

The Vth cranial nerve, the trigeminal, controls both sensory and motor functions: sensation of the forehead and face (including the inside of the mouth), and strength of the chewing muscles (temporalis*, masseters*, pterygoids*). Trigeminal nerve ancestry must be very old because as soon as it enters the pons, the Vth nerve takes a nose dive into the phylogenetically ancient medulla and upper cervical spinal cord. This descending tract of V synapses onto second order neurons which cross to the opposite side of the medulla before ascending to the contralateral thalamus. The descending tract of V lies dorsolaterally in the medulla, next to the *descending* sympathetic tract and the *ascending* spinothalamic tract carrying pain and temperature up from the opposite side of the body. An infarction here, called a Wallenberg* infarction, quite naturally produces ipsilateral facial numbness, contralateral pain and temperature loss of the body, and an ipsilateral Horner's.



The trigeminal nerve has three divisions: ophthalmic (V^1), maxillary* (V^2), and mandibular* (V^3). Fortunately, all motor function (chewing) is handled by one branch, the mandibular. Sensory divisions are demarcated as follows:

Temporalis Muscle: The muscle that bulges in the temples when you clench your jaws.

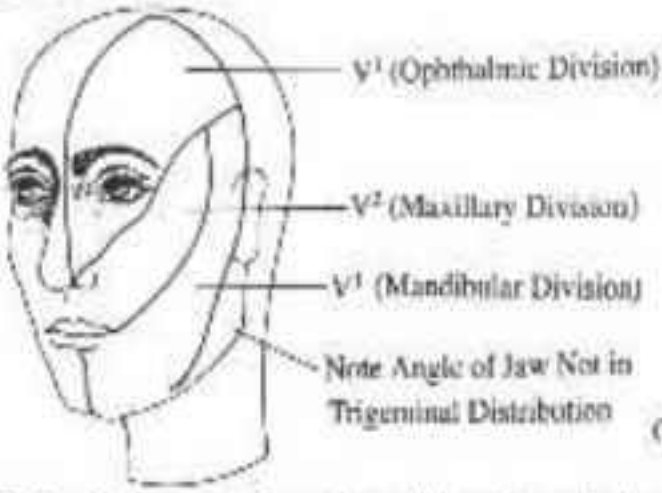
Masseters: From Greek, to chew.

Pterygoids: From Greek, 'shaped like a wing.' The pterygoid muscles open the mouth and move the jaw from side to side.

Wallenberg: German neurologist of the late 19th century.

Maxillary: The maxilla is the cheek bone.

Mandibular: The mandible is the jaw bone.

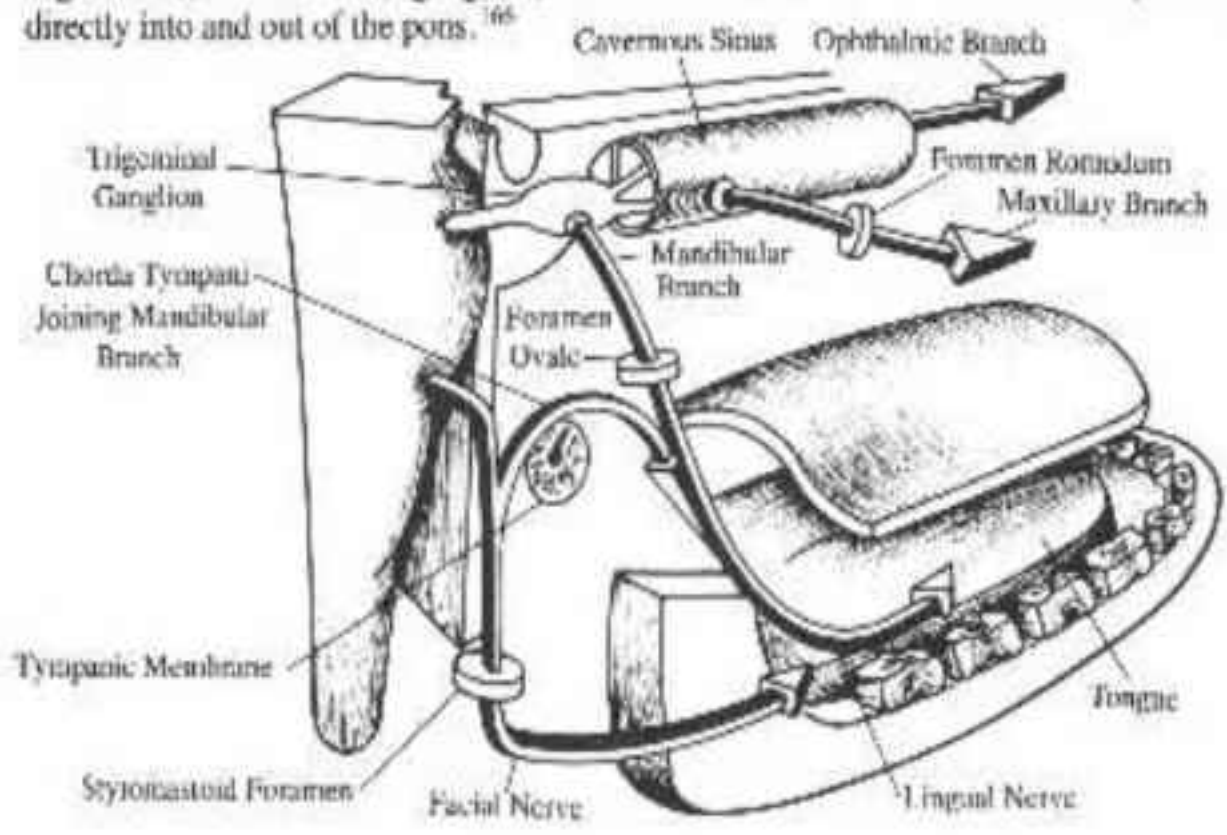




Onion skinning with maximal hypesthesia at the center of the bull's eye.

Note: 1) the posterior edge of the trigeminal reaches as far back as the ear; 2) the cornea is in the ophthalmic territory; 3) the mandibular division spares the angle of the jaw.[162] This last point is important when trying to decide if facial hypesthesia is due to a peripheral or a central Vth nerve lesion. If facial hypesthesia spares the angle of the jaw, the lesion is almost certainly extra-axial. Intra-axially, the trigeminal nerve dips deeply into the medulla in a well organized pattern: the forehead dips furthest and the mouth least. As a result, intrapontine lesions produce a pattern called 'onion-skinning' with maximal hypesthesia occurring over the nose and lips, and fading centripetally from this bulls-eye. Conversely, lesions in the low medulla often spare the lips and chin, affecting instead the forehead, cornea, and cheek.[164]

To get through the bony skull onto the face, each trigeminal division passes through an important foramen: the ophthalmic division through the superior orbital fissure accompanied by III, IV, and VI; the maxillary division through foramen rotundum ('fat Max'), and the mandibular (sensory and motor parts) through foramen ovale ('man has an oval face'). The ophthalmic division reaches the superior orbital fissure via the cavernous sinus, sharing a berth with III, IV, and VI. The maxillary division travels briefly in the wall of the cavernous sinus before departing for foramen rotundum, and the mandibular division heads straight for foramen ovale without entering the cavernous sinus.[165] Behind and below the cavernous sinus is a shallow depression called Meckel's cave, the three trigeminal divisions join into a large knot, called the trigeminal (or Gasserian) ganglion, from which the combined Vth nerve passes directly into and out of the pons.[166]



Intracavernous Lesions

By taking what appears to be a safe route through the cavernous sinus, III, IV, VI, V^1, and V^2 have unknowingly placed themselves in considerable jeopardy, despite being embedded within the dural layers of the cavernous sinus. Practically any cavernous sinus lesion—and there are lots of them—can indiscriminately injure these nerves during their long and lonely journey upstream against the torrents of gushing venous blood. Cavernous sinus thrombophlebitis*, aneurysms of the intracavernous portion of the internal carotid artery*, intracavernous meningiomas, carotid-cavernous fistulas*, pituitary tumors spilling laterally into the cavernous sinus—all may cause ophthalmoplegia with facial and forehead numbness.[170] The only good news is that jaw numbness doesn't occur since V^3 doesn't enter the cavernous sinus.

Trigeminal Neuralgia

One of the most painful conditions known to man is trigeminal neuralgia (tic douloureux). Patients suffer lightning jabs of horrible facial and jaw pain, usually precipitated by a trigger point along the gums or lips*. Fortunately, the pain rarely if ever awakens the patient from sleep.[172] The cause of trigeminal neuralgia is thought by many to be an arterial or venous loop thumping or rubbing against the trigeminal nerve entering the pons*, or sometimes a small plaque of demyelination (multiple sclerosis) within the brainstem.[174]

Patients with the vascular etiology benefit from a posterior fossa craniotomy to wedge a small sponge between the trigeminal nerve and the offending arterial branch.[175] Despite the severe symptomatology of trigeminal neuralgia, there is no hypesthesia of the face or atrophy† of the chewing muscles. If there is, look for a tumor infiltrating the trigeminal ganglion.

Cavernous Sinus Thrombophlebitis: A rapid, frequently fatal infection (fever, sepsis, increased intracranial pressure) that interrupts III, IV, VI, V^1, and V^2 bulges the eye forward, and occasionally damages the pituitary. Demands high dose antibiotics and usually steroids.[167]

Aneurysm of the Intracavernous Carotid Artery: Unlike aneurysms elsewhere, aneurysms of the intracavernous portion of the internal carotid artery dilate the entire arterial wall, not just a focal area. Because there is no single outpouching, intracavernous aneurysms rarely hemorrhage.[169]

Carotid-Cavernous Fistulas: Spontaneous or traumatic rupture of the intracavernous portion of the internal carotid artery creates a fistula (an abnormal passageway) between the high pressure carotid artery and low pressure carotid sinus. The ophthalmoplegia results from direct injury to III, IV, and VI, or more commonly from mechanical limitation of the eyeball, bulged forward by the raised pressure in the cavernous sinus. Listen for a loud bruit over the eye disclosing highly turbulent blood shortcutting through the fistula. Treatment requires occluding either the entire cavernous sinus or just the fistulous connection with one of several types of small balloons floated up the carotid artery by neuroradiologists using fluoroscopy (TV monitoring with xrays).[53]

Along the Gums or Lips: A cousin to trigeminal neuralgia is glossopharyngeal neuralgia. The patient experiences terrible jabs of throat pain when he swallows or coughs, movements which presumably stimulate a trigger point in the pharynx.[171]

Entering the Pons: Perhaps the pulsating artery rubs myelin off adjacent axons allowing short circuits or spontaneous discharges to occur in the trigeminal nerve.[173]

Atrophy: Shrinkage, wasting.

Testing the Vth Nerve

The only tricky part about testing the Vth nerve is the corneal blink reflex. Holding a wisp of cotton, place the heel of your palm on the patient's cheek and ask him to visually follow your other hand. This throws the cotton wisp out of focus and prevents reflex blinking to the threat of something being jabbed at the eye. Gently brush the cotton wisp against the cornea and gauge how sensitive the cornea is.

The masseter muscles are tested by feeling the angles of the clenched jaw. If one bony angle is more easily felt, there is probably atrophy of that masseter muscle. Visually check the temples and palpate for temporalis muscle atrophy. Have the patient open his mouth widely and try to close his mouth; you shouldn't be able to overcome the jaw-opening muscles, the pterygoids. For routine purposes I do not formally examine any of these muscles, only when I suspect brainstem or cranial nerve pathology. Same for the corneal reflex. Unless there is suspicion of posterior fossa pathology, simply brushing the cheek is usually adequate to detect asymmetries.



Temporalis Atrophy

Ptosis

(Oculomotor Nerve Palsy)







Temporalis atrophy (mandibular division) means that the oculomotor nerve lesion must be prior to the cavernous sinus (because the mandibular division does not enter the cavernous sinus).

VII: FACIAL NERVE

The VIIth nerve, the facial, controls all the facial and forehead muscles. The frontalis muscle wrinkles the forehead, orbicularis oculi winks the eye, and a dozen or more facial muscles afford an amazing repertoire of facial expressions. Get ready: upper facial weakness means lower motor neuron and lower facial weakness means upper motor neuron. This unfortunate semantic confusion stems from the curious bihemispheric control of the forehead. The VIIth nerve nucleus in the pons has two parts; the upper part controls the ipsilateral forehead and the lower part controls the ipsilateral cheek. The lower facial nucleus is controlled by the contralateral motor strip, so a right hemispheric lesion causes weakness of the left cheek. The upper facial nucleus, however, is controlled by both hemispheres (motor strips), so in order to paralyze the left forehead, you have to damage both hemispheres—or else damage the facial nerve itself.

Working backward, paralysis of the cheek and forehead on one side of the face indicates a lesion in the VIIth nerve somewhere between the pontine facial nerve nucleus and the facial muscles. In general, if the forehead is spared, then facial paralysis is due to a lesion in the descending corticopontine upper motor neuron. The term 'peripheral facial weakness' is synonymous with lower motor neuron weakness, but peripheral facial *nerve* weakness means a lesion of the facial nerve outside the brainstem.



Lower Motor Neuron Facial Palsy (Forehead Involved)

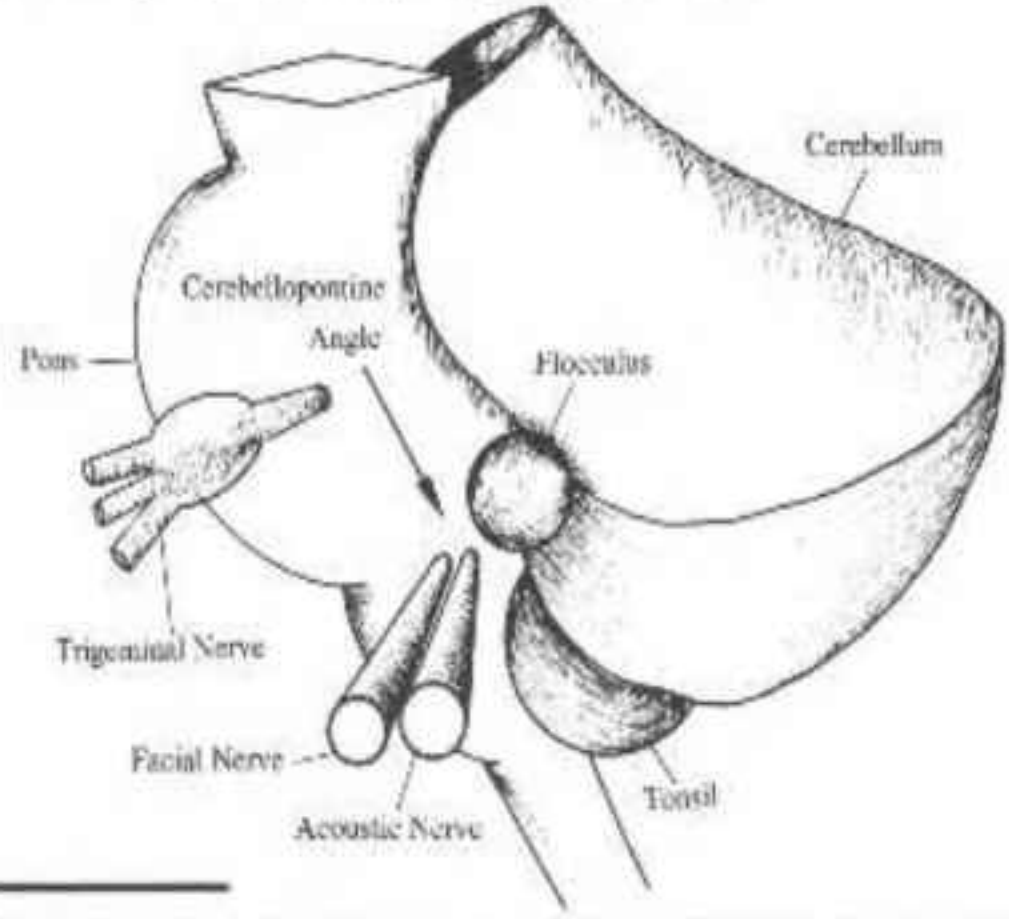
Eyelid closure (orbicularis oculi muscle) is weakened by both upper and lower motor neuron lesions, though more so by lower motor neuron lesions. Orbicularis oculi strength becomes important when one palpebral fissure* is open wider than the other; you have to decide if you're looking at orbicularis oculi weakness on one side or ptosis on the other. Since orbicularis oculi encircles the eye, a weak orbicularis oculi muscle leaves a sliver of sclera below the iris.[1,6] And when the patient squeezes his eyes shut, a weak orbicularis leaves more eyelash exposed. Now try prying the eyelids open; weakness of one should be apparent. Other concomitant signs of facial weakness (to be discussed), help implicate orbicularis oculi weakness through guilt by association, but still, don't forget to carefully check the other eye for miosis—evidence of a Horner's syndrome.

Palpebral Fissure: The separation between the two eyelids, derived from the Latin word palpo, to stroke, which the eyelid does to the eyeball.

If all this facial nerve anatomy weren't confusing enough, there's an additional anatomic twist to the facial nerve. As the facial nerve leaves its nucleus in the brainstem, other nerves briefly piggyback it on their way to: 1) the lacrimal gland, 2) the stapedius muscle (which dampens loud noises in the ear), and 3) the taste buds* (salt, sweet, sour, bitter). Ipsilateral loss of taste and tearing, and the presence of hyperacusis (noises sound too loud) confirm that your patient's facial weakness is lower motor neuron (but doesn't always distinguish between lesions in or out of the brainstem).[177]

Sometimes you can tell where the lesion is along the VIIth nerve by examining these three freeloaders. If tearing is gone, noises sound particularly loud in one ear, and taste for sugar and salt is lost, the lesion is quite proximal*. If tearing is spared, the lesion is slightly more distal; if only taste is lost, slightly more distal still; and if all three are preserved, the lesion is typically very distal, such as entrapment by a parotid gland tumor overlying the masseter muscle*.

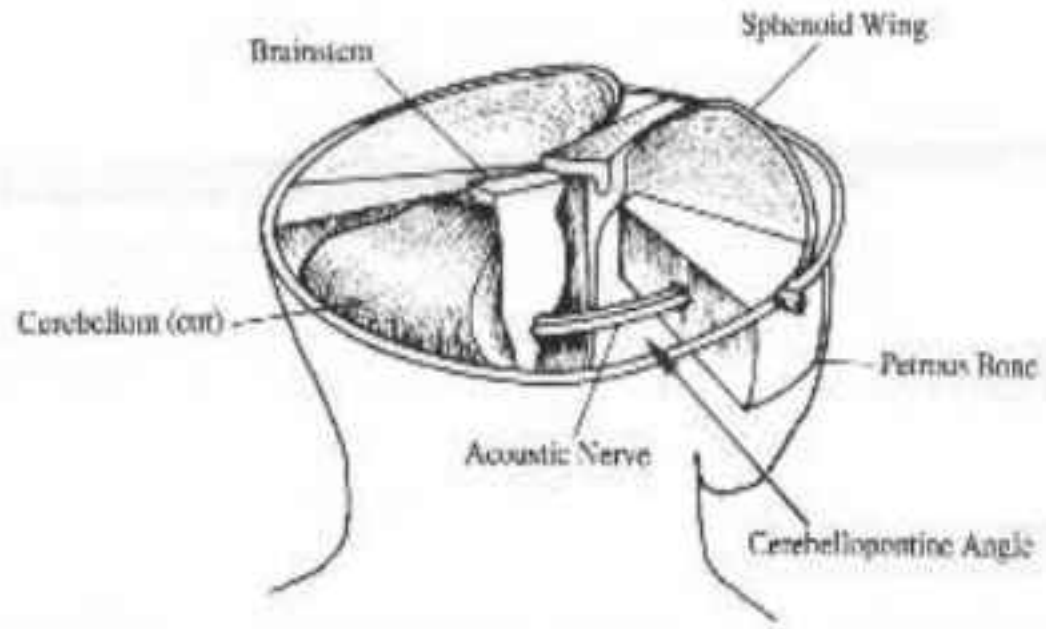
The VIIth, VIIIth, and Vth nerves exit the brainstem relatively close to each other and immediately find themselves in the cerebellopontine angle, a sizeable triangular space bordered by the cerebellum, pons, and temporal bone.



Taste Buds: Taste for the anterior 2/3 of the tongue travels along the VIIth nerve, while taste for the posterior 1/3 travels along the IXth cranial nerve, the glossopharyngeal. Most taste is actually smell; food without fragrance is relatively tasteless.

Quite Proximal: Whether hyperacusis is truly due to loss of the stapedius reflex is still controversial. As Adour points out, many Bell's palsy patients (see text below) have hyperacusis with a normal stapedius reflex, and conversely, many patients with no stapedius reflex fail to complain of hyperacusis.[178]

Masseter Muscle: If tearing, hearing, and taste are all okay, the lesion could also conceivably be very proximal – in the VIIth nerve nucleus before those three nerves join the facial nerve in the brainstem. Probably the most common reason, though, for peripheral facial palsy alone is partial VIIth nerve injury – selective enough to damage the facial fibers but not the three freeloaders.



Whenever you find peripheral facial weakness, you need to carefully check these two other cranial nerves (and the ipsilateral cerebellar hemisphere) to rule out an extra-axial posterior fossa tumor. Fortunately, 95% of the time acute peripheral facial weakness is due to Bell's* palsy, a poorly understood acute inflammatory attack* on the facial nerve within the facial canal, the bony tunnel in the temporal bone guiding the facial nerve to its exit at the stylomastoid foramen*. Excellent recovery usually takes place within weeks or months*. If the eyelid won't shut during the recovery phase, artificial tears are used to protect the cornea from drying out.

Involuntary Movements

A number of different involuntary movements affect the face: myokymia, blepharospasm, Meige's syndrome, hemifacial spasm, and focal seizures, each of which produces stereotyped movements, a feature which distinguishes them from the more random and chaotic chewing, smacking, pocketing, jaw opening, and tongue flickering movements of oral-facial dyskinesia (tardive dyskinesia).

The most curious involuntary movement is myokymia, a continuous, rapid, rippling of one cheek sometimes associated with facial contractions. It's not clear how or why the facial nerve becomes so irritable, but since Guillain Barre, multiple sclerosis, and malignant pontine tumors can all cause myokymia,[162] the site of irritability is probably in the facial nerve nucleus or facial nerve itself.

Bell: Sir Charles Bell, an Edinburgh surgeon in the early 1800's, was the first to show that the ventral roots of the spinal cord are solely motor (he cut them, paralyzing an animal's limb without causing loss of sensation).

Inflammatory Attack: The exact pathophysiology is controversial. Some believe the facial nerve becomes acutely demyelinated.[75] Others believe that inflammation swells the facial nerve.[180] And without adequate elbow room in the facial canal, the swollen facial nerve compresses itself enough to paralyze the face and forehead, often with pain behind the ear at the stylomastoid foramen.

Stylomastoid Foramen: Stylo means pole or stake (which the styloid process, a tiny bone protruding from the stylomastoid foramen, resembles). Mastoid means 'shaped like a breast.'

Within Weeks or Months: During the recovery phase of Bell's palsy, axons bound for the taste buds may accidently find themselves en route to the lacrimal glands. When these patients eat, they cry 'crocodile tears.'[180]

Blepharospasm is a recurrent involuntary spasm of eye closure (both eyes) with perhaps some spread into other facial muscles.[153]

Meige's (rhymes with beige) syndrome resembles bilateral blepharospasm but with more prominent involvement of the face; the whole face intermittently grimaces as if the patient had just sucked a lemon, or else the mouth may open involuntarily with an intense yawn.[154] Both blepharospasm and Meige's syndrome are probably a form of extrapyramidal movement disorder*.[156]

Hemifacial spasm is just that—recurrent spasms of one side of the face.[157] The lesion is usually in the peripheral VIIth nerve, just as it leaves the brainstem where the exposed facial nerve is thought to be irritated by a branch of the basilar artery thumping against it*.[191]



Note the simultaneous contraction of the corner of the mouth and orbicularis oculi.

Hemifacial Spasm
(Affecting Eye and Mouth)

Focal seizures of the face can mimic hemifacial spasm, but the facial contractions of focal seizures are much quicker and more chaotic in their rhythm. And like all seizures, the contraction phase is much quicker than the relaxation phase.

Facial tics also resemble hemifacial spasm, but, being a habit, tics can be voluntarily suppressed.

Trismus, involuntary spasm of jaw closure, is a classical sign* of tetanus. Tetanus is typified by widespread muscular spasms caused by a powerful toxin secreted by Clostridium tetani, a ubiquitous, anaerobic bacterium that contaminates devitalized

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Extrapyramidal Movement Disorder: Blepharospasm has also been reported with brainstem lesions.[155]

Thumping Against It: Whenever myelin is rubbed off adjacent axons, abnormal signals may result. If the signals trigger motor fibers, movements result (like hemifacial spasm), and if the abnormal signals trigger sensory neurons, pain (tic douloureux) or paresthesias. Three explanations have been offered for the abnormal signals. The abnormal signals may result from short circuiting between bare axons; bare axons may initiate spontaneous signals at the denuded spots; and finally, spontaneous signals from the denuded spots may 'kindle' the neuron's cell body in the brainstem.[188] (Kindling is a phenomenon by which occasional electrical impulses given to a nerve cell body can eventually make the cell body discharge spontaneously.)

Like trigeminal neuralgia, hemifacial spasm is often relieved by separating the offending arterial loop from the facial nerve.[189] Surprisingly, simply manipulating the facial nerve may help when there's no arterial loop rubbing against the facial nerve.[190]

Classical Sign: A highly characteristic, but not quite pathognomonic, sign.

wounds*. Look for involuntary spasms of other muscles besides the masseters, especially the abdominal muscles.

Examination

Testing the facial nerve is easily done during the interview. As the patient gently smiles, count the number of teeth on each side of midline. Compare the depth and crispness of each nasolabial fold. Is the corner of the mouth turned down slightly? Is one eye open wider than the other (look for a sliver of sclera above and below the iris) suggesting weakness of orbicularis oculi? Do the eyes blink synchronously? Looking for these signs of mild facial weakness, as well as checking eye movements, bulk of the temporalis muscles, speech, and use of the hands and arms, makes the interview more interesting and shortens your subsequent neurologic exam. The only things left to check are that both eyelashes can be buried equally, that the forehead muscles contract symmetrically, and if necessary, that both platysma* contract equally.

VIII: ACOUSTIC NERVE

The VIIIth nerve, the acoustic, does two sensory jobs. One is to relay hearing to the brainstem from the cochlea, and the other is to relay balance information from the labyrinth. Routine testing involves closing off one external ear canal and whispering in the other. Any impairment of hearing is pursued with an audiogram and an auditory evoked response* without relying on the relatively crude Weber and Rinne tests*.[192]

Devitalized Wounds: Like botulism, tetanus cannot grow in the presence of oxygen. Since tetanus is such a prevalent bacterium, it may contaminate any laceration. For tetanus to grow, the wound must have no oxygen, i.e., no blood supply. To prevent Clostridia from gaining a foothold in a wound, all devitalized tissue (tissue which has lost its blood supply) must be debrided (snipped away). Tetanus inoculation and subsequent booster injections protect against the tetanus toxin produced by the bacterium, but not against the infection itself, which requires penicillin therapy.

Platysma: A thin, broad muscle underneath the jaw, stretching over the whole front of the neck. You can see the platysma by asking the patient to lift his jaw and bare all his lower gums.

Auditory Evoked Response: A recording of the brain's electrical response to ten or so clicks per second delivered through earphones. Points along the auditory pathway in the brainstem produce detectable electrical signals. A delay of one of the signals pinpoints the lesion. (See chapter 44.)

Weber and Rinne Tests: These are bedside tests using a vibrating tuning fork to distinguish conductive hearing loss (middle ear) from sensorineural hearing loss (cochlea or VIIIth nerve). The Weber test consists of holding the stem of a vibrating tuning fork against the middle of the patient's forehead. If vibrations sound louder in the deaf ear, the deafness is due to a conductive, middle ear problem. Test this on yourself by plugging one of your external ear canals and humming.

In the Rinne test the stem of a vibrating tuning fork is held against the mastoid bone until the patient can no longer hear it. The tuning fork is then immediately held next to the external ear canal. If he can hear it then, air conduction is better than bone conduction. Hearing loss in that ear is therefore sensorineural.

To test the labyrinthine part of the VIIIth nerve, squirt one or two cc's of cold water into the external canal after otoscopically assuring yourself no wax will prevent the water from reaching the drum. The latency before nystagmus* begins, and the amplitude and duration of nystagmus all help document an impaired or dead labyrinth.[193] For quantitative* results and more meaningful information, obtain an electronystagmogram*.

The VIIIth nerve begins in the upper medulla as the cochleur and vestibular nuclei. Branches from each nucleus leave the brainstem laterally, traverse the cerebellopontine angle, and immediately enter the internal auditory canal accompanied by the facial nerve. At this point the closest nerve to the acoustic is, of course, the facial nerve. Yet, in tumors of the VIIIth nerve (acoustic neuromas), the first cranial nerve to be affected after the acoustic is usually not the facial, but the trigeminal nerve*.[194] The tumor begins in the internal auditory canal, creeps along the internal auditory canal toward the brainstem, bulges out into the cerebellopontine angle, and compresses the Vth nerve, resulting in loss of the corneal reflex. So if someone has unilateral (or even bilateral) hearing loss, check the corneal. If it's absent, the patient has an acoustic neuroma until proven otherwise. Even without loss of the corneal reflex, do an audiogram and auditory evoked response* in anyone with unexplained progressive hearing loss, because fully 10% of those patients will harbor an acoustic neuroma.[195]

The real tip-off to an acoustic neuroma is early loss of speech discrimination amidst background noise: the patient complains that he can't understand the person standing next to him at a noisy party, or that he has particular trouble hearing a phone conversation in a noisy phone booth.[196] Imbalance (labyrinthine part of the VIIIth nerve) in acoustic neuromas is usually mild because the tumor takes so long—up to 10–15 years—to produce doctor-seeking symptoms that the brain accommodates to the slow aberration of labyrinthine input.[197] With large acoustic neuromas, expect to see some nystagmus or ipsilateral cerebellar signs, and even papilledema if the tumor is large enough to obstruct the 4th ventricle.

Nystagmus: Cold or warm water injected into the ear canal stimulates movement of fluid within the labyrinth which the brain interprets as head movement (hence the vertigo). The eyes move because the labyrinths no longer stimulate each vestibular nucleus in the medulla equally. Since the vestibular nuclei are connected to the cranial nerves controlling eye movements, the eyes drift to one side and are yanked back to midline by the cerebral hemispheres, which you see as nystagmus.

Quantitative Test: Answers 'how much.' Qualitative tests answer 'yes/no.'

Electronystagmogram: An electrical recording of nystagmus after injection of warm or cool water into the external ear canal.

Trigeminal Nerve: Why the VIIth nerve is so resistant to compression is unclear. Maybe the VIIth nerve is elastic enough to stretch around the tumor, or maybe motor nerves are more resistant to compression than sensory nerves.

Auditory Evoked Response: If you don't have access to an AER, special xray views of the internal auditory canals may demonstrate widening of one internal auditory canal suggesting expansion by tumor.[59] Sophisticated audiometry (hearing test) is another useful screening test.[196] The CSF protein and the CAT scan should both be abnormal by the time the tumor extends from the internal auditory canal into the cerebellopontine angle.[197]

IX AND X: GLOSSOPHARYNGEAL AND VAGUS NERVES

IX and X, the glossopharyngeal and vagus, are like the proverbial Chinese laundry ("in by 9 and out by 10"), because IX is primarily sensory and X primarily motor. The glossopharyngeal nerve controls sensation of the posterior tongue and pharynx. The vagus controls the muscles of the pharynx and upper esophagus. I don't usually check the gag reflex without a history of dysarthria or dysphagia or signs suggestive of posterior fossa pathology. Once my interest is piqued, though, I unravel a safety pin and softly tap the back of the throat on each side*. There is usually no question of hypesthesia.

The motor half of the gag reflex consists of two vagal-innervated muscles: the soft palate and the pharyngeal curtain. The weak half of the soft palate hangs lower than its partner, especially when saying "ahh." When the patient swallows, watch the two vertical muscular curtains (or pillars) jut medially at the back of the throat. If one of them doesn't move, the ipsilateral vagus nerve is weak. A head lamp and a dental mirror allow visualization of the vocal cords, each of which is controlled by the ipsilateral vagus*. The rest of the parasympathetic vagus nerve wanders* into the chest and abdomen to slow the heart and to stimulate gastric acid secretion, pancreatic secretion, and gut peristalsis.



XI: SPINAL ACCESSORY NERVE

The XIth cranial nerve, the spinal accessory, is so named because it has two parts. The spinal part exits the upper cervical spinal cord and tracks back up through the foramen magnum into the posterior fossa where it joins the accessory part of XI exiting the medulla. The spinal accessory then does a U-turn back through the jugular foramen (accompanied by IX and X*) to innervate the ipsilateral sternocleidomastoid* and trapezius* muscles. On its way to the trapezius, the spinal accessory is

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On Each Side: Be sure not to tap too far laterally in the pharynx or you may puncture the carotid artery. (Which is why children should not be allowed to run around with pencils in their mouths. If they fall, the pencil may be driven into the carotid artery.)

Ipsilateral Vagus: The recurrent laryngeal branch of the left vagus nerve reaches the left vocal cord after looping under the aortic arch. Occasionally aortic arch aneurysms or mediastinal tumors interrupt the left recurrent laryngeal nerve along this detour. The right recurrent laryngeal nerve loops under the right subclavian artery.

Wanders: Vagus means to wander.

IX and X: Combined weakness of IX, X, and XI is called the jugular foramen syndrome.[39]

Sternocleidomastoid: Connects the mastoid bone to the sternum (breast bone) and clavicle.

Trapezius: Means four-footed.

joined by other other cervical roots (C3-4) which did not travel up through the foramen magnum.[202] Because of the spinal accessory's circuitous route, sternocleidomastoid and trapezius weakness may be due to lesions above or below the foramen magnum.

The accessory part of XI innervates the same muscles as the vagus, which is one reason it's called accessory (to the vagus).

Assessing sternocleidomastoid strength can be confusing. To test the left sternocleidomastoid you'd like to see it contract, so ask the patient to put his chin on his right shoulder and keep it there. Now, as you try to pull the whole face* back over to the left, watch (and feel) the left sternocleidomastoid. Note that by inserting on the mastoid bone behind the axis of rotation, the left sternocleidomastoid pulls the head to the right. Even more confusing is that a right hemispheric pyramidal tract (corticobulbar) lesion weakens the *right* spinal accessory nerve. So not only do the eyes 'look to the lesion', but so does the entire head*.





Normal
Sternocleidomastoid



Atrophic
Sternocleidomastoid

The trapezius muscle, forming the muscular incline along the side of the neck, helps shrug the shoulders. Trapezius examination, like any muscle examination, is a three-step procedure: look, feel, and test. First, look for asymmetry of the trapezius contours and check for one lower shoulder. Next, feel the bulk of each trapezius. Don't just pinch the skin; pretend the skin isn't there and grab the muscle belly. Next, have the patient shrug his shoulders about halfway and see if you can push one shoulder down.[204] Or better still, have the patient abduct his arms over his head. The weak trapezius should be obvious.[205]

Whole Face: Don't pull just the jaw over; you may dislocate it. Pull the cheek and jaw together.

Entire Head: For a week or so after a hemispheric stroke, the eyes and head tend to look toward the infarcted hemisphere, away from the hemiparesis, even when there is no hemianopia. Whether this ipsilateral sternocleidomastoid weakness—which runs counter to every other upper motor neuron lesion—represents true ipsilateral pyramidal tract innervation of the spinal accessory nerve or a double decussation is still debated.[203]



Trapezius Atrophy

Note Asymmetry of Trapezii One Lower Shoulder



Weakness of Arm Elevation



Trapezius Muscle

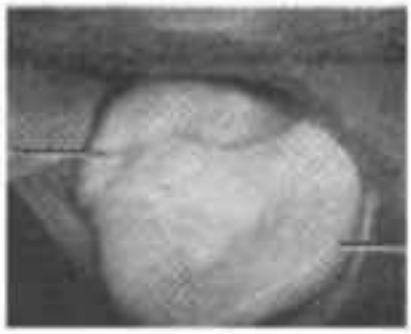
XII: HYPOGLOSSAL NERVE

The XIIth and final cranial nerve, the hypoglossal, supplies the tongue muscle*. Hypoglossal nerve damage causes ipsilateral tongue atrophy manifested by thinning of one side of the tongue and scalloping* of its edge. You may also see fasciculations* of that paralyzed half, but I have been luckier seeing fasciculations when both XIIth nerves are damaged. Many neurologists will only check for tongue fasciculations when the tongue is resting quietly on the floor of the mouth to avoid mistaking fine quivering when the tongue is extended for true fasciculations, which are coarser. Other neurologists are willing to diagnose coarse fasciculations even when the tongue is protruded. In any case, you can be more confident about unilateral fasciculations if the patient also has difficulty sticking his tongue into the ipsilateral cheek. Also, a unilaterally weak tongue should protrude to the suspicious side; the normal side of the tongue overpowers the weak side.



Tongue Deviation to Side of Weakness

Thinned, Scalloped



Atrophic Right Half

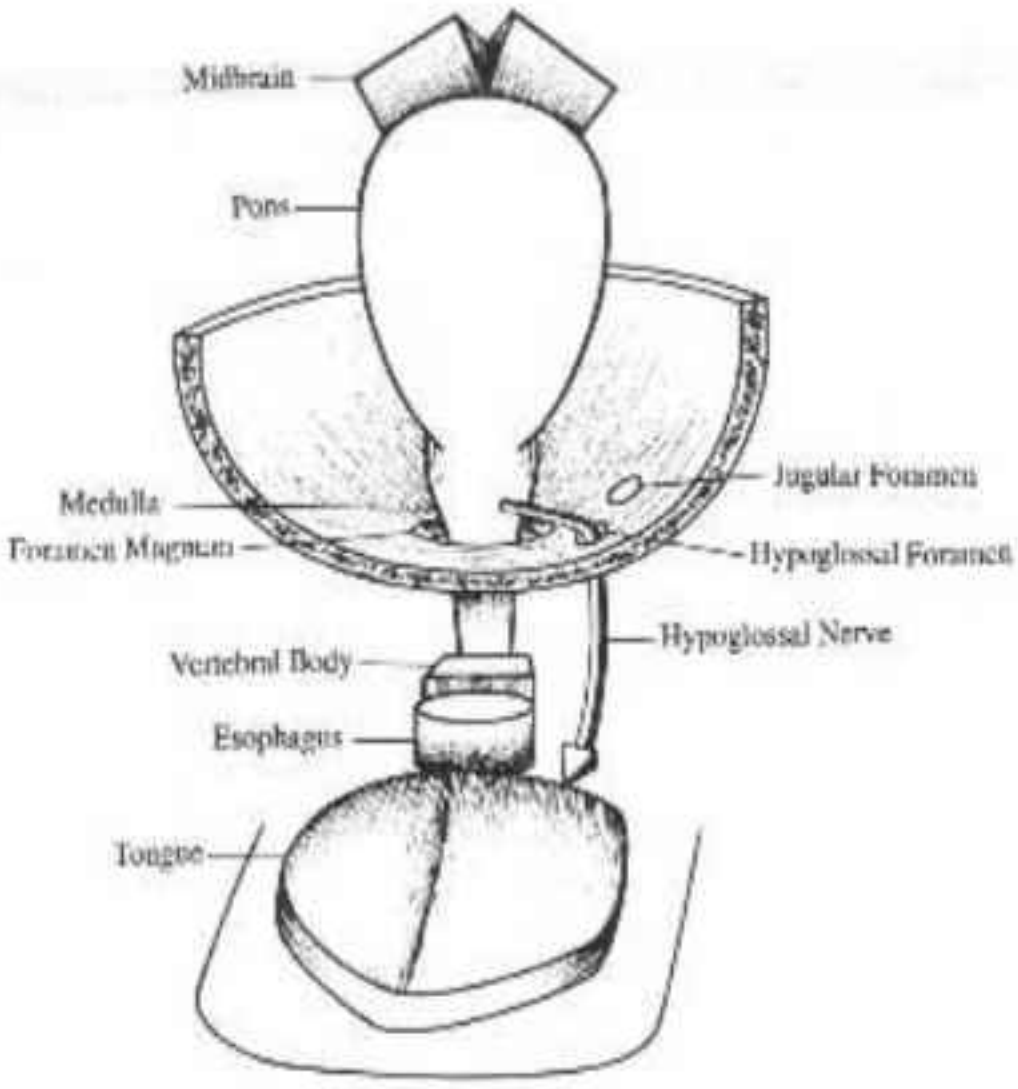
Bilateral weakness of X and XII—whether upper or lower motor neuron—causes severe dysphonia, dysarthria, and dysphagia. The upper and lower motor neuron forms of weakness are known as pseudobulbar and bulbar palsy, respectively (the bulb refers to the medulla). Bulbar palsy does not mean that the lesion is in the medulla, only that it involves the cranial nerves originating from the medulla—either in the medulla proper or along their peripheral pathways.

Distinguishing bulbar from pseudobulbar dysarthria takes some practice. Bulbar palsy sounds thick and deep like a 45rpm record played at 33rpm. Pseudobulbar palsy sounds stiff (spastic) and slow, not as mushy as bulbar dysarthria. Tongue atrophy and fasciculations would naturally point toward bulbar palsy. Because pseudobulbar palsy is usually due to small lacunar infarctions in both internal capsules, pseudobulbar palsy produces three other highly characteristic signs: weakness of the chewing muscles, a hyperactive jaw jerk, and 'emotional incontinence.' Patients laugh or cry at the slightest provocation, often without feeling the corresponding emotion.[207]

Tongue Muscle: When operating on the carotid artery, to remove a clot for example, surgeons must be careful to avoid the hypoglossal nerve to prevent mild postoperative tongue dysarthria.[208]

Scalloping: Synonymous with concave atrophy.

Fasciculations: Fascis means bundle; fasciculus, small bundle. Fasciculations—spontaneous and random twitches—are what small bundles of muscle fibers do when separated from their nerve. See chapter 23.


Midbrain
Pons
Jugular Foramen
Medulla
Foramen Magnum
Hypoglossal Foramen
Hypoglossal Nerve
Vertebral Body
Esophagus
Tongue

BRAINSTEM

DESPITE THE LONG TIME it took for us to get through the cranial nerves, they're really quite clear-cut once you know what you're looking for. Having found an abnormal cranial nerve, you must first decide if the lesion is in the lower motor neuron or in the descending upper motor neuron: is the cranial neuropathy a horizontal or a vertical one, an infranuclear* or a supranuclear one? Most of the time, a single abnormal cranial nerve represents a horizontal (infranuclear) lesion.

Cranial Nerve	How to Distinguish an Intranuclear from a Supranuclear Unilateral Cranial Neuropathy
Olfactory:	No such thing as a unilateral supranuclear loss of smell (i.e., must be in the olfactory nerve itself).
Oculomotor, Trochlear, Abducens:	No such thing as unilateral IIIrd or IVth nerve palsy. Rarely (very rarely) is a VIth nerve palsy ever due to a supranuclear lesion ('Posterior Internuclear Ophthalmoplegia of Lutz').[1] Supranuclear lesions affect both eyes with horizontal or vertical gaze palsies, or skew deviation.
Trigeminal:	Infranuclear lesions cause atrophy of the temporalis and masseter muscles and sensory loss that spares the angle of the jaw. Onion skinning with supranuclear lesions. Bilateral upper motor neuron lesions may make the jaw weak, but with an active jaw jerk and no atrophy. Unilateral pyramidal tract lesions may weaken the contralateral masseter and pterygoid, muscles.[2]
Facial:	Cannot wrinkle the forehead with lower motor neuron lesions. Unilateral upper motor neuron lesions spare the forehead. A paralyzed face that moves when laughing or crying suggests an upper motor neuron lesion. Loss of tearing, hyperacusis, and loss of taste indicate an infranuclear lesion.
Acoustic:	Unless the lesion is adjacent to the cochlear nucleus, unilateral deafness from a supranuclear lesion does not occur.
Glossopharyngeal:	Unilateral hypesthesia usually infranuclear (especially if the hypesthesia is severe).
Vagus:	Unilaterally, never (if there is such a thing in medicine) due to an upper motor lesion.[3] Bilateral vagus nerve palsy (without other cranial nerve sign signs): hard to tell, unless the gag is hyperactive (upper motor neuron).
Spinal Accessory	Lower motor neuron lesions cause atrophy of sternocleidomastoid and trapezius muscles.
Hypoglossal	Lower motor neuron lesions cause atrophy and fasciculations of the tongue.

Infranuclear: Anywhere between the cranial nerve's nucleus in the brainstem and its peripheral point of insertion.

You don't have to wait for the neurologic exam to start localizing lesions. As soon as you lay eyes on the patient, you should be looking for signs to construct an anatomic differential diagnosis. The name of the game is to single out the correct etiologic diagnosis from among a list of potential etiologies. Since each site in the anatomic differential diagnosis has its own etiologic differential diagnosis, unless you narrow the anatomic diagnosis to one or two spots, you'll end up living at the hospital trying to track down and rule out a dishearteningly long list of potential etiologies.

It's not enough to diagnose someone with a ptotic eyelid, inability to look up, down, and in, and a blown pupil as simply having a IIIrd nerve palsy, because you still have to answer: *Where* along the IIIrd nerve is the lesion? The anatomic differential diagnosis of a IIIrd nerve lesion still includes the superior orbital fissure, cavernous sinus, subarachnoid space, and midbrain. Instead of tracking down every etiology for each of these sites, first narrow the anatomic diagnosis by your history and physical so that you can focus on the etiologies for one or two anatomic sites. For example, if you can narrow the lesion to the cavernous sinus, your etiologic differential diagnosis would include, among other things, a pituitary tumor spilling over into the cavernous sinus. Translating that into English, you'd ask if she has noted any diminution of her periods or milk seeping from her breasts (amenorrhea/galactorrhea) to suggest a prolactin-secreting pituitary tumor. You might ask if she has recently become diabetic or noted any weight gain, hypertension, headaches, or impairment of peripheral vision to suggest Cushing's syndrome (chromophobe adenoma). See how much more specific your questions become once you know where the lesion is*?

Having decided from your exam that the patient's cranial neuropathy is due to an infranuclear lesion, remember: you can only conclude that there is something wrong somewhere between the cranial nerve's nucleus in the brainstem and its peripheral point of insertion. It *is* possible for the lesion to be in the brainstem,[4] but to be sure that the lesion is in the brainstem, you have to intersect the cranial nerve with one of the long tracts: the pyramidal tract, the spinothalamic tract, or the posterior column on the *opposite* side of the body.

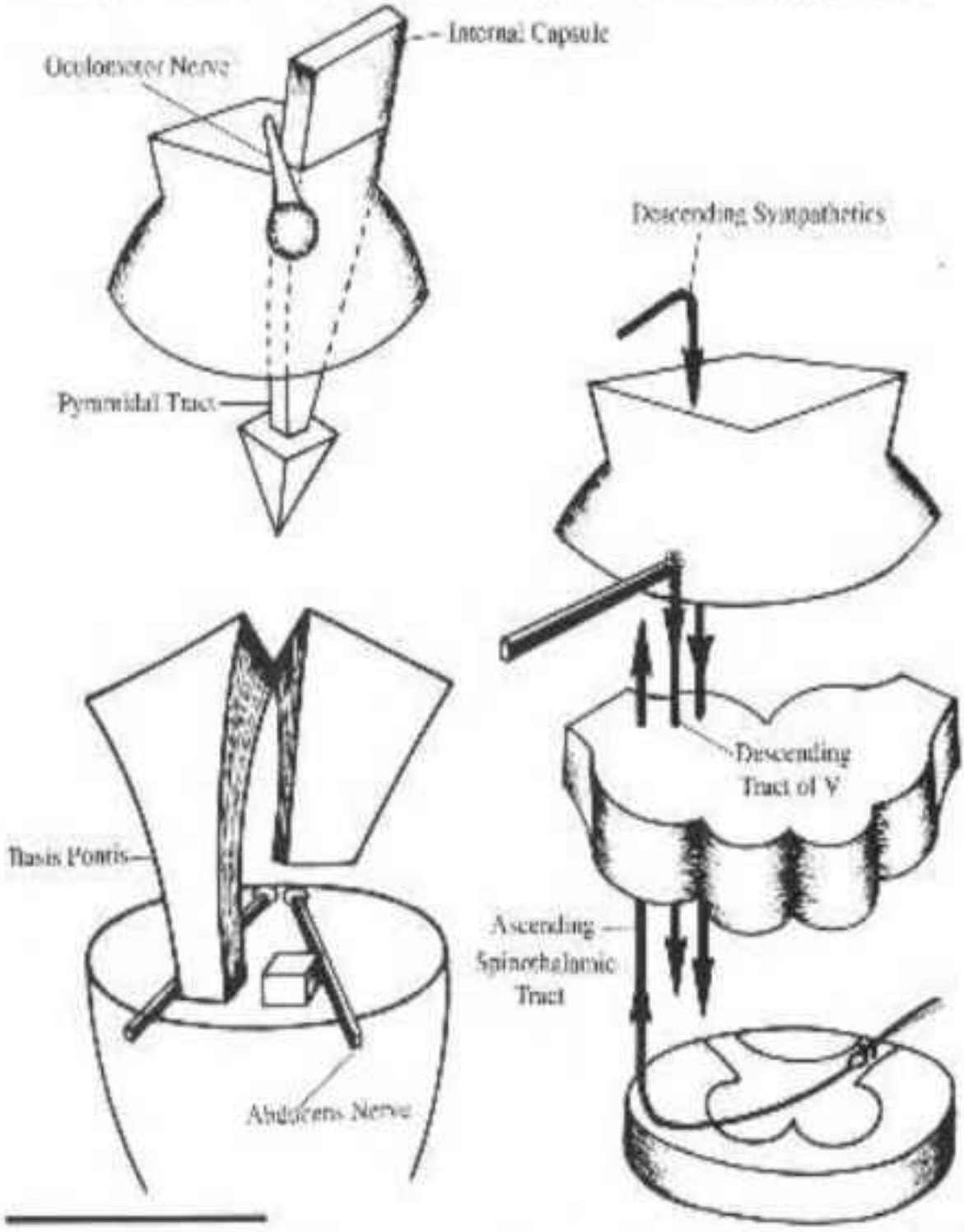
Where the horizontal subsystem (the cranial nerve) and the vertical subsystem (the long tract) intersect—i.e., in the brainstem—is considered the site of dysfunction. We assume that whatever is causing the cranial neuropathy is also causing the contralateral long tract signs, i.e., that the patient does not have two separate lesions. The anatomic explanation for the signs being contralateral is obvious from the fact that the pyramidal tracts and posterior columns do not cross until the lower medulla, the spinothalamics having already crossed immediately on entering the spinal cord.

Intra-axial dysfunction does not necessarily mean that the *lesion* is intra-axial, only that the neurologic disturbance is intra-axial. The combination of a cranial nerve and contralateral long tract only declares that the brainstem is the *presenting* site of dysfunction, not necessarily the primary site. Extra-axial masses may occasionally compress the brainstem enough to give cranial nerve and contralateral long tract signs.

Where the Lesion Is: Admittedly, at times, doctors do successfully localize the lesion in reverse: by considering each etiologic diagnosis for each anatomic site and then asking the necessary questions to rule out each etiology. This is not only a time consuming and expensive way to localize lesions but also a little risky, because you have to rely more on subjective reporting by the patient, and less on objective physical signs.

CROSSED CRANIAL NERVE AND LONG TRACT SIGNS

Three sets of crossed cranial nerve and long tract signs occur commonly—one for the midbrain, one for the pons, and one for the medulla. In the midbrain, the combination is a IIIrd nerve and a contralateral hemiparesis (pyramidal tract); in the pons, a VIth (or a VIth and VIIth*) and a contralateral hemiparesis;[6] and in the medulla, a Vth nerve (pain and temperature), contralateral loss of pain and temperature (spinothalamic tract), and ipsilateral Horner's (sympathetic tract descending through the medulla),[7] a constellation called the Wallenberg or lateral medullary syndrome*.



VIth and VIIth: Sometimes an intra-axial VIth nerve lesion is large enough to intercept the looping VIIth nerve, too, with resulting forehead and facial weakness.[5]

Lateral Medullary Syndrome: A medial medullary infarction does occur, but rarely enough to be reportable. Signs include XIIth nerve palsy (atrophy and weakness of half the tongue) and contralateral hemiparesis.[8]

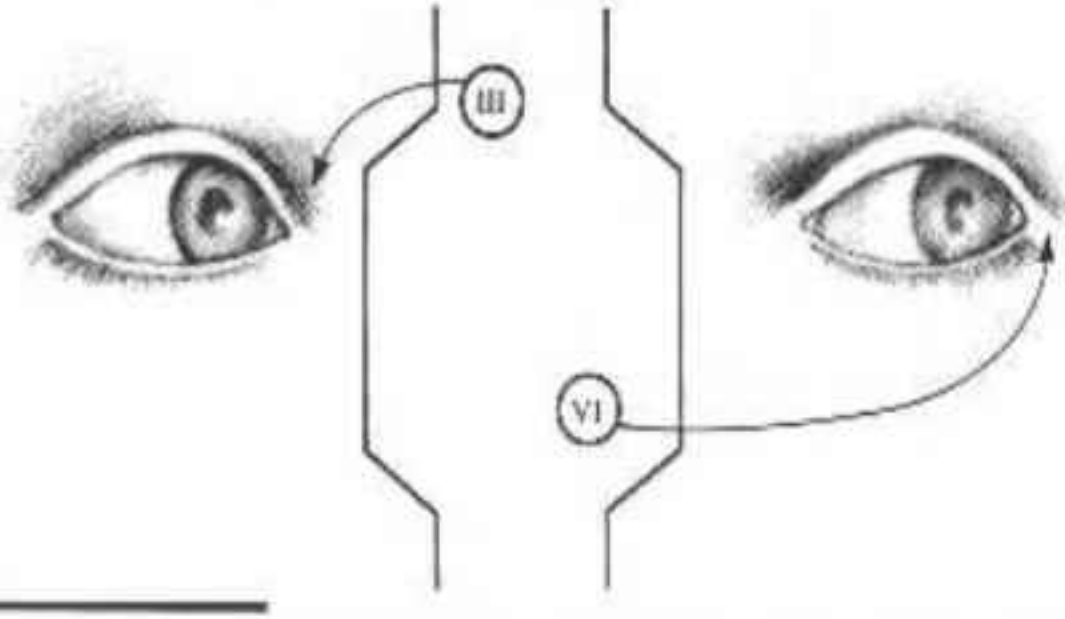
A hemiparesis does not occur in a Wallenberg stroke because the pyramidal tracts are outside the distribution of the posterior inferior cerebellar artery (the 'PICA'), an important branch of the vertebral artery. After supplying the lateral medulla, the PICA continues on to supply the inferior cerebellar peduncle and the ipsilateral cerebellar hemisphere. So occlusion of the PICA not only produces ipsilateral facial numbness, ipsilateral Horner's, and crossed pain and temperature loss, but also ipsilateral limb ataxia. Hiccups and mild dysarthria and dysphagia frequently occur in lateral medullary strokes from ischemia of the neighboring vagus nucleus. Involvement of the nearby vestibular nucleus in the upper medulla commonly causes coarse, rotary nystagmus.

SINGLE BRAINSTEM SIGNS

Besides combining a cranial nerve and contralateral long tract*, you can localize lesions to the brainstem—or at least to the brainstem and its intimate cerebellar connections—with the following single signs: internuclear ophthalmoplegia, skew deviation, upbeat nystagmus, downbeat nystagmus, and probably coarse horizontal nystagmus.

Internuclear Ophthalmoplegia

Understanding internuclear ophthalmoplegia requires some anatomic groundwork. Looking left involves two cranial nerves: the left VIth (for the left lateral rectus muscle) and the right IIIrd (for the right medial rectus muscle). This was a serious evolutionary problem for Mother Nature, because the IIIrd nerve nucleus is high up in the midbrain and the VIth nerve nucleus is down in the lower pons. There had to be a way to yoke the two cranial nerves. Her solution was the pontine (or para-abducens) gaze center* and the medial longitudinal fasciculus.[10]



Cranial Nerve and Contralateral Long Tract: The one exception to this rule of brainstem localization is an XIth nerve palsy and contralateral hemiparesis, a combination that could result from a lower or an upper motor neuron lesion, because the XIth nerve is probably controlled by the *ipsilateral* pyramidal tract.[9] Rarely a clinical issue because medullary lesions causing an ipsilateral XIth nerve palsy and contralateral hemiparesis seldom, if ever, occur.

Pontine Gaze Center: Another, more acceptable but also more cumbersome name for the pontine gaze center is the PPRF: Paramedian zone of the Pontine Reticular Formation.

Here's what happens. When you want to saccade left to look at a target, your right frontal lobe sends the instruction down a still mysterious frontopontine tract* to the pontine gaze center.[13] The pontine gaze center relays the signal to the adjacent VIth nerve nucleus. From the VIth nerve nucleus exit two neurons, one headed to the (ipsilateral) lateral rectus muscle, and the other, called the medial longitudinal fasciculus, up the opposite side of the brainstem to the contralateral IIIrd nerve nucleus*. Since the medial longitudinal fasciculus (MLF) begins and ends in the brainstem, an MLF lesion automatically localizes the lesion to the brainstem.

There are three signs for a *pontine* medial longitudinal fasciculus lesion, or internuclear ophthalmoplegia*. The first is weakness of one medial rectus muscle, because the medial longitudinal fasciculus can't transmit its message up to the IIIrd nerve nucleus to pull the eye medially. To bring out a subtle medial longitudinal fasciculus lesion have the patient glance from side to side as you watch carefully for a slight lag of the adducting eye.[14]

The second sign of a pontine internuclear ophthalmoplegia is nystagmus, often just one or two chugs, in the abducting eye. The reason for the nystagmus is still being speculated about*.

The third criterion for an internuclear ophthalmoplegia is retained ability to converge, demonstrating that the reason for the medial rectus weakness on adduction is not in the oculomotor nerve or medial rectus muscle itself. Convergence bypasses the medial longitudinal fasciculus, being mediated instead by a small midbrain nucleus which extends a short axon directly to each IIIrd nerve nucleus, thus avoiding the medial longitudinal fasciculus altogether.[17] If you can't demonstrate this last finding—retained ability to converge—don't worry; a lot of old people can't converge anyway,[18] or else we explain away the absence of convergence by assuming that the MLF lesion is in the midbrain, injuring the convergence center just before the MLF plugs into the oculomotor nucleus.[19]

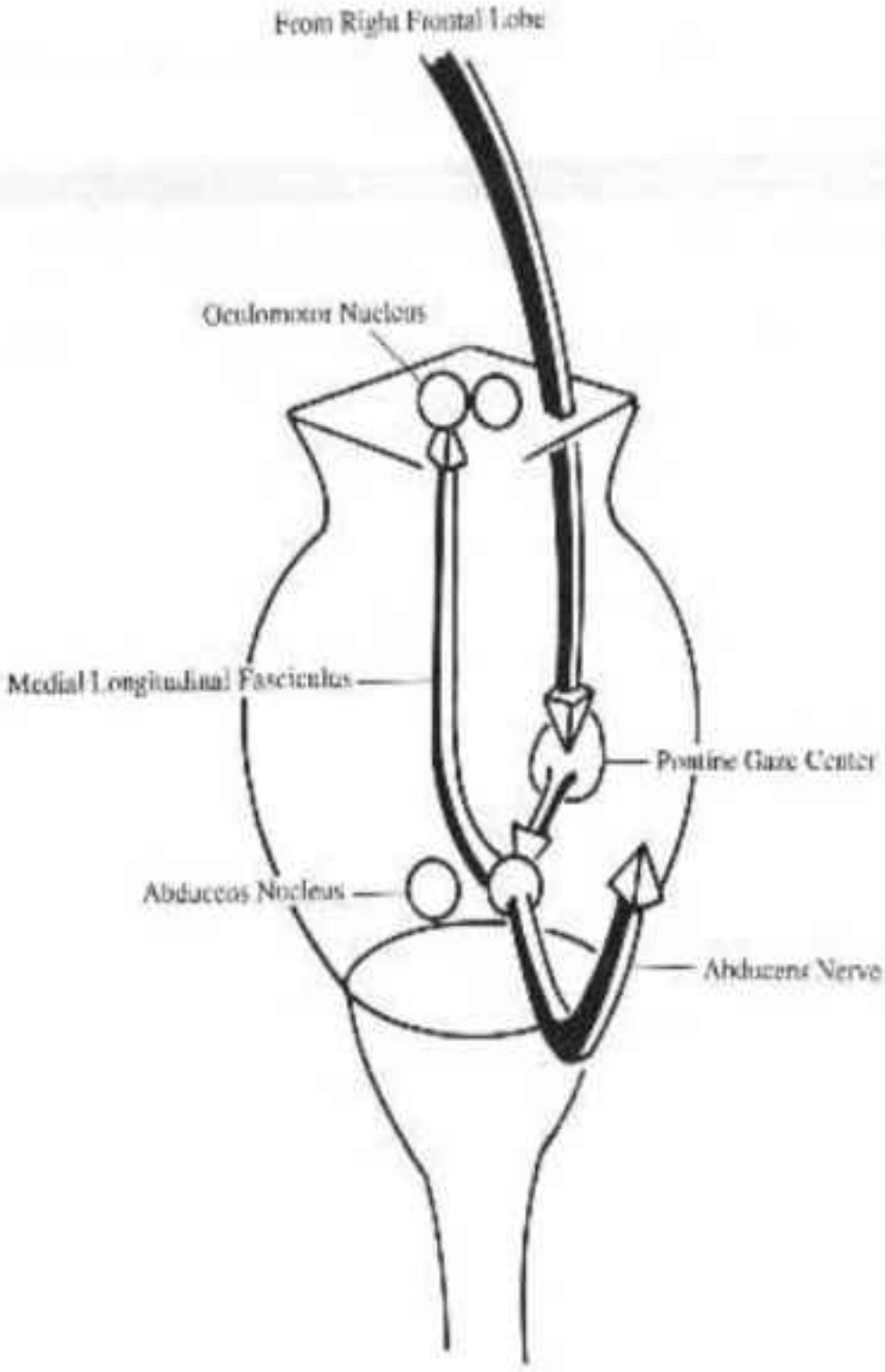
To diagnose an MLF lesion (and thereby a brainstem lesion) in a comatose patient, you obviously cannot rely on the patient to move his own eyes. You, therefore, must do it for him by somehow stimulating the VIth nerve nucleus. This is done by stimulating the inner ear labyrinth with either the 'doll's eyes' maneuver or a stronger stimulus, 'ice water calories.'

Mysterious Frontopontine Tract: The exact pathways for this frontopontine tract are still being mapped through the midbrain and upper pons.[13] Unlike saccades to a target, it's less clear which cortical area initiates saccades to open space ("Look left").[13]

Contralateral IIIrd Nerve Nucleus: Those two neurons leaving the VIth nerve nucleus—one to the lateral rectus and the other to the contralateral IIIrd nerve nucleus—mean that an isolated VIth nerve palsy cannot be due to a lesion in the VIth nerve nucleus. Such a lesion would also damage the exiting medial longitudinal fasciculus and prevent the contralateral IIIrd nerve nucleus from adducting the contralateral eye. When neither eye can cross the midline like this, the patient has a 'gaze palsy.'

Internuclear Ophthalmoplegia: The term 'internuclear' refers to the lesion's location between the IIIrd and VIth nerve nuclei.

Speculated About: One theory (among several[17]) is that the MLF normally inhibits the contralateral medial rectus muscle during lateral gaze. Without MLF inhibition, the abducting eye drifts back toward the midline and then gets jerked back again to its lateral position.[18]



Intact doll's eyes means that the eyeballs move conjugately in their sockets as the head is rotated or snapped from side to side*. (What you actually see is the eyeballs

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From Side to Side: This is the real reason the labyrinths were designed—not for balance, but to keep the eyes locked on target when the head moves, called the vestibulo-ocular reflex.[20] Without functioning labyrinths—a common threat in the days of streptomycin (an early TB medicine)—patients suffer from oscillopsia: the world jiggles when they ride in a car along bumpy roads.[21]

Losing the adjoining saccule and the utricle can be life-threatening to scuba divers. Without these two structures to tell them which way is up, scuba divers must either maintain visual contact with the surface or watch which way their expired bubbles float. Otherwise, they risk swimming downward to their death. Scuba divers with normal labyrinths face the same risk if they get down so deep that buoyancy robs them of their sense of gravity. And of course, diving in murky water compounds the risk because divers can no longer see the surface or their air bubbles.

lagging behind the sudden head rotation.) The same conjugate eye movements are elicited by injecting ice water into one or the other external ear canal after elevating the head of the bed 30 degrees to maximize stimulation of the horizontal labyrinth. By cooling the endolymphatic fluid, ice water sets up convection currents within the semicircular canals. These convection currents depress the signals leaving the labyrinth*.[22] As a result, the eyes drift toward the depressed labyrinth. Here's why:

Normally, each set of labyrinths *continually* sends signals via the acoustic nerve to the vestibular nucleus. As it turns out, each vestibular nucleus is hooked up to the *contralateral* VIth nerve nucleus. In other words, each set of labyrinths is continually 'pushing' the eyes away from it. So, when cold water inhibits the labyrinths on one side, the eyes drift toward the cold water, where they remain until the cold water wears off*.



In an unconscious patient with, for example, a right internuclear ophthalmoplegia, the right eye won't adduct across midline with doll's eyes or cold calorics. If *neither* eye deviated past midline—a gaze palsy—the lesion would then be in the ipsilateral VIth nerve nucleus (assuming the labyrinth and acoustic nerve were working).

Leaving the Labyrinth: Warm water would have *increased* the signals by making the endolymphatic fluid flow in the opposite direction.

Wears Off: Cold calorics in a *conscious* patient elicit nystagmus as the cerebral cortex jerks the deviated eyes back to midline.[23] The mnemonic 'COWS' (Cold Opposite, Warm Same) refers in a *conscious* patient to the direction of the eye jerk—the eyes gravitate toward the ice water and jerk away from it, and conversely, gravitate away from warm water, but jerk toward it. When cold calorics are used to assess *comatose* patients, forget the term COWS because you'll confuse 'cold-opposite' to mean the eyes should drift away from the ice water, which is wrong—the eyes move *toward* the ice water. (If you want a mnemonic, use 'cold contracts, pulling the eyes toward it.')

Vertical Nystagmus

Upbeat and downbeat nystagmus point to brainstem—or combined brainstem and cerebellar—dysfunction (occasionally to cerebellar dysfunction alone).[24] Downbeat nystagmus, especially in the primary position, is typical of lesions affecting the medulla (and cerebellar flocculus and nodulus), such as Arnold Chiari. Occasionally lesions elsewhere in the brainstem, interrupting connections to and from the vestibular nucleus, produce downbeat nystagmus, too.[25] Upbeat nystagmus is less localizable than downbeat nystagmus, but may represent disrupted brainstem connections to the cerebellar vermis and flocculus*.[27]

Ocular bobbing[28] and ocular dipping[29] are two coarse variants of vertical nystagmus. In ocular bobbing, the eyes bob down and drift up; in ocular dipping, the eyes drift down and jerk up. Ocular bobbing usually signifies structural brainstem pathology, but potentially reversible etiologies, like liver failure, have also been reported.[30] Not enough autopsies have been performed on patients with ocular dipping to be sure of the exact pathophysiology.

Skew Deviation

Skew deviation means one eye is up and the other is down in all directions of gaze (unlike a IVth nerve palsy*). The (supranuclear) lesion for skew deviation is usually pontine, but midbrain and medullary lesions have also been reported.[32] Pontine lesions causing skew deviation frequently interrupt the upper pontine reticular activating system driving the patient into coma. Which means you have to look carefully for skew deviation in stuporous or comatose patients; your patient often won't be awake enough to complain about it. Look at the patient's eyeballs from the side. Is one eye looking lower, i.e., skew? If so, concentrate on the other signs you'd expect from pontine lesions, like a gaze palsy, abducens palsy, internuclear ophthalmoplegia, absent corneal reflex, absent jaw closure, ataxia*, and hemiparesis.

Cerebellar Vermis and Flocculus: Don't forget that vertical nystagmus only means brainstem or cerebellar-brainstem dysfunction. The cause of that dysfunction doesn't have to be a *structural* brainstem lesion. Drugs, for example, are a frequent cause of upbeat nystagmus (especially upbeat nystagmus that occurs only when the patient looks up) and downbeat nystagmus, too.[26]

IVth Nerve Palsy: A IVth nerve lesion also skews the eyes, but the skew is correctable by tilting the head, something that can't be done with true skew deviation.

Occasionally, dysfunction of one eye muscle (from a retro-ocular mass, myasthenia gravis, thyroid eye disease, etc.) may mimic a skew, but proptosis of the eye, the conscious state, and the absence of pontine, cerebellar, or long tract signs should direct your initial investigation to local orbital diseases.

Skew deviation has rarely been reported from vestibular lesions.[31]

Ataxia: Ataxia may come from two different sources: from destruction of the cerebellum or destruction of the cerebellar afferents passing through the pons. (Obviously, ataxia is only demonstrable in awake or mildly stuporous patients.)



Coarse Horizontal Nystagmus

Truly accurate localization of horizontal nystagmus requires sophisticated eye movement monitoring to carefully examine the velocity and acceleration of the slow and jerk phases. At the bedside, a reasonably helpful rule is that coarse horizontal nystagmus is central—from either the brainstem or brainstem/cerebellum. (Fine horizontal nystagus may also be central, as mentioned in chapter 20.)

TWO MORE CROSSED CRANIAL NERVE AND LONG TRACT COMBINATIONS

Though I mentioned there are three important crossed cranial nerve and long tract syndromes of the brainstem, there are really five, but I needed to explain the pontine gaze center and medial longitudinal fasciculus before explaining the other two. If a patient cannot look left with *either* eye, a condition called a gaze palsy to the left or a gaze preference to the right, the lesion is generally in one of two locations: either in the right hemisphere (usually the frontal lobe) or the left side of the brainstem—in the left pontine gaze center or left VIth nerve nucleus*.[35] If the patient also has a left hemiparesis, then the lesion is in the right hemisphere ("the patient looks at the lesion"); a right hemiparesis places the lesion on the left side of the pons*. This would be a fifth type of crossed brainstem combination.

The last combination is the 'one and a half' syndrome in which a patient with a gaze palsy also has an internuclear ophthalmoplegia when looking away from the gaze palsy. The anatomic explanation is a lesion in the pontine gaze center (or abducens nucleus) large enough to intercept the medial longitudinal fasciculus crossing from the opposite side.[35]

VIth Nerve Nucleus: If doll's eyes or cold calories can bring the eyes across midline, then the lesion must be in the pontine gaze center, not in the VIth nerve nucleus. Doll's eyes and cold calories move the eyes by stimulating the VIth nerve nucleus directly; lesions of the pontine gaze center do not prevent vestibular instructions from reaching the contralateral VIth nerve nucleus (more about this later).

Left Side of the Pons: Occasionally (rare enough to be reportable), patients who hemorrhage into one hemisphere will, for uncertain reasons, look away from the lesion.[36]





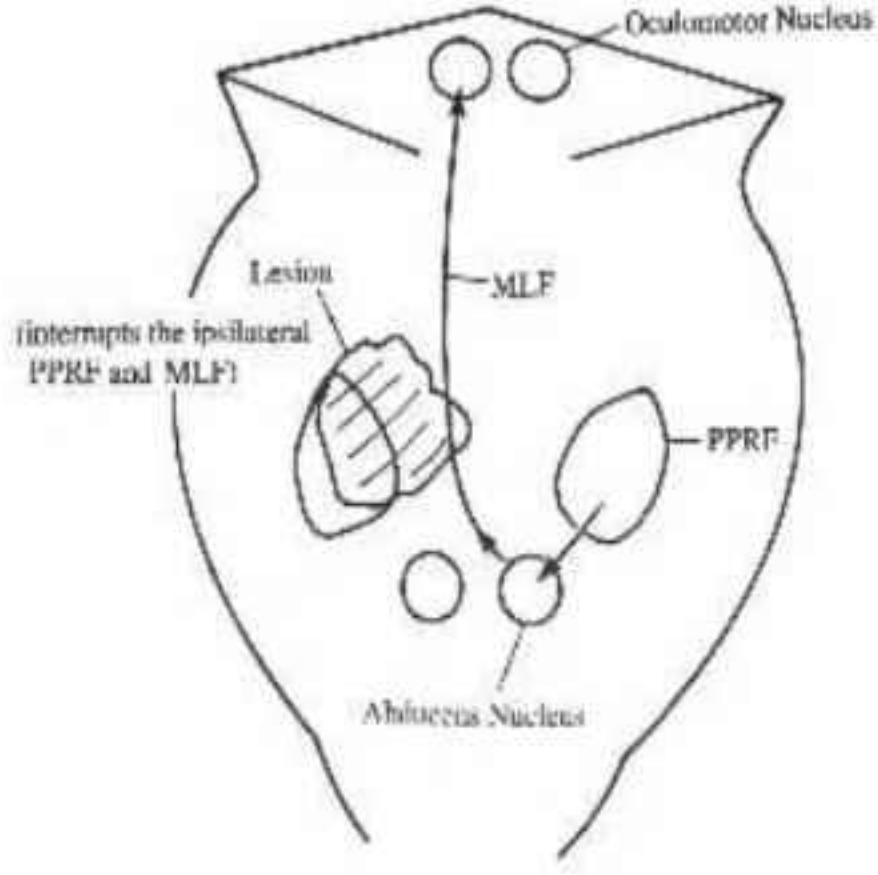




Right Gaze Paresis



Right Internuclear Ophthalmoplegia



PARINAUD'S SYNDROME

We've discussed two types of brainstem syndromes—ones involving the IIIrd nerve, VIth nerve, VIIIth nerve, Vth nerve, and pontine gaze center, all of which depend on a vertical tract for brainstem localization, and others, like internuclear ophthalmoplegia, vertical nystagmus, and skew deviation, which don't. The brainstem can be implicated in still another way by using two horizontal signs which intersect in the dorsal midbrain directly beneath the pineal gland and 3rd ventricle. This dorsal midbrain syndrome, called Parinaud's syndrome, consists of inability to look up and generous sized pupils unreactive to light but reactive to accommodation. Such a curious combination of signs is readily predictable from the proximity of the midbrain upgaze center* to the slip of optic tract fibers transmitting light intensity to the midbrain pretectum. Inability to look up alone is strongly suggestive of midbrain dysfunction†, but the combination of upgaze palsy and unreactive pupils demands dorsal midbrain localization where the two pathways converge. The preservation of pupillary constriction during accommodation (light-near dissociation) is due to the more ventral, protected location of accommodation fibers bound for the oculomotor nucleus from the occipital lobes.[37]

On vigorously attempted upgaze in Parinaud's syndrome, the upgaze center fires so hard at the superior rectus subdivision of the oculomotor nucleus that impulses 'overflow' into other regions of the oculomotor nucleus, regions controlling the other extrinsic eye muscles. When all these other muscles contract, the eyes are sucked back into their sockets which you see as rhythmic retraction of the eyeballs, called nystagmus retractorius.[38] The easiest way to elicit this is to ask the patient to follow a downward moving optokinetic tape. As you watch from the side, you'll notice that the eyes retract with each upward saccade to the next target.

The convergence center lying next to the upgaze center is also commonly affected in Parinaud's syndrome. Even though the combination of upgaze paresis, generous sized pupils, and light-near dissociation points immediately to the dorsal midbrain, gild the lily anyway by looking for nystagmus retractorius and inability to converge‡.

Midbrain Upgaze Center: The main midbrain center controlling vertical saccades (both upward and downward) is the rostral interstitial nucleus of the medial longitudinal fasciculus.[39]

Strongly Suggestive of Midbrain Dysfunction: Sometimes the eyes won't move up or down because of lesions above the midbrain in the supranuclear tracts descending from the cerebral hemispheres. Two good examples are Progressive Supranuclear Palsy and oculogyric crisis from phenothiazines.

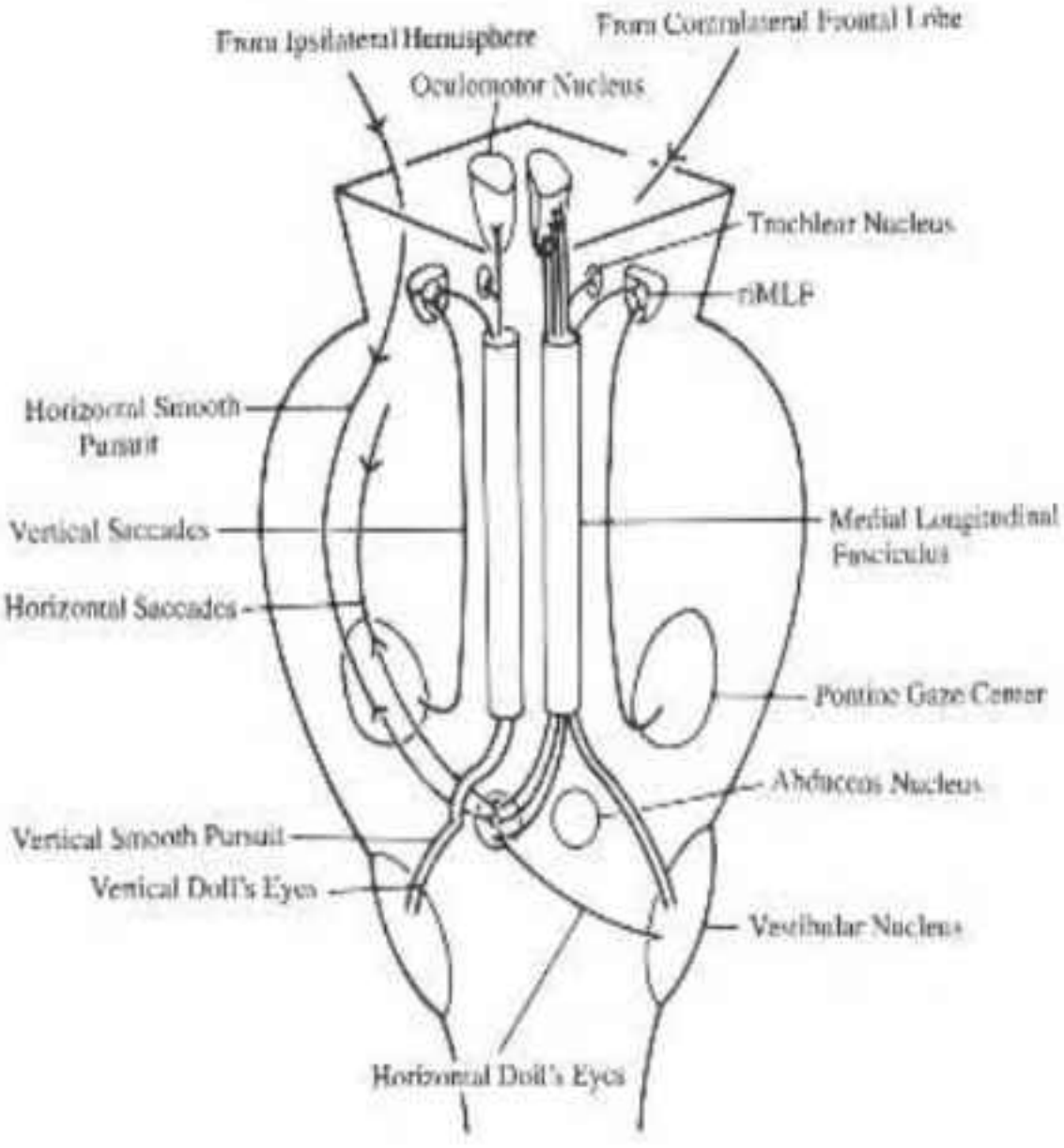
Inability to Converge: The control of conjugate eye movements is surprisingly complex, in part, because the eyes move conjugately for three purposes: to glance (saccade) at something, to pursue a moving target (smooth pursuit), and to keep the eyes focused on a target while the head is moving (vestibulo-ocular reflex). Each type of eye movement uses a different pathway to reach the oculomotor, trochlear, and abducens nuclei in the brainstem. To complicate matters, each type of eye movement may use one pathway for horizontal eye movements and a slightly different pathway for vertical eye movements.

All eye movements are generated by cranial nerve nuclei in the brainstem: the oculomotor and abducens for horizontal gaze, and the oculomotor and trochlear for vertical gaze. The supranuclear control of these brainstem nuclei begins in the cortex or in the inner ear labyrinths and descends (or ascends in the case of the labyrinths) to specialized 'middle management' nuclear centers in the

brainstem before finally reaching the IIIrd, IVth, and VIth nerve nuclei. The middle management nuclei are the Paramedian Pontine Reticular Formation (PPRF) for horizontal saccades and horizontal pursuit, the Rostral Interstitial Nucleus of the Medial Longitudinal Fasciculus (riMLF) for vertical saccades and vertical pursuit, and the vestibular nucleus for horizontal and vertical doll's eyes (vestibulo-ocular reflex).

Saccades: The best worked-out pathways are for horizontal and vertical saccades. As mentioned, saccades to a target begin in the frontal eye fields. From the frontal eye fields, saccadic instructions descend through several different pathways to the contralateral PPRF.[39] The PPRF is itself divided into a rostral and caudal division, based on the fact that rostral PPRF lesions impair horizontal saccades, while caudal PPRF lesions impair both horizontal and vertical saccades.[40] One interpretation might be that rostral PPRF fibers controlling horizontal saccades exit the PPRF *through* the caudal PPRF, and that the caudal PPRF controls vertical saccades.

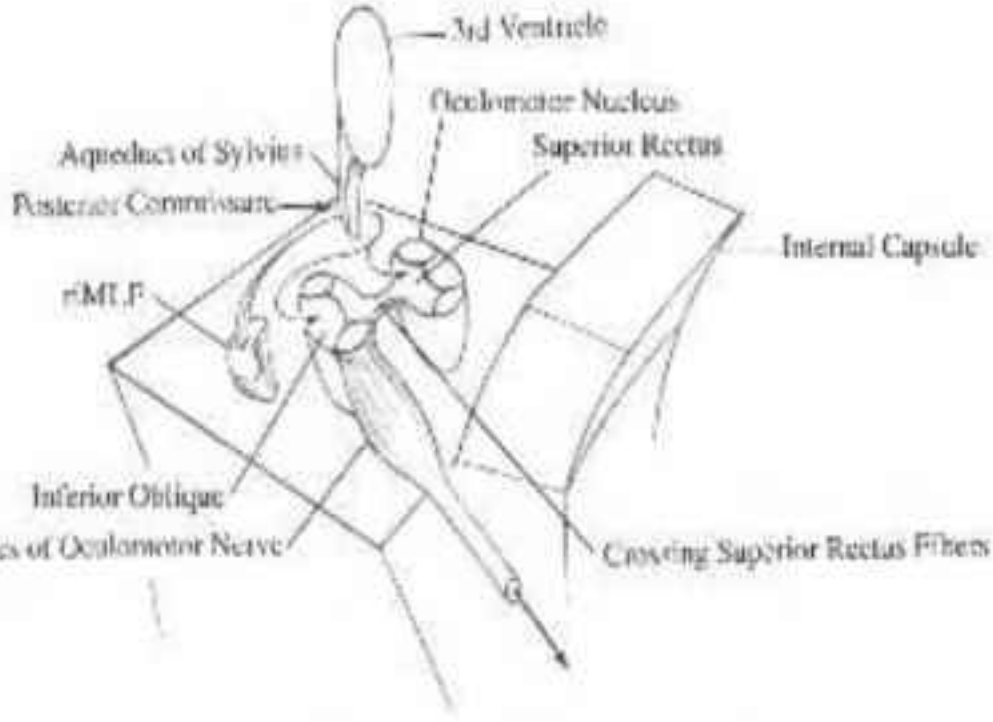
The rostral PPRF sends its horizontal saccadic instructions to the ipsilateral VIth nerve nucleus which then relays the instructions in two directions: out the ipsilateral abducens nerve to the lateral rectus muscle, and up the contralateral medial longitudinal fasciculus to the contralateral oculomotor nucleus (medial rectus muscle).



Vertical saccades differ from horizontal saccades in three important ways: first, vertical saccades exit the caudal PPRF and ascend ipsilaterally to the midbrain in a tract separate from the medial longitudinal fasciculus. In other words, lesions of the medial longitudinal fasciculus do not affect vertical saccades.[41] Second, unlike horizontal saccades, vertical saccades completely bypass the adjacent VIth nerve nucleus, which is understandable since the abducens nerve doesn't participate in vertical eye movements.[42] Third, vertical saccades ascend from both PPRF's up both sides of the brainstem. A unilateral brainstem lesion will not affect vertical saccades.

Vertical saccades ascend to the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF) and perhaps also to the interstitial nucleus of Cajal.[43] Both of these nuclei are adjacent to the oculomotor nucleus in the midbrain. Each riMLF controls upgaze for the ipsilateral eye by stimulating the superior rectus and inferior oblique muscles in a rather roundabout way. Paradoxically, each riMLF does not initiate upgaze in the ipsilateral eye by simply stimulating the ipsilateral IIIrd nerve nucleus, because each oculomotor nucleus does not, as you'd expect, innervate the ipsilateral eye. It turns out that each superior rectus subnucleus controls the *contralateral* superior rectus muscle by sending its nerve fibers through the contralateral superior rectus subnucleus into the contralateral IIIrd nerve.

In order for both eyes to look up at the same time, both riMLF's fire, each riMLF stimulating the ipsilateral eye (superior rectus and inferior oblique muscles) via the following pathway. Each riMLF sends a small fiber bundle through the posterior commissure (behind the aqueduct of Sylvius) to the contralateral side of the midbrain where the fiber bundle bifurcates, one part innervating the adjacent superior rectus subnucleus (contralateral to the riMLF), and the other part recrossing in front of the aqueduct of Sylvius to innervate the inferior oblique subnucleus (ipsilateral to the riMLF). Since the superior rectus subnucleus innervates the contralateral eye, each riMLF stimulates upgaze in the ipsilateral eye.[44]



The posterior commissure (behind the aqueduct of Sylvius) is where dorsal midbrain lesions cause upgaze palsy as part of Parinaud's syndrome.

Fibers for downgaze saccades are thought to leave the riMLF, synapse immediately onto the ipsilateral inferior rectus subnucleus, and then decussate to the contralateral trochlear nucleus via a pathway caudal to the posterior commissure.[45] This anatomic separation of the commissures for upward and downward saccades enables lesions in the posterior commissure to impair upward saccades without impairing downward saccades.

Slow Eye Movements: Horizontal and vertical slow eye movements are generated during pursuit of a moving object (like a small optokinetic tape) and during doll's eyes maneuver (the vestibulo-ocular reflex).

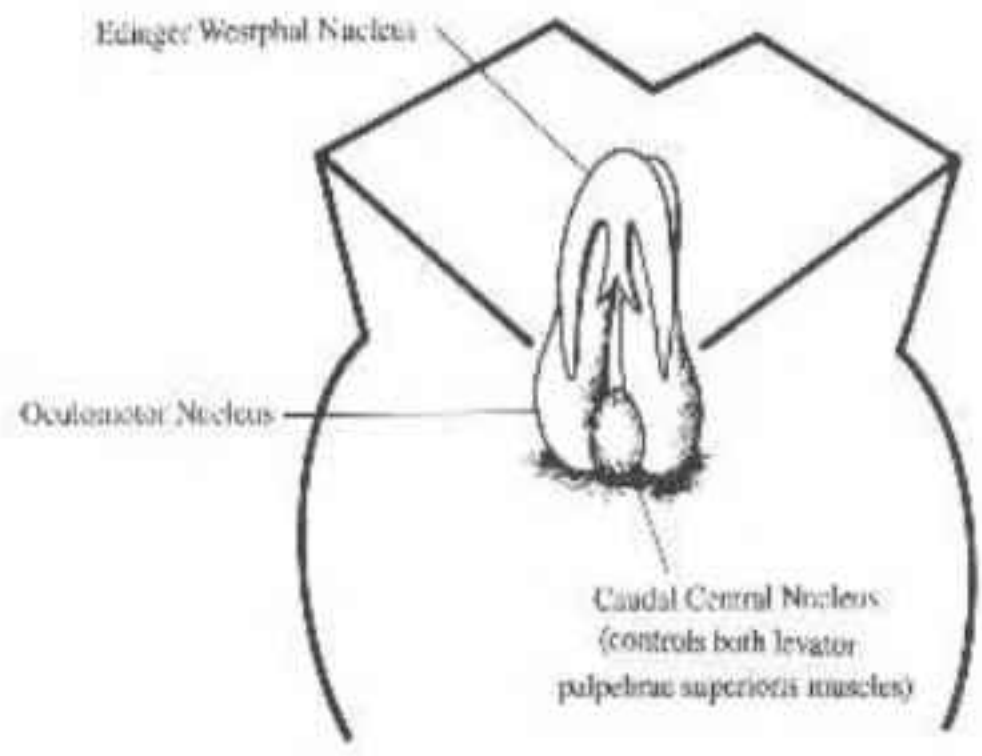
All horizontal signals—saccades, pursuit, and vestibulo-ocular—touch synapse in the VIth nerve nucleus in the lower pons. Horizontal smooth pursuit signals reach the VIth nerve nucleus only after descending from the parieto-occipital cortex through uncertain pathways to an ipsilateral brainstem center for horizontal pursuit (perhaps the PPRF[46]). Horizontal vestibulo-ocular movements begin in the vestibular nucleus and immediately cross to the contralateral VIth nerve nucleus, bypassing the contralateral PPRF.[47]

Because some patients with MLF lesions have no disturbance of adduction during pursuit or doll's eyes,[48] it's thought that the cerebellum also plays a role in horizontal (and vertical) smooth pursuit.

Vertical slow eye movements are also generated during pursuit and doll's eyes maneuver. Like vertical saccades, vertical pursuit is generated by riMLF. But unlike vertical saccades, vertical slow eye movements ascend *in* the MLF (and probably in the superior cerebellar peduncle too) to reach the riMLF.[49] What's less clear is how vertical pursuit signals from the cortex get to the brainstem and where they synapse in the brainstem before entering the MLF.

Vertical doll's eyes signals begin in the vestibular nuclei and ascend in the ipsilateral MLF (and superior cerebellar peduncle), but unlike either vertical saccades or vertical pursuit, vertical vestibulo-ocular signals synapse directly onto the trochlear and oculomotor nuclei without first synapsing in the riMLF.[50]

Oculomotor Nerve Complex: Of the five extrinsic eye muscles innervated by the oculomotor nerve, only two have clinically important representations within the oculomotor nucleus: levator palpebrae superioris and the superior rectus. Both levator palpebrae superioris muscles are controlled by a *single* midline subnucleus, the caudal central nucleus, lying at the caudal end of the oculomotor nucleus. A small lesion along the dorso-caudal oculomotor nucleus may, therefore, cause bilateral ptosis.[51] Conversely, unilateral ptosis cannot be due to a nuclear IIIrd nerve lesion. Unilateral ptosis can only occur after the oculomotor fibers have left the nucleus: as the fascicles of the oculomotor nerve traverse the midbrain or after the oculomotor nerve has exited the midbrain.



The superior rectus submucleus lies medially in the IIIrd nerve nucleus, making it easy for superior rectus fibers to decussate through the contralateral superior rectus submucleus and enter the contralateral oculomotor nerve.[52] The result of this unusual wiring is that a 'nuclear IIIrd' not only paralyses the ipsilateral eye, but also upgaze in the contralateral eye.[53] Likewise, bilateral upgaze palsy due to a lesion in the posterior commissure (i.e., Parinaud's syndrome) can be mimicked by a lesion in one superior rectus submucleus, a condition called pseudo-Parinaud's.[54]

Strictly speaking, a nuclear IIIrd should only paralyze upgaze in the contralateral eye when that contralateral eye is abducted, because the inferior oblique muscle elevates the eye when the eye is adducted. Hoyt, however, says that upgaze can been abolished with superior rectus weakness alone, because the inferior oblique is only a minor contributor to upgaze.[55] When both elevators of one eye are paralyzed (superior rectus and inferior oblique), however, the patient has 'double elevator palsy.'

Parasympathetics: Light intensity is interpreted by the Edinger Westphal nucleus, a single, midline submucleus of the oculomotor nucleus. Light signals in each optic tract reach the Edinger Westphal nucleus via small branches which enter the brachium conjunctiva (superior cerebellar peduncles) to synapse ipsilaterally into two important pretectal nuclei: the subcentiform nucleus and the olivary nucleus. The olivary nucleus projects to the contralateral side of the Edinger Westphal complex; the subcentiform nucleus projects to both sides of the Edinger Westphal complex.[55]

Lesions of the pretectal nuclei produce the second important feature of Parinaud's syndrome: generous sized pupils fixed to light.

The Edinger Westphal complex consists of three major columns (one central and two lateral) along the dorsum of the oculomotor nucleus. Parasympathetic fibers exiting each side of the Edinger Westphal nucleus join the multiple fascicles of the intra-axial oculomotor nerve. Small midbrain lesions damaging the oculomotor fascicles may sometimes spare the parasympathetic fascicles, causing a pupil-sparing oculomotor nerve palsy.[57] All these fascicles converge at the cerebral peduncle to form the oculomotor nerve. At this point, where the oculomotor nerve exits the brainstem, parasympathetics fibers lie dorsomedial in the oculomotor nerve.

Extra-Axial Oculomotor Nerve: The oculomotor nerve coorses under the posterior communicating artery before entering the cavernous sinus. The oculomotor nerve then travels within the dural leaves of the lateral wall of the cavernous sinus, above the trochlear nerve, above the maxillary and frontal divisions of the trigeminal nerve, and lateral to the abducens nerve. In the proximal cavernous sinus, the oculomotor fibers occupy the interior of the oculomotor nerve, and the parasympathetics occupy the perimeter. This anatomic arrangement makes infarctions (which damage the interior of the nerve) more likely to produce pupil-sparing opthalmoplegia, and compressive lesions more likely to produce opthalmoplegia with a dilated, fixed pupil.

At or before the superior orbital fissure, the oculomotor nerve divides into a superior and inferior branch, the superior branch going to the superior rectus and the levator palpebrae superiorus muscles, the inferior branch innervating the remainder: the ciliary muscle, the iris sphincter, and the medial rectus, inferior rectus, and inferior oblique muscles.[58] Because pupillary fibers lie inferiorly in the distal cavernous sinus, masses in the distal cavernous sinus may produce pupil-sparing opthalmoplegia, mimicking infarctions of the oculomotor nerve.[59]

Another important reason cavernous sinus lesions spare the pupil is that sympathetics also travel through the cavernous sinus: from the intracavernous carotid artery, briefly onto the abducens nerve, and then onto V^1 to enter the orbit. The small pupil in a IIIrd nerve palsy may actually be a superimposed Horner's syndrome.[60]

Localizing Oculomotor Nerve Lesions

Midbrain Syndromes:
- Supranuclear:
  - Internuclear ophthalmoplegia (MLF).
  - Parinaud's syndrome (posterior commissure): Upgaze palsy with intact Doll's, generous sized fixed pupils, convergence insufficiency, nystagmus retractorius, Collier's sign.
  - Double elevator palsy with retained Doll's eyes (riMLF outflow, not the riMLF itself because downward pursuit and saccades are still intact).
- Nuclear:
  - Unilateral IIIrd nerve palsy and contralateral superior rectus palsy (any ptosis or unreactive pupil must be bilateral).
  - Pseudo-Parinaud's syndrome (superior rectus subnucleus).
  - Bilateral ptosis (not seen with supranuclear lesions).
- Fascicular:
  - Unilateral complete or pupil-sparing ophthalmoplegia (fascicular IIIrd).
  - Complete IIIrd and contralateral hemiparesis (cerebral peduncle).
  - Complete IIIrd and contralateral hemiataxia (superior cerebellar peduncle).
  - Complete IIIrd and contralateral hemichorea (red nucleus).

Extra Axial but Proximal to the Cavernous Sinus:
- Complete (internal and external) ophthalmoplegia (vulnerable parasympathetics).
- Mandibular (V^3) involvement: sensation along the jaw (but not the angle of the jaw) with weakness and atrophy of the chewing muscles.
- Pupil-sparing ophthalmo*plegia* has almost never been reported with aneurysms, but pupil-sparing ophthalmo*paresis* has.[91]

Cavernous Sinus Syndromes:
- Cannot involve the mandibular division of the trigeminal.
- May get pupil-sparing even with compressive lesions, especially if the lesion is in the anterior cavernous sinus or the oculomotor nerve palsy is incomplete.
- Primary misdirection of the IIIrd nerve (i.e., no history of prior trauma).[52]

Superior Orbital Fissure Syndrome:
- III, IV, VI, and V^1.

Orbital Apex Syndrome:
- Superior Orbital Fissure Syndrome plus Optic Neuropathy.

Muscle or Neuromuscular Junction:
- Bilateral ptosis.
- External ophthalmoplegia (III).
- Pseudo-internuclear ophthalmoplegia.[92]
- Total bilateral internal and external ophthalmoplegia (III, IV, and VI).

RETICULAR ACTIVATING SYSTEM

WE'VE ALREADY DISTINGUISHED being awake from being alert—conscious versus attentive. The cortex and thalamus are necessary for attentiveness; what awakens you? It took a surprisingly long time before Magoun and Moruzzi answered this simple question (1949 to be exact[1]) by magically arousing cats from a deep sleep with electrodes implanted in their midbrain. The cats awakened to the electrical stimulation of their reticular activating system, a thick network of cells densely scattered in the upper pons and midbrain amidst the IIIrd nerve nuclei and two medial longitudinal fasciculi.

COMA

By allowing us to awaken, the reticular activating system in the midbrain and upper pons is the single most important square inch of the nervous system. Every effort, therefore, must be made to protect the reticular activating system, even though the threat to it is usually concealed by the coma itself. Without the patient's conscious cooperation, you are forced to make judgments about the etiology of his coma without a full complement of signs, signs which you relied upon for confident diagnosis in awake patients.

That's only part of the problem. The real problem is that the reticular activating system can be assaulted from three separate directions: from above by supratentorial lesions; from behind by cerebellar and 4th ventricular lesions; and from in front by mass lesions (tumors and aneurysms) or by basilar artery thrombosis.

What makes the assessment of coma easy is that each type of insult to the reticular activating system has its own characteristic pattern of signs. What makes it difficult is that the patterns aren't always clinically obvious unless specifically looked for. Moreover, some signs in comatose patients do not have the same significance as they do in conscious patients. For example, upgoing toes in a comatose patient do not always imply a structural lesion. Upgoing toes—which simply mean that the pyramidal tracts aren't working properly—may result from seizures or blood-borne insults like drug overdose, sepsis, and internal organ failure.

Another problem with examining comatose patients is that the familiar spastic catch may not always be there to indicate a pyramidal tract lesion. The tone may be normal or flaccid as long as the lesion—and the advancing pressure head in front of the lesion—remain above the level of globus pallidus. But once the advancing front of high pressure reaches about the level of globus pallidus, the tone begins increasing rapidly, reaching a peak called decerebrate rigidity as the lesion or its pressure front extend downward into the midbrain and pons. But—here comes the confusion—as

soon as the lesion (or its pressure front) reaches the level of the vestibular nucleus at the ponto-medullary junction, the tone suddenly becomes *flaccid**.

Another confusing bit of neurophysiology stems from the general rule that consciousness is controlled by the reticular activating system in the upper brainstem and attention by the cortex and thalamus. Chronic hihemispheric lesions allow consciousness, but not awareness: the patient may open his eyes, look about, and withdraw from pain, but he won't make any meaningful contact with his environment. However, *acute* bihemispheric lesions (and occasionally even acute unihemispheric ones) can also send someone into temporary coma. How this can happen is unclear, but presumably acute hemispheric lesions suddenly 'deafferent' the reticular activating system. That is, after the reticular activating system normally awakens the cortex, the cortex returns the favor by stimulating the reticular activating system to *maintain* consciousness. Acute bihemispheric lesions precipitate frank coma apparently by acutely depriving the reticular activating system of ongoing cortical stimulation.

Fortunately, the eyes are a big help in sorting out coma due to brainstem compression. Supratentorial brainstem compression does not affect eye movements until late (when oculomotor nerve palsy develops), but posterior fossa compression of the brainstem affects eye movements early with almost any ophthalmoplegia imaginable: unilateral VIth nerve palsy, bilateral VIth nerve palsies, a gaze palsy in one direction, gaze palsy in both directions, skew deviation, internuclear ophthalmoplegia, and coarse nystagmus.

Blood pressure and respirations are two very important systemic signs in assessing brainstem function. Both are controlled by rugged medullary centers;[3] unless these centers succumb early to a direct assault by sedatives or a direct blast from an adjacent cerebellar mass, they'll doggedly increase their output until overwhelmed by steadily increasing pressure from above. Presumably this is Nature's way, called the Cushing reflex*, of responding to brainstem ischemia and hypoxia.[4]

Flaccid: Besides coordinating labyrinthine signals to keep us vertical and to keep our eyes locked on target when our heads move, the vestibular nucleus projects an important bundle of fibers, the vestibulospinal tract, downward into the spinal cord to stimulate our 'antigravity' muscles. The more recently created thalamus and basal ganglia use this enthusiastic vestibulospinal tract to their own advantage by simply harnessing the vestibular nucleus with finely-tuned inhibitory signals. Unbridled decerebrate rigidity quite naturally ensues when these inhibitory signals are intercepted by deep thalamic, midbrain, and upper pontine lesions or by massively elevated intracranial pressure (all of which probably interrupt the central tegmental tract in the brainstem').

Cushing Reflex: Harvey Cushing is to this day revered as the greatest neurosurgeon in history. When at the turn of the century Cushing applied for the post of neurosurgeon at Johns Hopkins University, no such post existed and only a handful of brain tumors had ever been operated on at Johns Hopkins (all the patients died). Incredibly, doctors were still arguing whether low blood pressure was the cause of shock. In fact, it took a courageous man like Cushing to suggest that during operations the blood pressure ought to be continually measured instead of relying on an anesthetist's fingertip on the radial artery. (This rash idea was summarily rejected by Harvard Medical School, but the idea clicked anyway.)

No blood transfusions were being administered when Cushing started, and there was, as yet, no clear way to stop the brain, with the consistency of jello, from oozing and hemorrhaging during routine neurosurgical operations. Nowadays, thanks to Cushing and Bovie, neurosurgeons have an electrical tweezer to coagulate bleeding points.

UNILATERAL SUPRATENTORIAL HERNIATION

The archetypal insult to the reticular activating system, the one that all other types are compared to, is temporal lobe herniation. During herniation, the medial edge of the temporal lobe bulges over the free edge of the tentorium into the incisura, mashing the midbrain*. Though protectively cradled between the temporal lobes, the midbrain must always be wary of either temporal lobe forcing its way into the incisura. Any expanding unihemispheric mass will bulldoze normal brain tissue toward areas of lower pressure, usually the opposite side of the cranial vault*. But after pressure in the opposite hemisphere rises enough to prevent further midline shift, supratentorial structures seek shelter in the relatively low pressure posterior fossa by creeping toward the incisura surrounding the midbrain.



Clinically, this well-choreographed shift of cerebral structures produces a consistent sequence of signs: the patient quickly slides from early agitation into deepening stupor and eventual coma. As the internal capsule is squeezed, the patient becomes increasingly hemiparetic*. Respirations begin to quicken and become more labored.[6] The blood pressure, especially the systolic pressure, rises rapidly during its uphill fight to supply the brainstem with more blood. The pulse also rises at first but then, with increasing medullary compression, slows into the 40–50 beats per minute range.[7] Don't rely too heavily on the exact pulse rate at any one specific time; more important is a *changing* heart rate, either increasing or decreasing over minutes to hours.[8] Suddenly, the hemiparesis is no longer just a hemiparesis, but frank decerebrate posturing. Respirations are now deep and fierce. You quickly lift up the eyelids to discover that the pupil opposite the decerebrate side is now slightly larger and sluggish to light. The temporal lobe has just herniated across the free edge of the tentorium, enough to clip the IIIrd nerve exiting the midbrain.

Mashing the Midbrain: Herniation over the free edge of the tentorium gives supratentorial herniation its other name: transtentorial herniation.

Cranial Vault: Remember that the pathologic lesion can be very small. For example, a small tumor, critically placed at the foramen of Monro, can obstruct the lateral ventricle, and the lateral ventricle can act as the mass.

Increasingly Hemiparetic: You can verify the hemiparesis by simply watching the patient spontaneously use one side more than the other. If that doesn't work, try lifting the patient's arms and yelling encouragement to keep them up. If the patient is too comatose to test arm drift, firmly squeeze each sternocleidomastoid and watch for asymmetrical arm use as he thrashes about or tries to remove your hand.

Sometimes the hemiparesis is on the *same* side as the cerebral lesion. What happens is that the herniating temporal lobe pushes the midbrain against the opposite tentorial edge, notching the contralateral cerebral peduncle and causing a hemiparesis *ipsilateral* to the herniating temporal lobe. The notch in the contralateral cerebral peduncle is called Kernohan's notch.[9]

One word of caution: don't wait for the dilated pupil to diagnose herniation—you might as well wait in the morgue. Once herniation has taken place, it may take too long to mobilize your therapy to save him. Conversely, if you can step in before he has herniated, the patient has an excellent chance of making a full, or at least functional, recovery. So be especially careful at night when the nurse calls you to report that the patient's blood pressure is rising. Since she didn't awaken him to check for a falling level of consciousness or a worsening hemiparesis, you may not be alerted to impending herniation.

CENTRAL HERNIATION

Bilateral hemispheric masses, such as non-communicating hydrocephalus or bilateral subdural hematomas, also shove supratentorial structures toward the incisura. The combined pressures on the midbrain from both hemispheres results in a vertical attack from 12 o'clock high, thereby avoiding the internal capsules and an asymmetrical hemiparesis. Otherwise, the sequence of events for central herniation is the same as for a unihemispheric mass: agitation evolving into coma, increasing respirations, bilateral stiffening evolving into decerebration, progressive hypertension, and changing pulse rate, all culminating in bilaterally dilated pupils sluggishly reactive or unreactive to light.

With advancing downward compression on the pons and medulla, the patient eventually loses his doll's eyes, ice water calorics, corneal and gag reflexes, and finally, his decerebrate rigidity and respirations. But again, don't wait for pupillary dilation, ophthalmoplegia, and absent corneals before diagnosing brainstem compression by a supratentorial mass.

Sometimes, symmetrically increased intracranial pressure can cause unilateral or bilateral VIth nerve palsies by vertically compressing the brainstem. How bilateral hemispheric masses can exert pressure on the pons without first going through the midbrain (with either a IIIrd nerve palsy or internuclear ophthalmoplegia) is somewhat of a mystery. One explanation is that pressure from 12 o'clock high shoves the whole brainstem caudally. The VIth nerve is sensitive to downward tugging because of its long upward course—all the way from lower pons up the clivus into the cavernous sinus.[9] (Others think the brainstem becomes ischemic.[10]) Unilateral hemispheric masses do not, in general, cause "false localizing" VIth nerve palsies, because a herniating temporal lobe shoves the midbrain obliquely to the side, causing a IIIrd nerve palsy.

Not uncommonly, direct vertical compression of the midbrain by a dilated 3rd ventricle may cause early loss of upgaze, and generous, sluggish pupils—Parinaud's syndrome—before the other signs of increasing intracranial pressure.

INTRAVENTRICULAR HEMORRHAGE

The orderly progression of signs for supratentorial masses is ignored by intraventricular hemorrhage. With a direct route to the lower brainstem through the aqueduct of Sylvius, blood in the ventricles causes a rapidly deepening coma, bypassing the usual sequential signs of rising intracranial pressure. Intraventricular hemorrhage is a difficult clinical diagnosis, but suspect it when the stroke begins with a headache (and

vomiting*), and progresses rapidly from hemiparesis to coma without decerebration, hyperventilation, rising blood pressure, or changing heart rate, signs that normally accompany progressive supratentorial brainstem compression.

POSTERIOR FOSSA HERNIATION

Posterior fossa herniation won't look anything like supratentorial herniation. In its most malicious form, you may be stroking your chin trying to figure out why the patient looks a little restless when he suddenly stops breathing and dies. No warning, no nothing. The reason for this difference in presentation stems, as usual, from anatomy. Compared to the posterior fossa, a tight little cubby hole bordered by immobile bone and a rigid tentorial tarp, the supratentorial space is a billowy cavern that, up to a point, will shift and squeeze to accommodate extra intracranial pressure†. It takes far less mass in the posterior fossa to fatally compress the brainstem because the pressure rises very high, very rapidly. It's a bit like blowing air into a small steel football instead of inflating a regular leather one. The ultimate internal pressure may be the same, but less air and less time is needed for the small steel football than for the larger leather one. Like the bladder inside a football, supratentorial structures accommodate the extra pressure until the exterior cover (the skull) says, enough is enough. Lateral ventricles compress, blood vessels compress, white and gray matter compress, the whole brain may even shift across midline—all of which graciously gives you characteristic signs and enough time to recognize them.

The brainstem, in contrast, is firmly bound on each end and further restricted from bowing forward by the clivus. The brainstem does not have the mobility to forestall early and rapid development of life-endangering distress. Furthermore, *each* brainstem region is nakedly vulnerable to posterior fossa compression. By directing its assault upward against the midbrain, horizontally against the pons, or downward against the medulla, a posterior fossa mass can produce a confusing, or at least unfamiliar, cluster of signs.

Vomiting: Any increase in intracranial pressure causes vomiting.

Extra Intracranial Pressure: In other words, the supratentorial space has more compliance than the posterior fossa. Compliance is the amount of pressure rise for each cc of fluid you inject into the cranium.[1]

Pontine Compression

Pontine compression is terribly important to recognize because surgical relief is frequently life-saving. Telltale *horizontal* signs of pontine compression are readily predictable from pontine structures:

Affected Pontine Structure:	Horizontal Sign:
1) Lower end of the reticular activating system (upper pons)	1) Early coma
2) Pontine gaze center or abducens nucleus	2) Gaze palsy (often bilateral)
3) Abducens nerve (before leaving the pons)	3) Lateral rectus palsy (also frequently bilateral)
4) Medial longitudinal fasciculus	4) Internuclear ophthalmoplegia*
5) Vth nerve as it exits the pons	5) Absent jaw closure and absent corneal reflexes
6) Facial nerve nucleus	6) Facial paralysis (one or both sides, including the forehead)
7) Vestibular nucleus	7) Skew deviation*, coarse nystagmus*

Vertical signs in extra-axial pontine compression are less predictable than horizontal ones, because the vertical signs depend on whether the pontine compression occurs above or below the vestibular nucleus. If pontine compression occurs above the vestibular nucleus, tone is increased or even decerebrate. If pontine compression is directed at or extends below the vestibular nucleus, tone is flaccid. But in neither type of pontine compression, above *or* below the vestibular nucleus, will there be early hemiplegia because the pontine pyramidal tracts in the basis pontis lie far forward, protected from the relatively distant cerebellar or 4th ventricular mass.[13] The tip-off to pontine compression—if you need one, what with all the horizontal signs—is that the midbrain-controlled pupils remain small and reactive*, and the medullary-controlled blood pressure, respirations, swallowing, and gag reflex are still maintained*.

Dysarthria almost always accompanies pontine compression for any number of reasons: interrupted cerebellar connections, interrupted corticobulbar fibers (pseudobulbar palsy), or associated compression of the IXth, Xth, and XIIth cranial nerve nuclei in the upper medulla (bulbar palsy).

Internuclear Ophthalmoplegia: If the patient is comatose, you'll need ice water calorics to demonstrate each of these ophthalmoplegias (internuclear ophthalmoplegia, gaze palsy, and abducens nerve palsy.)

Skew Deviation: Skew deviation probably results from a disruption of brainstem tracts connecting the vestibular nucleus with the IIIrd, IVth, and VIth nerve nuclei.[7]

Coarse Nystagmus: Whether coarse nystagmus results from an interruption of brainstem pathways or cerebellar-brainstem connections is unclear.

Small and Reactive: Large pontine lesions, like pontine hemorrhage, constrict the pupils to pinpoint size (0.5 mm), probably by intercepting all the descending sympathetics and leaving the midbrain parasympathetics free to constrict the pupils via the IIIrd nerve.

Still Maintained: The respirations may become irregular in cadence and depth with pontine compression (especially if pharyngeal weakness intermittently obstructs the upper airway), but not apneic, a sign more often of medullary damage.

Remember the signs of pontine compression. You're going to need them when a stuporous patient is rolled into the emergency room with a history of sudden occipital headache, vomiting, ataxia, and pontine compression. The patient, almost always hypertensive, will probably die if you don't recognize his cerebellar hemorrhage*. If you do, operative drainage will allow him to walk away relatively unscathed. His chances are good if you can make the diagnosis before he fatally herniates upward against the midbrain or downward against the medulla.

The pons is almost always compressed from behind by 4th ventricular or cerebellar masses, occasionally from the side by tumors arising directly from the Vth or VIIIth cranial nerve, and only very rarely from in front by tumors attached to the clivus.

Medullary Compression

Medullary compression, unlike pontine compression, produces early loss of blood pressure, respirations, swallowing, gag, and corneal reflexes (where the descending tracts of V dip into the medulla). Now that we're below the vestibular nucleus, the limbs are clearly flaccid. Though the level of consciousness may simply be restless agitation*, the patient is *usually* stuporous or comatose from either simultaneous pontine compression or non-communicating hydrocephalus from 4th ventricular obstruction.[15] The pontine compression that almost always accompanies medullary compression causes: ophthalmoplegia, absent corneal reflexes, absent jaw closure, and facial palsy. The pupils during all this remain undaunted because they're controlled by the still unaffected midbrain.

Upward Herniation

Upward herniation against the midbrain, a rare clinical entity, almost always follows on the heels of pontine, or pontomedullary, compression.[16] Only isolated lesions of the anterior vermis, already poking up through the posterior incisura, can expand early enough to directly compress the midbrain before the pons. All of which means you should have recognized the evolving signs of pontine compression and contacted the neurosurgeon before upward herniation occurs. You should have already seen the early coma, ophthalmoplegia (VIth nerve palsy, gaze palsy, internuclear ophthalmoplegia, or skew deviation), absent jaw closure, poor corneals, and facial weakness before both pupils dilate and fix to light. (The tone may be stiff or flaccid depending on whether the vestibular nucleus was compressed.)

Upward herniation is always a threat when posterior fossa masses compress the 4th ventricle. Any neurosurgical attempt to reduce intracranial pressure by inserting a shunt tube into a lateral ventricle may suddenly lower the supratentorial pressure enough to herniate the posterior fossa upward through the incisura.

Cerebellar Hemorrhage: The patient has three reasons to vomit: acute increase in intracranial pressure (non-communicating hydrocephalus from 4th ventricular obstruction), direct irritation of vomiting centers in the medulla,[12] and acute irritation of the vestibular nucleus causing vertigo and nausea.

Restless Agitation: A purely medullary lesion will not cause coma because the reticular activating system is in the midbrain and upper pons—not the medulla.

Problems Recognizing Posterior Fossa Herniation

The most common difficulty in diagnosing posterior fossa herniation is recognizing the *absence* of early hemiplegia, a sign which distinguishes posterior fossa herniation from the two other major structural causes of coma: brainstem strokes and unilateral supratentorial herniation. Progressively deepening coma without a hemiplegia, typical of posterior fossa herniation, does occur in central (symmetrical bihemispheric) herniation, but early ophthalmoplegia should steer you toward the posterior fossa.

Don't be fooled because the patient's arms and legs aren't grossly ataxic. The patient may be too lethargic to test for limb ataxia, and not uncommonly, the ataxia is predominantly truncal; unless you take the time and effort to walk the patient before he becomes stuporous, you may overlook a cerebellar mass.[17]

It is also easy to miss the significance of flaccidity, a sign of lower pontine or medullary compression. Flaccidity is mistakenly attributed to sedative overdose or organ failure, or even to bilateral cortical dysfunction (like bihemispheric strokes).

Typical sedative overdose produces a pupil-sparing coma with flaccid quadriparesis, shallow respirations, hypotension, and a poor gag reflex—just like medullary compression. Moreover, doll's eyes are absent in both sedative overdose* *and* pontomedullary compression (compressing the vestibular nucleus and the VIth nerve nucleus). Fortunately, cold calorics can usually distinguish drug overdose from pontomedullary compression. Being a stronger stimulus than head rotation, cold calorics can usually—but not always[10]—overcome drug-inhibited gaze centers, but not compressed ones. Despite these different responses to cold calorics, distinguishing drug overdose from pontomedullary compression by neurologic exam alone can be very tricky; you don't want to have to make a living doing it.

You should now begin to understand why posterior fossa herniation is such a great impostor. While upward herniation causes the same decerebration and pupillary dilation as supratentorial herniation, pontomedullary compression may disguise itself as a drug overdose. To add insult to injury, cerebellar tonsil herniation through the foramen magnum may even cause a stiff neck, mimicking meningitis.

BILATERAL CORTICAL DYSFUNCTION WITHOUT ELEVATED INTRACRANIAL PRESSURE

The final group of coma-causing lesions disrupts both hemispheres without raising the intracranial pressure, and without damaging the reticular activating system in the upper brainstem. The blood-borne insults of this group—drugs, toxins and metabolites—tend to skip the midbrain and pons and selectively affect the medulla and autonomic nervous system. The resulting signs depend on whether the medulla and autonomic nervous system are stimulated or depressed by the insult. For example, depressed sympathetics produce small pupils; stimulated sympathetics produce large pupils (as well as fever, tremulousness, flushing, and cardiac arrhythmias). Likewise, a stimulated medulla results in hyperventilation, tachycardia, hypertension, increased tone, and hyperactive reflexes, and a depressed medulla, apnea, bradycardia, hypotension, and flaccid limbs with hypoactive reflexes.

The differential diagnosis of coma with normal brainstem function and without signs of increased intracranial pressure is outlined below:

Sedative Overdose: In fact, unless the doll's eyes *are* absent, the coma is probably not due to sedatives!

	Bihemispheric Cerebral Cortex
Drugs*:	Anticonvulsants, neuroleptics, opiates, sedatives, vitamins, alcohol, methanol, heavy metals
Infection:	Viral encephalitis, meningitis, sepsis
Genetic:	Porphyria
Immunologic:	
Tumor:	
Trauma:	Concussion**
Mechanical:	
Organ Dysfunction:	
Systemic:	Hypotension, malignant hypertension, heat stroke
Skin:	
Neuro:	Nonconvulsive status epilepticus
Eyes:	
Ears:	
Endo:	Myxedema coma, hypercalcemia, hypoglycemia, diabetic ketoacidosis, nonketotic hyperglycemia
Resp:	Hypoxia
Card:	Severely reduced cardiac output
GI:	Liver failure
RE:	
Uro:	Renal failure, hypernatremia, hyponatremia
Gen:	
Vasc:	Bihemispheric strokes Subarachnoid hemorrhage
Heme:	
Bone:	
Coverings & Connective Tissue:	

Drugs: Whether drugs and metabolic toxins precipitate coma by directly shutting down the reticular activating system, or by shutting down the cortex and thereby depriving the reticular activating system of stimulation, is anybody's guess.[20] I find it easier to structure the etiologic differential diagnosis by using both cerebral hemispheres as the target instead of the reticular activating system.

Concussion: A concussion is a brief loss of consciousness after trauma with no focal neurologic signs. A transient cortical sign or a transient hemiparesis upon awakening suggests a cortical contusion (bruise).

The cortex is particularly vulnerable to being smacked up against the skull or being scraped along the notched and ridged floor of the skull, as any boxer knows. Likewise, post-traumatic brainstem signs with intact hemispheres suggest that the brainstem was twanged against the clivus, an image that almost makes you want to wear your seatbelt.

What distinguishes most of these illnesses from increased intracranial pressure, posterior fossa herniation, and sedative overdose, is the normal tone, normal brainstem function*, and brisk respirations.

Liver failure can be a particularly annoying problem because liver failure may cause hyperventilation and occasionally decerebration,[22] a combination typically associated with increased intracranial pressure.

Despite all the natural fluster and anxiety they evoke, comatose patients can be very interesting to sort out. You already know how to examine the brainstem: pupillary reaction (midbrain), eye movements (pons), and respirations and blood pressure (medulla). Additional pontomedullary signs include jaw closure, corneal reflexes, facial weakness, and gag reflex. Armed with the five recognizable patterns of coma—unilateral supratentorial herniation, central herniation, posterior fossa herniation, sedative overdose, and bihemispheric dysfunction without elevated intracranial pressure—you can propose any one of these patterns of assault on the reticular activating system and then use the exam to confirm your hypothesis.

In general (with more to be said in chapter 37), the approach to localizing the site of any coma-causing lesion is first to decide if the midbrain is structurally intact: make sure that the pupils are still reactive and that each eye can move medially—if necessary, using doll's eyes or cold calorics. If the midbrain is still all right, the only other place where a structural brainstem lesion can disrupt the reticular activating system is in the upper pons. So, next look for signs you'd expect from a pontine lesion: internuclear ophthalmoplegia, skew deviation, gaze palsy, VIth nerve palsy, weakness of jaw closure, and facial palsy. If the midbrain and pons are working, the cause of the coma is probably supratentorial.

Now all you have to do is distinguish lesions that produce high intracranial pressure from those that don't. Clinically, the signs that best distinguish high pressure supratentorial lesions from normal pressure ones are the tone, respirations, and blood pressure. A stiffening hemiparesis, especially decerebration, with hyperventilation and a rising blood pressure should immediately alert you to increasing intracranial pressure. Liver failure may also cause decerebration (usually bilateral) and hyperventilation, but not the rising blood pressure. Hyperventilation without stiffening tone or rising blood pressure should tip you off to hypoxia, systemic acidosis, or local CSF acidosis from meningitis.

It's easy to become rattled when comatose patients blast through the emergency room doors. But don't let all the hysteria sway you from methodically taking the vital signs, asking the circumstances in which the patient was found, doing a brief general physical exam, and carefully sorting out the neurologic signs. It sounds like a silly platitude to say that your conclusions depend on an accurate neurologic exam, but unless you focus individually on the level of consciousness, the midbrain, the pons, the medulla, and the long tracts, you won't feel confident in your ability to handle the situation. It's too easy amidst the commotion of an emergency room to order the wrong tests, forget to administer the right drugs, and underestimate the urgency of the situation.

Normal Brainstem Function: There are some exceptions, of course. Very uncommonly, drugs or organ failure may cause dysconjugate gaze on doll's eyes or cold caloric testing.[23]

SPINAL CORD AND ROOTS

SPINAL CORD

IT HAS ALWAYS BEEN A MARVEL to me how a structure smaller in cross-section than a dime can still be large enough to contain all the nerves necessary for neurologic function below the jaw. Today's casually accepted understanding of spinal cord physiology sprouts from roots deep in the 19th century. By 1800, the only certainty about spinal cord function was that nerves transmit electricity. No one knew that ventral nerve roots had a different function from dorsal roots, that axons were connected to cell bodies, or even that neurons were physically separate from each other; in fact, no one even knew what a cell was.

Deciphering cord physiology began in 1811 when Dr. Charles Bell (of Bell's palsy fame) discovered the purely motor function of the ventral root, followed eleven years later by Francois Magendie's demonstration of total anesthesia without paralysis upon cutting the dorsal root. It took until 1838 before Schwann (describer of the Schwann cell) and Schleiden recognized cells as the fundamental structure of tissue. Though Robert Remak had by that time traced the connection of peripheral axons to neuronal cell bodies in the ventral horn, the entire neuronal structure—dendrite, axon, and cell body—was not fully described until the Civil War by Otto Dieters. By that time Benedict Stilling had developed the technique of slicing microscopically thin sections, and the burgeoning wool industry was able to provide the necessary dyes for staining microscopic tissues.

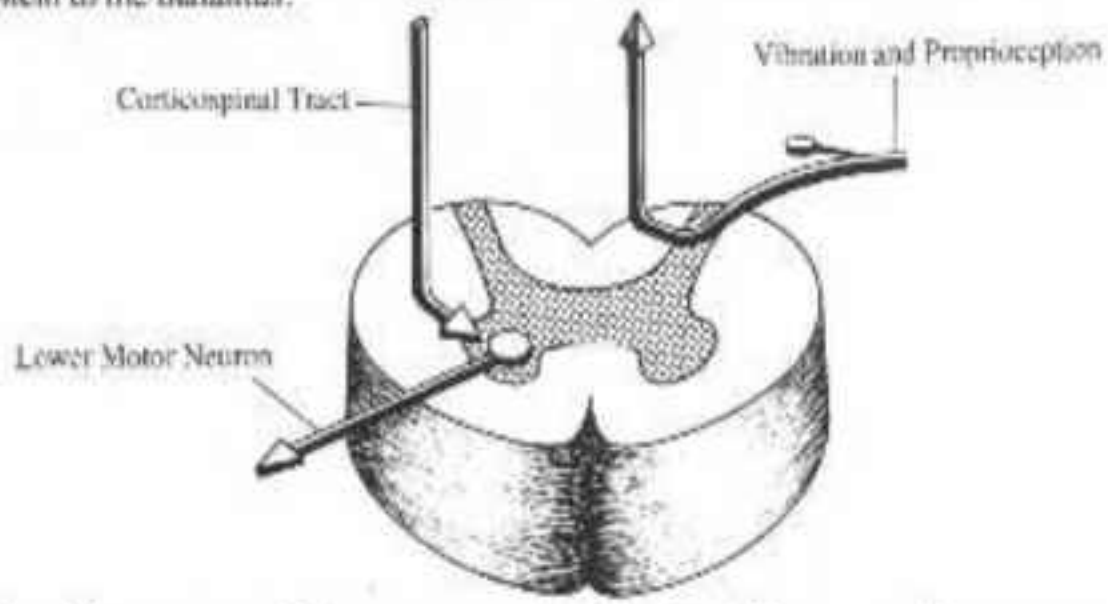
The fundamental concept that electricity travels along individual neurons, not along a dense cobweb of fused dendrites, wasn't confirmed until 1877. In that year Forel demonstrated that when a single neuron is killed, only those processes attached to that cell body die. Another decade passed before Ramon y Cajal showed that electrical impulses travel in one direction: from the dendrites, through the cell body, and out the axon.

Spinal cord white matter contains adjacent columns of ascending sensory axons and descending corticospinal axons. Corticospinal fibers are located in each half of the spinal cord at approximately 3:00 and 9:00, one column for each side of the body. The primary sensory modalities of pain, temperature, touch, vibration, and proprioception (joint position sense) are carried to the spinal cord via peripheral nerves. Just before reaching the spinal cord, peripheral nerves sort themselves out into sensory and motor roots. Each sensory root carries the four modalities of sensation from a specific area of the body called a dermatome. As soon as sensory roots enter the spinal cord, fibers carrying vibration and proprioception separate from those carrying pain and temperature. Proprioceptive and vibratory fibers enter the dorsal columns*, and

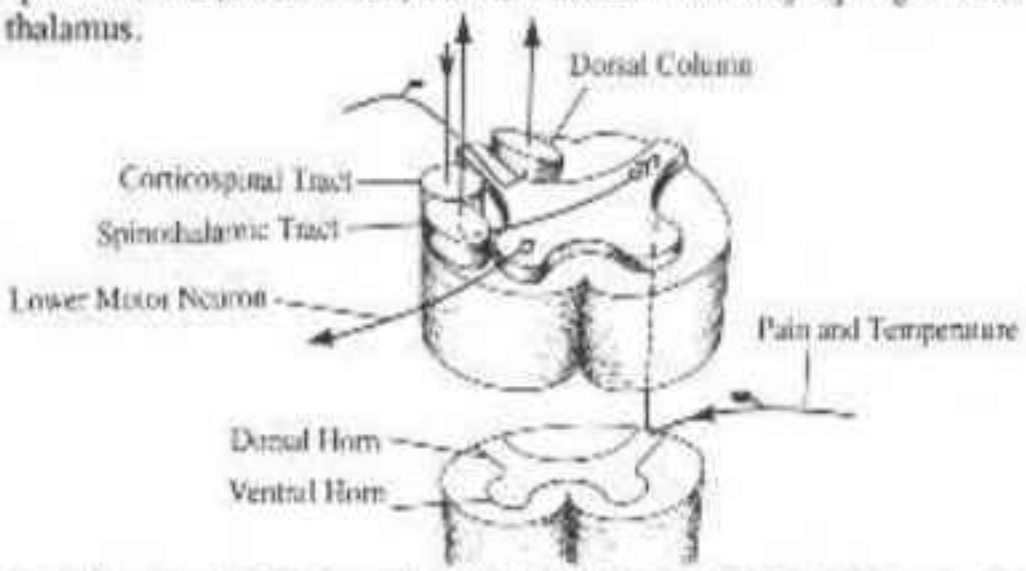
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Dorsal Columns: The dorsal columns have traditionally been thought to carry vibration and proprioception, but experimental and clinical evidence is mounting that these two sensations ascend in tracts lying slightly lateral to the dorsal columns, in Morin's pathway. What the dorsal columns really do is still speculative.

ascend ipsilaterally to their first synapse in nucleus gracilis and cuneatus situated at the junction of the brainstem and spinal cord. A proprioceptive or vibratory neuron, then, begins in the toe and extends all the way to the brainstem without a single synapse! Only after synapsing in the lower medulla do proprioception and vibration cross, continuing their ascent in the contralateral medial lemniscus* through the brainstem to the thalamus.



Pain and temperature fibers upon entering the dorsal horn ascend one or two segments* before synapsing onto second order neurons. After deciding they have received an intense enough bombardment of pain impulses, these second order pain and temperature neurons discharge across the center of the spinal cord to the contralateral spinothalamic (anterolateral) tract and ascend without synapsing to the contralateral thalamus.



The first order neuron is shown ascending 1-2 levels before synapsing. In some cases, the second order neuron (and not the first order neuron) may ascend 1-2 levels as it crosses through the cord.

Touch goes up both the anterolateral and posterior columns, but still ends up in the same contralateral thalamic nucleus as pain, temperature, vibration, and proprioception, namely the ventral posterolateral nucleus of thalamus. From the ventral posterolateral thalamus, sensory fibers continue *up* the internal capsule to the sensory strip in the parietal lobe.

Lemniscus: Ribbon.

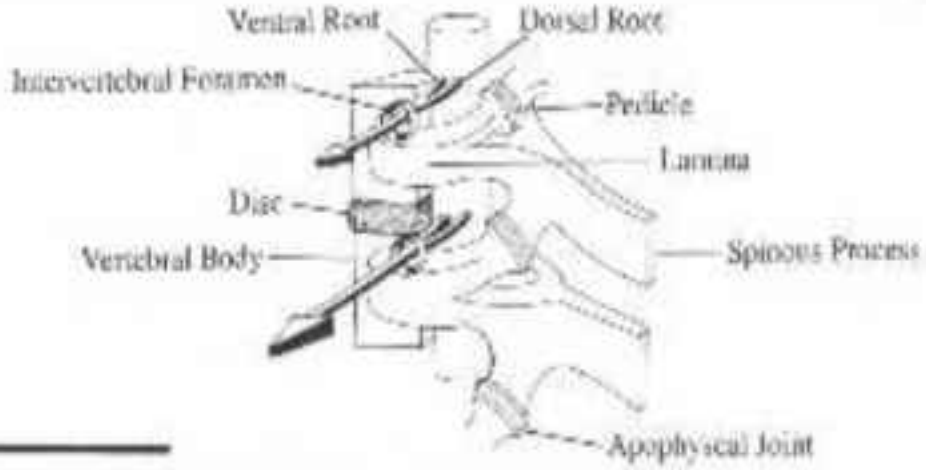
Segment: The short section of spinal cord corresponding to a root is called a segmental level.

These three vertical tracts—corticospinal tract, spinothalamic tract, and posterior column—constitute the 'long tracts.' Since all three long tracts extend from the spinal cord to the cerebral cortex, simply finding a hemiparesis or sensory loss over one half of the body is not enough to indicate a lesion in the spinal cord. To localize a long tract sign to the spinal cord, i.e., to diagnose a myelopathy*, requires that you also find a simultaneous horizontal sign that intersects at least one of the long tracts in the spinal cord. Such a horizontal sign is either a sensory root or a motor root, and preferably both to be sure. Sometimes you have to settle for an absent deep tendon reflex as the only horizontal root sign.

Unlike the brainstem, there is no single pathognomonic sign indicative of a myelopathy*—only the combination of a long tract and root. The combination of a *peripheral nerve* and a long tract does not localize a lesion to the spinal cord, because peripheral nerves do not intersect the spinal cord—only roots do. For example, a spastic paraparesis and an atrophic hand are due to a cervical myelopathy if the hand atrophy represents a C8/T1 radiculopathy*. If, however, the hand is suffering from an ulnar nerve lesion, you're back to square one; the spastic paraparesis is due to a bilateral pyramidal tract lesion anywhere between the thoracic spinal cord and bilateral cerebral cortex. We were spared this dilemma in the brainstem because there are no root/peripheral nerve distinctions. All horizontal signs stem from the cranial nerves.

ROOTS

As you can see, the roots provide a powerful tool for localization. A few minutes studying their anatomy will save hours of clinical quandary. There are two (left and right) sets of roots (motor and sensory) for each vertebral body, plus an extra set in the cervical region. Beginning at the first cervical level (C2*), motor and sensory roots join to form a common root which exits through the intervertebral foramen located above the corresponding vertebra. At the 7th cervical vertebra, an extra C8 root exits below the C7 vertebra. From here on down the roots exit beneath the corresponding vertebra.



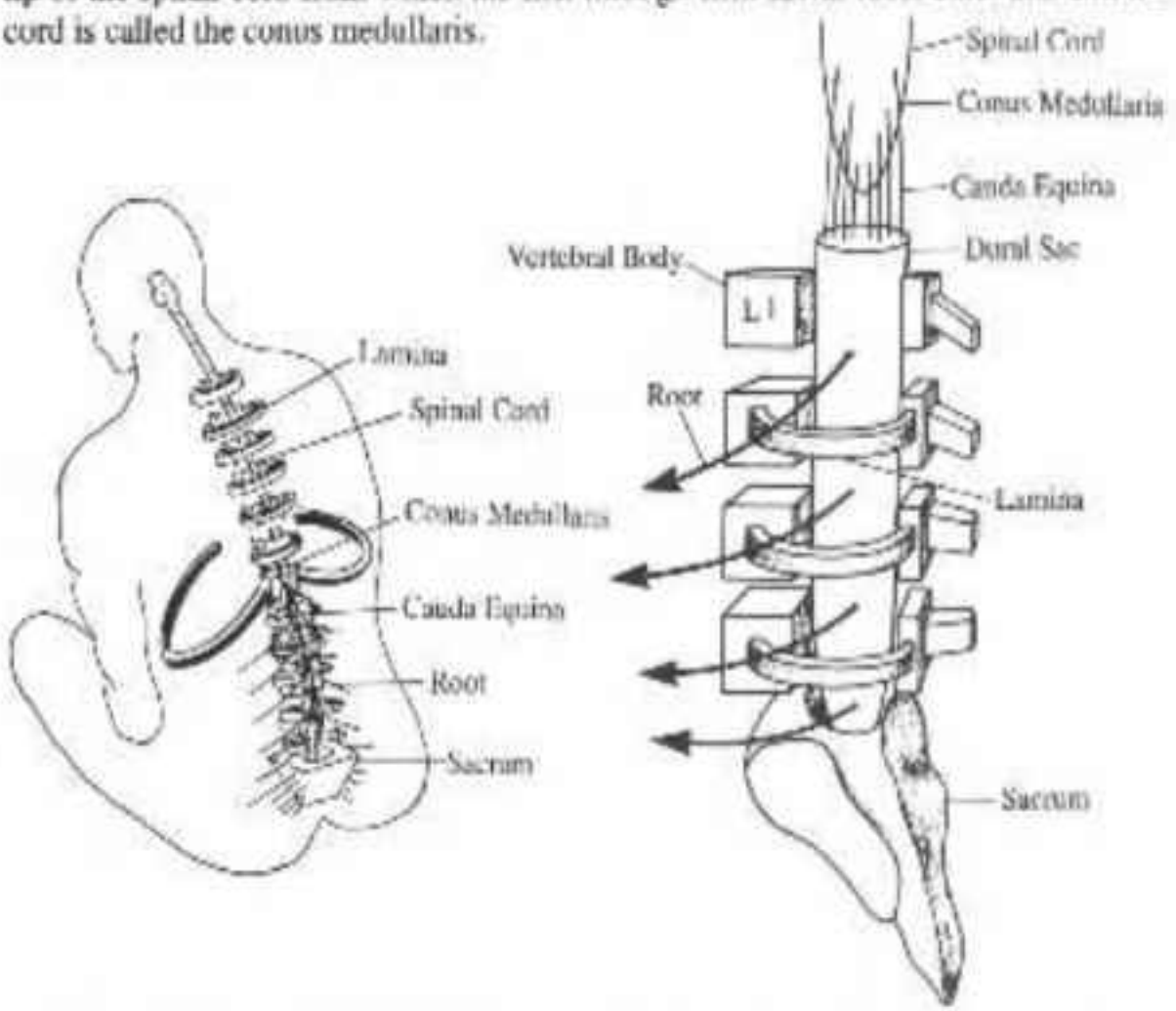
Myelopathy: Spinal cord disturbance. Myopathy is a muscular problem.

Indicative of a Myelopathy: There is one, almost pathognomonic 'symptom-sign' of posterior column pathology called Lhermitte's sign. When the patient flexes his neck (presumably stretching disturbed posterior columns), he experiences a sudden, brief jolt of electrical tingling in his arms, trunk, or legs.[7]

Radiculopathy: Weakness or sensory loss due to a root lesion. I tend to use the term radiculopathy interchangeably with segmental level, but there is an anatomic difference.

C2: C1 root is a purely motor root, there is no dorsal sensory root for C1.

The spinal cord ends at about the first lumbar vertebra (L1). In the fetus, spinal cord segments and exiting roots did match up alongside their corresponding vertebral foramina. But as the fetus and vertebral column lengthened, the spinal cord did not keep pace so that the bottom tip of the spinal cord, the conus medullaris, wound up opposite the L1 vertebra. In order, then, for lumbar and sacral roots to exit beneath their corresponding vertebra, the roots must continue down the spinal canal on their own. The bushy tail of axons that descends four or five vertebrae before leaving the spinal canal is known as the cauda equina (cauda = tail, equina = horse). The bottom tip of the spinal cord from which the first through fifth sacral roots enter and exit the cord is called the conus medullaris.



It would have been beautiful if Mother Nature had organized the roots so that each muscle was innervated by a single root. Instead, she designed the motor system so that one root may innervate five or six different muscles, and the same muscle may be innervated by several different roots. And to make matters worse, when the roots leave the spinal cord they don't just make a beeline for their muscle. Instead, upon leaving the spinal column the roots huddle into a God-awful looking tangle called a plexus in which the roots divide and redistribute themselves into peripheral nerves. We can moan and groan over the unnecessary complexity, but we do the very same thing. You look at a good-sized railroad terminal, and, just as each root leaves the cord in a nice orderly fashion, so do trains leave from nicely labeled tracks. But no sooner are the trains out of the station than they enter a plexus of intertwining tracks—the switching yard—before finally distributing themselves to their proper outgoing track. As a result of redistribution within the plexus, any peripheral nerve contains motor and sensory fibers from several different roots, and much of neurology is simply distinguishing weakness or sensory loss due to a root lesion from that due to a peripheral nerve lesion.

LOWER MOTOR NEURON SIGNS

Before making the distinction between root and peripheral nerve, however, you must be certain that the weakness is a lower motor neuron problem (anywhere from the neuronal cell body in the ventral horn to its insertion in the muscle), and not an upper motor neuron (pyramidal tract) or primary muscle problem. In other words, the anatomic differential diagnosis of weakness includes the pyramidal tract, anterior horn cell, root, plexus, peripheral nerve, neuromuscular junction, and muscle.

Upper motor neuron signs you recall are spasticity, weakness (preferably hemiparesis), slowing of rapid alternating movements, hyperreflexia, and a Babinski. Lower motor neuron lesions (root or peripheral nerve) cause: 1) muscular atrophy*, 2) fasciculations, 3) hypotonia, 4) weakness in a peripheral nerve or root distribution, and 5) diminished reflexes.

EXAMINING FOR LOWER MOTOR NEURON SIGNS

Tone you know how to test; just look for a floppy, flaccid limb. To detect atrophy, hold both the patient's hands by their fingertips, palms down, letting the thumbs hang. Look for scalloping of the first dorsal interosseous[4] muscle. Have the patient adduct his thumbs to bunch up both first dorsal interossei. Now feel them. If one is softer, that first dorsal interosseous is mildly atrophied.



1st Dorsal Interosseous Atrophy



Atrophic Thenar Eminence

Turn the hand over and look at the thenar and hypothenar eminences. Do they create a central depression in the palm so that a teaspoon of water would puddle there? Feel abductor digiti quinti and then feel the underlying metacarpal bone through the muscle. If you feel the bone easier on one side, abductor digiti quinti is atrophied. Do the same for the thenar eminence (opponens, flexor pollicis brevis[5], and abductor pollicis

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Atrophy: Prolonged disuse of a limb for whatever reason may also cause muscles to atrophy.[3] To be sure that your patient's atrophy is a lower motor neuron problem, you need to look hard for fasciculations, and for the *absence* of pyramidal tract signs: spasticity, loss of fine motor control, hyperreflexia, and Babinski reflex.

Interosseous: The dorsal interosseous muscles anchor themselves on the metacarpal bones to spread the fingers; the ventral interossei pull the fingers together. (Meta = beyond, carpos = wrist: bones beyond the wrist.)

Flexor Pollicis Brevis: Pollicis = thumb, brevis = short. Flexor pollicis brevis flexes the metacarpal-phalangeal joint across the palm. Flexor pollicis *longus* flexes the interphalangeal joint.

brevis*). Does one thenar eminence feel softer; can you feel the underlying metacarpal bone better on one side?

With the palms up, hold the patient's arms in front of him. Look for scalloping of flexor carpi ulnaris. Pronate the arms and look for flattening of brachioradialis. Palpate* the biceps for softening. Grasp the pectoralis muscles* and feel for softening. Look at each triceps in profile; does the triceps smoothly merge into the elbow, or is it scalloped and atrophied just above the elbow? Look at the profile of the deltoids* and feel their consistency. Standing behind the patient, look for scalloping of the posterior deltoid, supraspinatus, and infraspinatus muscles*. Compare the two scapular spines; is one excessively prominent? To appreciate softening in all these muscles, palpate with your whole hand and palm, not just your fingertips. If you're not sure which muscle is softer, imagine yourself standing in line at the Giant—which muscle would you buy?



Scalloped Triceps



Flexor Carpi Ulnaris Atrophy (medial forearm)





Supraspinatus and Infraspinatus Atrophy

Abductor Pollicis Brevis: Thumb abduction lifts the thumb away from the palm, perpendicular to thumb flexion.

Palpate: To palpate something means more than just to feel it. Palpation is a search for *all* the qualities of an object: its size, shape, temperature, surface texture, and internal consistency. Sighted people feel; blind people palpate.

Pectoralis Muscle: The chest muscle underneath the breast (pectus = breast bone).

Deltoid: Named after its shape—like the Greek letter delta.

Infraspinatus Muscle: Supra and infraspinatus are the two muscles above and below the scapular spine.

In the legs, look for flattening of the quadriceps muscle or scalloping along its medial side; feel the quads for softening. The tibialis anterior muscle should rise above the edge of the tibial* bone. If not, there's atrophy. Turn the patient over. Does one gluteus* have more atrophic wrinkles or is one buttock obviously flatter than the other? Go to foot of the bed and look at the contour of the buttocks. Is the 'gluteal skyline' symmetrical?[4] Feel the ischial bone through the gluteus; is the gluteus softer on one side? Look for scalloping of the hamstrings* and feel down to the femur for softening. Does one gastrocnemius* appear flattened? Slide your palm along the gastrocs for any flattening and then palpate them for flabbiness. Circumferential measurement of the leg muscles is also adequate, but won't detect softening, a reliable sign of atrophy.



Flattened Gluteus Maximus



Tibialis Anterior Atrophy



Quadriceps Atrophy



Medial Gastrocnemius Atrophy

Tibia: Shin bone (pipe in Latin).

Gluteus: Greek: buttock.

Hamstrings: Ham is an Anglo-Saxon term for the gluteal and posterior thigh region.

Gastrocnemius: Gastroc = stomach (like gastric acid); knemē = leg.

Fasciculations are spontaneous, random contractions of thin strips of muscle, usually too small to move a joint. The muscle must be fully at rest to call a spontaneous muscular twitch a fasciculation. If the muscle is not resting, the contraction is not truly spontaneous and therefore not a fasciculation. If fasciculations are not present at rest, smack the muscle with your reflex hammer, or have the patient contract the muscle vigorously and watch for them after he relaxes the muscle.

The presence of fasciculations means that something is wrong with the lower motor neuron. Theoretically, the abnormality may be in the spinal cord (in the ventral horn) or anywhere along the peripheral nerve up to the point of insertion, but almost always fasciculations result from proximal insults—either in the cell body within the ventral horn or in the root. Rarely are fasciculations due to peripheral neuropathies*.[6]

Deep tendon reflexes are diminished in lower motor neuron weakness, but the degree of diminution matches the weakness. Reflexes depressed out of proportion to weakness usually means a peripheral neuropathy (chapter 25).

ANATOMY

The clinically useful radicular divisions of the upper extremity are as follows: C5 controls the shoulder girdle muscles (deltoid, supraspinatus, infraspinatus, and rhomboids*) and partially innervates serratus anterior*, biceps, and brachioradialis. C6 innervates the biceps, brachioradialis, supinator, and wrist extensors. C7 controls the triceps and finger extensors. C8 controls the hand—the grip muscles, the thumb, the finger extensors (with help from C7), and together with T1, the interossei, lumbricals*, and thenar and hypothenar muscles*.

Peripheral nerves to the upper extremity are rather splintered, especially around the shoulder girdle: the dorsal scapular nerve controls the rhomboids; the suprascapular nerve controls supra and infraspinatus; the axillary nerve controls the deltoid; and the long thoracic nerve controls serratus anterior. All of these muscles are supplied by the C5 root (C6 and C7 help C5 supply serratus anterior). The biceps is supplied by the

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Peripheral Neuropathies: Why fasciculations result more commonly from proximal that peripheral lesions is an interesting question, especially since it appears that the aberrant electrical impulses originate, at least in some cases, within the *distal* parts of peripheral nerves.[7]

Rhomboids: Rhombus means wheel in Greek; the addition of 'oid' for some reason changes the meaning to a figure resembling a parallelogram with unequal sides, the shape of the rhomboid muscle. The rhomboids (situated underneath the trapezius muscles) pull the scapulae toward the vertebral column.

Serratus Anterior: The edge of this muscle where it inserts on the ribs has a serrated, saw-tooth appearance. Serratus anterior keeps the scapula fixed to the rib cage, providing a solid base of support for arm movement.

Lumbricals: Small muscles in the hand which help extend the fingers (chapter 25).

Thenar and Hypothenar Muscles: Muscles that begin and end in the hand—the interossei, lumbricals, abductor digiti minimi, flexor pollicis brevis, abductor pollicis brevis, and opponens pollicis—are known as the intrinsic hand muscles.

Theoretically, T1 supplies the small intrinsic hand muscles, and C8 supplies the long finger flexors like flexor digitorum superficialis, flexor digitorum profundus, and flexor pollicis longus. In practice, though, there is so much dual innervation of the intrinsic hand muscles that for all intents and purposes, the hand is a C8/T1 structure.

musculocutaneous nerve, while the radial nerve supplies the triceps, supinator, brachioradialis, and wrist and finger extensors. Note that the radial nerve supplies no intrinsic muscles in the hand, which means that hand atrophy cannot be due to a radial nerve lesion.



Dorsal Scapular Nerve



Suprascapular Nerve



Median Nerve



Radial Nerve



Ulnar Nerve

The ulnar nerve supplies only two muscles in the forearm, both of which have ulnar in their name: flexor carpi ulnaris and ulnar half of the flexor digitorum profundus*. In the hand the ulnar nerve supplies abductor digiti quinti, adductor pollicis, the third and fourth lumbricals, and all the interossei—in other words, all the intrinsic muscles except the first two lumbricals and the three thenar muscles.

Flexor Digitorum Profundus: Profundus means deep, hence, a muscle deep to the flexor digitorum superficialis. Flexor digitorum profundus flexes the distal phalanx; flexor digitorum superficialis flexes the proximal interphalangeal (PIP) and metacarpal-phalangeal (MP) joints.

The median nerve in the forearm supplies pronator teres* and all the finger, thumb, and wrist flexors* except for flexor carpi ulnaris and the ulnar half of flexor digitorum profundus. The only muscles in the hand supplied by the median nerve are the radial two lumbricals and the thumb muscles: opponens pollicis, flexor pollicis brevis, and abductor pollicis brevis.

ROOT VERSUS PERIPHERAL NERVE

Once you're certain the weakness is lower motor neuron (by finding atrophy, fasciculations, hypotonia, and hypoactive reflexes), you're ready to establish an anatomic differential diagnosis. Since every muscle in the body below the chin is simultaneously innervated by a root and a peripheral nerve, the anatomic differential diagnosis encompasses the root (or segmental level) and the peripheral nerve innervating that muscle. Which means you have to know the root and peripheral nerve innervation of every clinically important muscle in the body.

After deciding which root and which peripheral nerve to focus on, you're ready to sort out which one is causing the lower motor neuron signs. The general idea is to find a weak muscle, and 1) establish the anatomic differential diagnosis between the peripheral nerve and root, 2) propose that the weakness is due to a lesion in the peripheral nerve, and then 3) try to disprove your hypothesis by looking for a weak muscle that is not supplied by the peripheral nerve, but *is* supplied by the root in question. If you find that all the weak muscles are supplied in part by the same root, then the weakness is radicular. (Or else, unlikely, but it happens, the patient has something wrong with both peripheral nerves.)

Upper Extremity

The two most common root versus peripheral nerve problems in the arm are hand atrophy and wrist drop. Suppose a patient complains that one of his hands is weak and you find atrophy of the first dorsal interosseous and abductor digiti quinti. These muscles are supplied by both the ulnar nerve and C8/T1 roots, so is the atrophy due to an ulnar nerve lesion or a C8/T1 radiculopathy? Unlike C8 and T1 which supply all the intrinsic hand muscles*, the ulnar nerve supplies all the intrinsics *except* the thumb: flexor pollicis brevis, abductor pollicis brevis, and opponens pollicis which are all supplied by the median nerve. So, you initially propose that the atrophy of first dorsal interosseous is due to an ulnar nerve lesion. Now try to disprove it by looking for weakness outside the ulnar nerve distribution but still in the confines of the C8/T1 roots. Turn the hand over and check the opponens, flexor pollicis brevis, and abductor pollicis brevis muscles in the thenar eminence. If there is also atrophy and weakness in these median innervated muscles, then the first dorsal interosseous and abductor digiti quinti weakness are due to a C8/T1 root or segmental cord lesion (unless the

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Teres: Smooth, round.

Wrist Flexors: There are three parallel sets of muscles which control wrist flexion and extension. They pair up as follows: flexor carpi radialis/extensor carpi radialis; palmaris longus/extensor digitorum; flexor carpi ulnaris/extensor carpi ulnaris. Combined action of flexor and extensor carpi radialis abducts the wrist; flexor and extensor carpi ulnaris team up to adduct the wrist.

Intrinsic Hand Muscles: Surprisingly enough, opponens pollicis also receives a significant contribution from C7.

patient is unlucky enough to have both an ulnar and a median neuropathy*) since both the thenar and hypothenar muscles are C8/T1 innervated muscles



1st Dorsal Interosseous Atrophy

Thenar Eminence Atrophy



How about a patient with a wrist drop (weakness of wrist and finger extensors): is this due to a radial nerve injury or C6 radiculopathy? Propose it's due to a radial neuropathy and check a C6 muscle not innervated by the radial nerve, like the biceps. If the biceps is normal, the wrist drop is probably not due to a root lesion, so go back and check the other radial innervated muscles: triceps, supinator, and brachioradialis. If the triceps is weak*, the wrist drop cannot be due to a C6 lesion (triceps is a C7 muscle) and must therefore be due to a radial neuropathy.



Testing Triceps



Testing Wrist Extensors



Testing Brachioradialis

Ulnar and Median Neuropathy: This situation occurs primarily with polyneuropathies (all the nerves in the body are affected—chapter 25), but in that situation the atrophy involves both hands symmetrically.

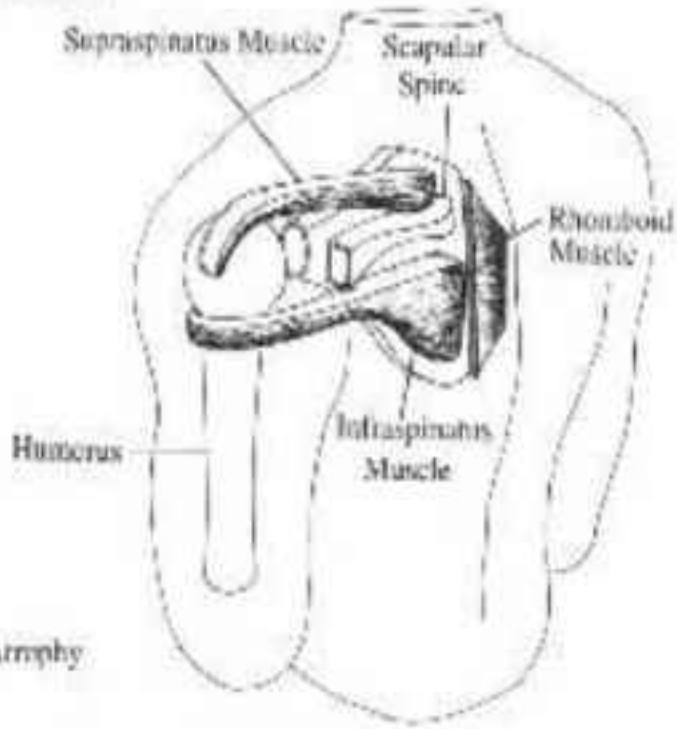
Triceps is Weak: Actually, in most radial nerve injuries, the triceps is normal, because most radial nerve injuries occur in the spiral groove, distal to the branchpoint for the triceps.

In testing the supinator muscle, be sure to fully extend the arm. With the elbow flexed, wrist supination is not performed by the supinator muscle, but by the much more powerful biceps*. (Next time you use a screwdriver, gauge the difference in strength with the arm extended and flexed; feel your biceps contracting during flexed supination.) Similarly, brachioradialis flexes the elbow, but only when the thumb points upward; the biceps flexes the elbow with the palm upward. Also, be careful when testing the grip in the presence of a wrist drop. The grip is *always* weak with a wrist drop, because no one has a normal grip if the wrist isn't fully extended. If you forget to lift the wrist into a fully extended position before testing the grip, you may be fooled into thinking that more than a simple radial nerve injury is present.

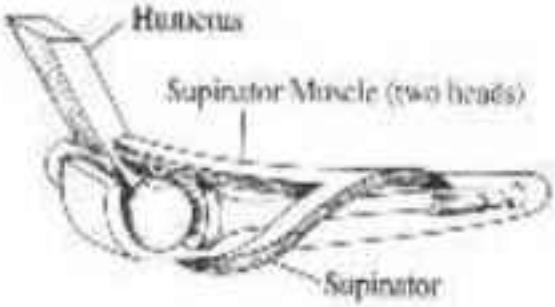
Suppose the patient has a weak deltoid: C5 or axillary nerve? Since the axillary nerve supplies only the deltoid (and the clinically unimportant teres minor), it's easy to disprove an axillary neuropathy by finding weakness in other C5 muscles—supraspinatus, infraspinatus, and rhomboid muscles.



Supraspinatus, Infraspinatus, and Deltoid Atrophy



Biceps: Wrist supination works by an undeniably brilliant development of the radius and ulna bones. While the ulna remains anchored, the radius spins, flip-flopping the wrist from pronation into supination, and vice-versa. The biceps supinates the forearm by inserting into the medial side of the radius bone and spinning the radius when the biceps contracts.





Supraspinatus abducts the arm for the first 15 degrees, deltoid thereafter. Infraspinatus externally rotates the flexed arm as in a tennis backhand swing. Test infraspinatus by tucking the patient's elbow into his side, and then having the patient push the back of his wrist against your hand.



Testing Supraspinatus



Testing Deltoid



Testing Infraspinatus →

When testing the deltoid, give the patient a mechanical advantage by first allowing him to fully abduct his elbows (muscles are strongest when fully contracted). To maximize *your* mechanical advantage, place your hands as far away from the moving joint as possible, in this case, over the elbows. Then *pull* the elbows down, don't yank them.

The rhomboids pull the scapulae toward the spine in a military stance. Begin examining the rhomboids by checking that one scapula hasn't shifted away from the spine. Feel for rhomboid atrophy by palpating the ribs through the rhomboid muscle. To test its strength have the patient put his hand on his hip and push his elbow backward against your hand. With the hand on the hip the scapula and humerus function like a single bone, allowing you to push the scapula laterally along the chest wall by pushing against the patient's elbow. As the patient pushes backward against your hand, try to rotate the scapula away from the vertebral column.

Serratus anterior (C5,6,7) is examined by having the patient push against a wall while you look for 'winging' of the scapula (lifting of the scapula from the chest wall).



Winging of the Scapula



Teating Rhomboid

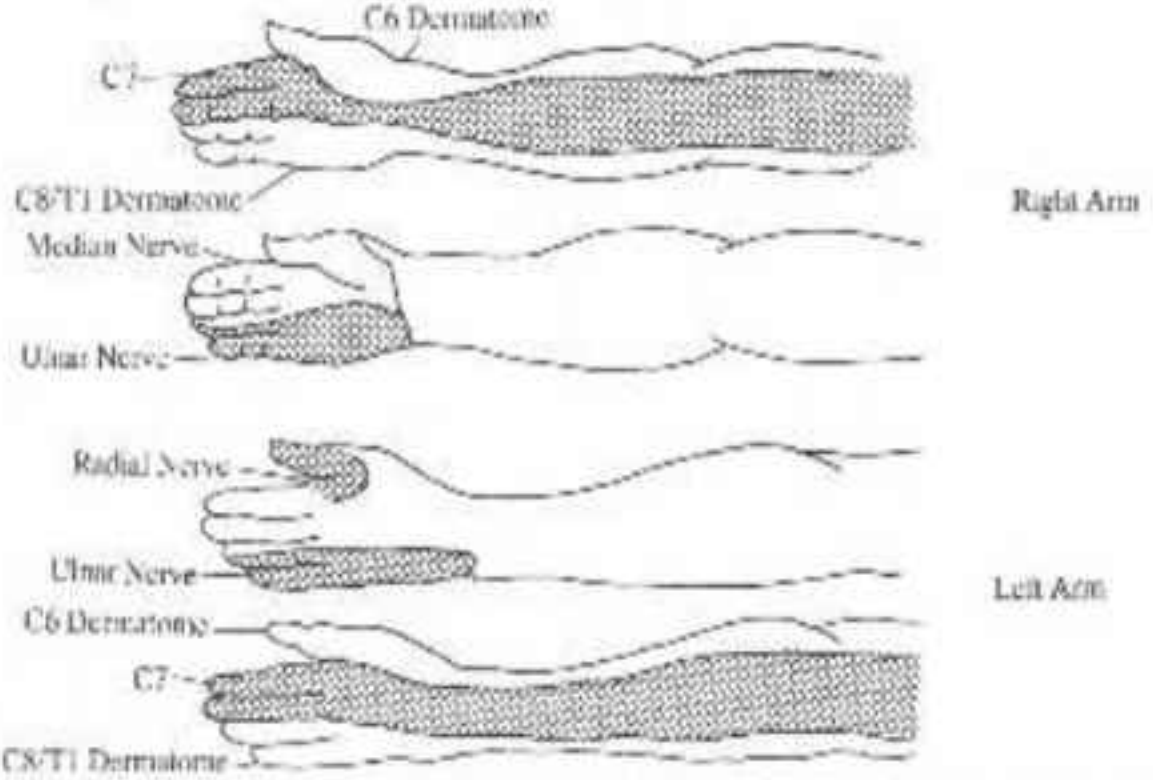
When you have difficulty distinguishing root from peripheral nerve lesions on the basis of atrophy and weakness, you'll have to resort to sensory disturbances. If the sensory loss were ever clear (which it never is), the task of distinguishing root from peripheral nerve would be easier than using motor signs, because the peripheral nerves and roots supplying the same muscle usually supply different areas of skin*. In the patient with atrophy of the first dorsal interosseous (ulnar nerve vs C8/T1), the sensory part of the ulnar nerve splits the ring finger and stops at the wrist, while the

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Different Areas of Skin: The area of skin supplied by a root (or segmental level) is called a sensory dermatome. Unfortunately, sensory dermatomes vary considerably from patient to patient.[7]

Sensory nerves in the hand are pretty reliable and often produce sharper borders than sensory dermatomes. Pay attention to these nerve distributions next time you awaken with a numb hand.

C8 sensory root supplies the entire ring finger and extends up the medial forearm. (T1 supplies the medial arm and axilla.) In the patient with a wrist drop (radial nerve vs C6), both the radial nerve and C6 supply the posterior thumb, but C6 also supplies the anterior surface of the thumb (median nerve territory) and radial aspect of the forearm. (In fact, radial nerve injuries usually produce only a small patch of sensory loss at the crotch of the index finger and thumb.) In the patient with deltoid weakness (axillary nerve vs C5), the axillary nerve supplies the skin over the lower half of the deltoid, while C5 extends beyond this local area.



Distinguishing sensory roots from sensory nerves is more of a problem when sensory loss is the only finding. Is sensory loss over the thumb a C6 sensory radiculopathy or a median neuropathy? The median nerve supplies the entire radial half of the palm, splitting the ring finger and stopping at the wrist. C6 supplies the anterior and posterior thumb, but only the thumb, and extends up the radial side of the forearm. The median nerve supplies the palmar surface of the index and long fingers; C7 supplies the front and back of these two fingers and extends up the back of the forearm. Also, C7 does not split the ring finger.

Not uncommonly you may have to rely on a unilaterally absent biceps or triceps reflex to diagnose a radiculopathy*. The biceps reflex is C6, brachioradialis reflex C6, and triceps reflex C7. Reflexes are lost early in radiculopathies because the afferent limb of the reflex arc is heavily myelinated and compression of the root—the most common cause of radiculopathies—affects the most heavily myelinated axons first, translating into lost reflexes. The thickly myelinated vibratory and proprioceptive axons are next affected, and later, the pain and temperature axons which are smaller, less thickly myelinated. To confirm this order of sensory loss, next time your arm or leg falls asleep (from peripheral nerve compression), see if you can still feel a pin but not a vibrating tuning fork.

Radiculopathy: If the muscle is completely paralyzed, a unilaterally absent reflex is not a radicular sign because the lesion could also be in the muscle or peripheral nerve. To be a radicular sign, the reflex should be depressed out of proportion to the weakness.

Brachial Plexus

How about another common clinical problem. The patient has a weak grip (C8). You postulate as one possibility a median neuropathy of the grip muscles: flexor digitorum superficialis, flexor pollicis longus, and radial half of flexor digitorum profundus, but you also find weakness of the biceps (C6) and deltoid (C5). This pattern does not fit a single peripheral nerve, and multi-radiculopathies are pretty rare. In this case the lesion is likely in the brachial plexus* lying deep within the supraclavicular fossa* just proximal to the shoulder joint. Confirm this anatomic diagnosis by examining the two nerves which take off before the plexus forms: dorsal scapular nerve to the rhomboid muscle and the long thoracic nerve to serratus anterior. If both muscles are normal, the lesion must be distal to their departure from the C5 root, i.e., in the brachial plexus.

One relatively common, nontraumatic insult to the brachial plexus is a poorly understood immunologic condition called brachial neuritis which can affect any nerve exiting the brachial plexus.[8] In the presence of sudden unexplained pain around the shoulder associated with upper extremity weakness that doesn't fit a single root or single peripheral nerve, and spares the rhomboids and serratus anterior, consider brachial neuritis. You can be even more suspicious by finding tenderness (due to presumed inflammation) within the brachial plexus. Stick one hand high up into the patient's axilla while compressing the brachial plexus from above with your other hand in the supraclavicular fossa. If tenderness is present on the weak side but not the other side, the lesion is probably in the brachial plexus, and likely brachial neuritis.

The lower portion of the brachial plexus may be kinked in a condition called the thoracic outlet syndrome. Some people are born with an extra rib jutting out from the 7th cervical vertebra. This extra rib becomes a high hurdle for cervical roots en route to the arm. In other patients, a fibrous band attached to the normal first thoracic rib acts like the extra cervical rib. In either case, the brunt of compression is borne by the lower portion of the brachial plexus (C8–T1), manifesting as hand atrophy. Vascular symptoms in the hand (Raynaud's phenomenon, embolic occlusion) may also occur if the brachial artery is compressed.

The thoracic outlet syndrome is a difficult diagnosis to prove clinically. The most popular physical sign is a positive Adson's maneuver: with your fingertips on the patient's radial pulse, slowly lift his wrist upward and backward so that the patient looks like he is about to pass a football. If the radial pulse disappears, and the patient develops numbness and tingling along the medial arm and hand, the Adson's manuever is positive.[9] Surgical removal of the offending cervical rib and any fibrous bands is usually curative.[10]

Damage to the upper brachial plexus damages the C5 and C6 root fibers controlling the shoulder girdle muscles, and the biceps, brachioradialis, and supinator muscles, a condition called Erb's palsy. This occurs when the shoulder is forcibly stretched away from the neck (as happens during a difficult birth). The arm hangs at the patient's side, internally rotated. In Klumpke's palsy, the lower brachial plexus is injured (C8/T1 fibers), resulting in a weak and atrophied hand.

Brachial Plexus: Brachium is arm, plexus is braid.

Supraclavicular Fossa: The shallow depression above the clavicle (clavicle = key).

Lower Extremity

In the leg the most common root versus peripheral nerve problem is foot drop: weakness of tibialis anterior, an L4-5 muscle supplied by the deep peroneal nerve. Distinguishing between these two anatomic possibilities requires a working knowledge of the peripheral nerves in the leg. The sciatic* nerve cascades out of the sciatic notch in the buttock, and like a waterfall plummets down the back of the leg, then curves under the medial malleolus* into the foot.

Below the knee the sciatic nerve continues as the posterior tibial nerve. The reason for the name change is that a major branch, the common peroneal nerve, parts company from the sciatic just above the popliteal fossa*. The common peroneal wraps around the fibular head while the posterior tibial nerve (the direct extension of the sciatic) continues straight down the calf, supplying the gastrocnemius, tibialis posterior, flexor hallucis* longus, and, after sweeping into the foot, the intrinsic foot muscles. The common peroneal* divides at the fibular head into two branches: 1) the deep peroneal nerve supplying tibialis anterior, extensor hallucis longus, and extensor digitorum, and 2) the superficial peroneal nerve supplying peroneus longus and the skin over the shin and dorsum of the foot.



Sciatic Nerve
Posterior Tibial Nerve



Common Peroneal Nerve



Common Peroneal Nerve

Foot drop (tibialis anterior weakness), then, can be due either to an L5 root or a common peroneal nerve injury. Sensation won't distinguish the two since both L5 and the common peroneal nerve supply roughly the same area over the dorsum of the foot. Nor will the reflexes help much either, because the knee jerk is L4 and the ankle jerk

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Sciatic: From ischion, the Greek hip joint.

Malleolus: Ankle (malleolus means hammer in Latin).

Popliteal Fossa: The shallow depression behind the knee joint.

Hallucis: Big toe.

Peroneal: Peroneal is Greek; Fibula is Latin—both mean buckle or fastener, which the fibula appears to do to the ankle and knee.

is S1*.[11] First propose that the foot drop is due to a common peroneal injury and look for an L5 muscle outside the common peroneal territory. Such a muscle is tibialis posterior which inverts the foot when the foot is plantar flexed. (Tibialis anterior helps invert the foot when the foot is dorsiflexed.) The tibialis posterior tendon is palpable coursing alongside the medial malleolus to insert on the medial undersurface of the foot. Weakness of tibialis posterior makes a foot drop an L5 root lesion, while a normal tibialis posterior strongly suggests focal compression of the common peroneal nerve at the fibular head.[12] Other muscles partly innervated by L5 are the hamstrings, gluteus maximus, and gluteus medius (hip abductor). Confirm peroneal compression by firmly pressing or tapping the common peroneal nerve where it courses around the fibular head; it should be tender there, but not in the opposite leg (see Tinel's sign, chapter 25).

There is a third, and not that uncommon, anatomic possibility for foot drop: sciatic nerve. In addition to tibialis anterior and peroneus longus weakness, look for weakness of the hamstrings, gastrocnemius, tibialis posterior, and foot intrinsics (toe flexors), i.e., the patient's foot should be weak in *all* directions: flexion, extension, inversion, and eversion. The only leg muscles not supplied by the sciatic nerve are above the knee—the psoas* muscle (supplied by an unnamed nerve from the lumbar plexus), the quadriceps (femoral nerve), and the thigh adductors (obturator nerve). Gluteus maximus may also be normal since it is supplied by the inferior gluteal nerve, not the sciatic, but proximal injuries to the sciatic often damage the neighboring inferior gluteal nerve, too. Look for focal tenderness of the sciatic by palpating deep in the sciatic notch where the sciatic nerve exits the pelvis.

The only other frequent root versus peripheral nerve problem in the leg is quadriceps weakness—L4 versus femoral nerve. Both supply the quadriceps, the skin over the thigh, and the knee jerk. But L4 also partially innervates adductor magnus (the thigh adductors are innervated by the obturator nerve), tibialis anterior, and peroneus longus, all beyond the control of the femoral nerve. To help confirm a femoral neuropathy, palpate for femoral nerve tenderness along the femoral canal (under the inguinal ligament).



Obturator Nerve



Femoral Nerve

S1: There is an L5 tendon reflex of the medial hamstring muscle. With the patient prone, flex the knee and rest his tibia on your upper arm. Locate the medial hamstring tendon with your thumb and tap it. With the patient supine, flex his knee slightly and let the leg rotate out to find the medial hamstring tendon.

Psoas: Greek: loin. Filet mignon is the psoas muscle of a castrated bull. The steak is particularly tender because it never been used to flex the hips during mounting and mating.

Mechanical Root Signs

Two maneuvers provide additional evidence of root disease—straight leg raise and cervical compression. A straight leg raise is positive when you elicit pain, or preferably sudden resistance with pain, while flexing the patient's fully extended leg. This maneuver stretches the roots supplying the sciatic nerve (L5, S1, and S2).[15] If you elicit similar, but less severe pain by lifting the *contralateral* leg (the 'crossed straight leg' test), you can be quite confident of a compressive radiculopathy.[15] If the straight leg test is negative, stretch the sciatic further by pulling back on the toes (the patient should wince) and then (if he didn't wince) indenting the popliteal fossa with your fingers, called the 'bowstring sign.' Conversely, when you flex the patient's hip with the knee bent, the sciatic isn't stretched, and the patient should experience little or no pain. With the knee flexed, force the head of the femur into the acetabulum by pulling the heel medially (Patrick's maneuver). If the patient now complains of pain, his pain is from the hip joint, not the root.

Two maneuvers somewhat diagnostic of the upper lumbar roots are hyperextension of the hip[15] or flexion of the knee over the foot of the examining table.[16] Both of these maneuvers stretch the L1–4 roots (but also the lumbosacral plexus and femoral nerve).[17]

You can elicit mechanical root signs in the neck by, instead of stretching the root, pinching it. With both palms, firmly press down on top of the patient's head. This compresses the vertebral column and, with it, the vertebral foramina through which the roots exit the spinal canal. You can exaggerate the narrowing by first tilting the patient's head to one side and *then* compressing the cervical vertebral column. Sometimes merely twisting the neck or bending it backward will pinch the root. If any of these maneuvers reproduces the patient's pain, especially if that pain radiates from the neck into the shoulder, scapula, arm, or hand, then the lesion is likely originating in the root. Presumably an osteophyte or herniated disc is rubbing against the root as it passes through the vertebral foramen. On the other hand, if rotation, flexion, extension, and/or abduction of the *shoulder* reproduces the pain, the problem is an orthopedic one in the shoulder joint.[18] Feel specifically for tenderness of the shoulder joint capsule by sliding your fingertips along the chest wall high up into the axilla while pushing the shoulder downward with your other hand. Or try pushing the humeral head into the shoulder joint by draping his arm over your shoulder and driving the humeral head into the shoulder joint with both your palms.

EXAMINING THE LEG

It's sometimes easier to remember the leg muscles if you reduce the leg into its three joints: hip, knee, and ankle, each of which has a flexor and an extensor. The extensor of the hip is gluteus maximus; flexor of the hip, psoas. The flexor of the knee is the hamstrings; the extensor, quadriceps. The dorsiflexors of the ankle are tibialis anterior and extensor hallucis longus; the ankle plantar flexor, gastrocnemius. The ankle is also capable of inversion and eversion: the ankle invertor is tibialis posterior; the evertor, peroneus longus. Another way to view (and examine) the leg is that there are three muscles down the front (psoas, quadriceps, and tibialis anterior), and three up the back (gastroc, hamstrings, and gluteus) with an ankle evertor and invertor thrown in.

The roots are conveniently organized in the sequence for walking. You begin each step by flexing the hip (psoas: L1,2,3), then extending the knee (quadriceps: L2,3,4),

and then dorsiflexing the foot (tibialis anterior: L4,5). You propel yourself forward by extending the hip (gluteus maximus: L5,S1,S2), and then stepping off with gastrocnemius (S1,2).

Begin the leg exam by having the patient lie flat on his back. After looking for atrophy and fasciculations, ask the patient to lift the leg with the knee bent* (psoas). Grasp the knee and push the leg down, concentrating on your gut exertion. Do both sides. Now, while on the patient's right side, put your left elbow behind the patient's right knee and grasp his left knee cap. Instruct the patient to keep the right leg stiff (quadriceps); you shouldn't be able to overcome a locked knee. Again, compare both sides. Now have him cock his feet back. Feel the bulk and firmness of tibialis anterior, and try to forcibly plantar flex the foot; it shouldn't budge. After doing both sides go to the foot of the bed (with the feet still dorsiflexed) and look at the big toes. Are both pulled back equally far? If not, one extensor hallucis longus is weak. Pull both big toes simultaneously. Extensor hallucis longus is a useful muscle because it is one of the few leg muscles small enough to be overpowered, permitting easy detection of mild weakness. In addition, it's a pure L5 muscle.



Testing Psoas



Testing Tibialis Anterior



Testing Quadriceps



Weak Extensor Hallucis Longus

With the Knee Bent: You can test hip flexion with the knee straight, but you'll also be testing rectus femoris (part of the quadriceps muscle).

Peroneus longus is tested by standing on the medial side of the patient's foot, having the patient evert the foot while you forcibly try to pull it medially. Now stand on the lateral side and try to pull the inverted foot laterally to test tibialis posterior (be sure the foot is plantar flexed). Have the patient curl his toes down while you try to pull them back (flexor hallucis longus and flexor digitorum longus). Verify gastrocnemius strength by asking the patient to step hard on the gas; see if you can prevent it. Now bend the knee and place one hand on his knee to stabilize it, the other hand on the Achilles tendon. Ask him to pull his heel toward his butt (hamstring function), and you concentrate on your gut. Finally, put both legs flat on the bed and have the patient dig his heels into the mattress (gluteus function). You shouldn't be able to lift his heel off the bed without lifting the whole body off the bed, too.



Testing Peroneus Longus



Testing Tibialis Posterior



Testing Gastrocnemius



Testing Hamstrings



Testing Gluteus Maximus

Examination of the gastrocnemius in a supine patient is frequently fruitless; it is such a powerful muscle that fully 20-25% of its strength must be lost before you can detect any weakness. To demonstrate mild weakness of the gastroc, have the patient walk on his toes. Ask him to lift one knee in the air and, while holding your hand for balance, to then raise up on the toes of his other foot. At this point you can also test tibialis anterior and extensor hallicus longus by having the patient rock back on his heels and heel walk.

The hamstrings and gluteus maximus may also be examined with the patient prone. Ask the patient to flex both legs about halfway. Grab both heels from the foot of the bed and instruct the patient to pull both heels as hard as he can toward his butt as you check that both halves of the hamstrings contract. The weak hamstrings will be readily apparent. Now ask him to lift one knee off the mattress (with the knee flexed or bent). Even without forcibly pushing the leg down, you can determine if one gluteus is weak by seeing how high he lifts each knee*.

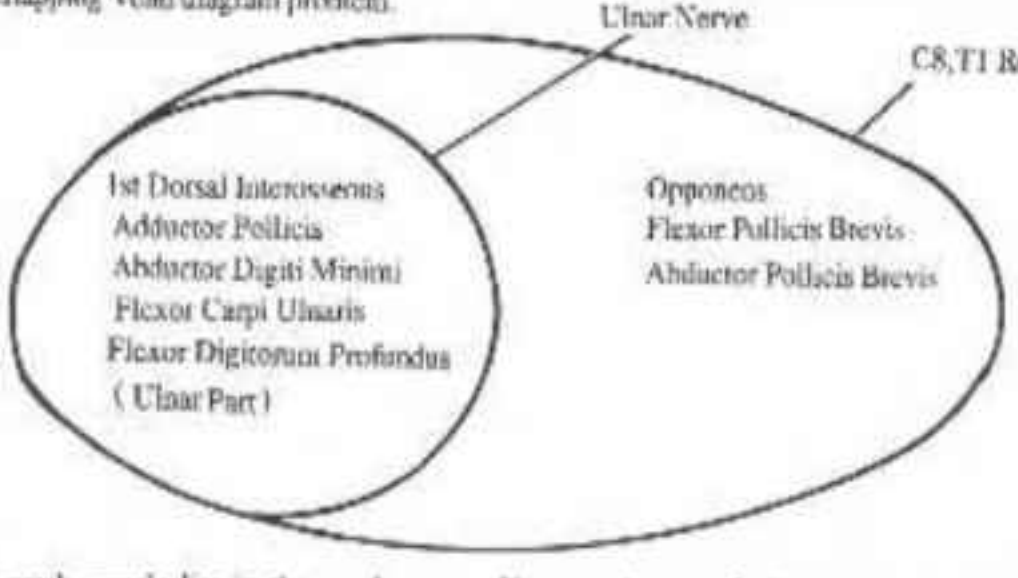


Testing Hamstrings



Testing Gluteus Maximus

Knee: For you right hemispheric people, the problem of distinguishing peripheral nerve from root is an overlapping Venn diagram problem.



The weak muscle lies in the overlap zone. You now have to find a weak muscle outside the overlap zone. Sometimes, as in ulnar neuropathies, one circle is entirely inside the other.

SPINAL CORD SYNDROMES

To diagnose a myelopathy, you need to combine long tract signs with root, or segmental, signs. The root signs necessary for spinal cord localization are not always obvious, particularly in two classic spinal cord syndromes: the Brown-Sequard* and the Anterior Spinal Artery syndrome. Both syndromes disturb half of the cord: Brown-Sequard—the left or right half; Anterior Spinal Artery—the anterior half.

BROWN-SEQUARD

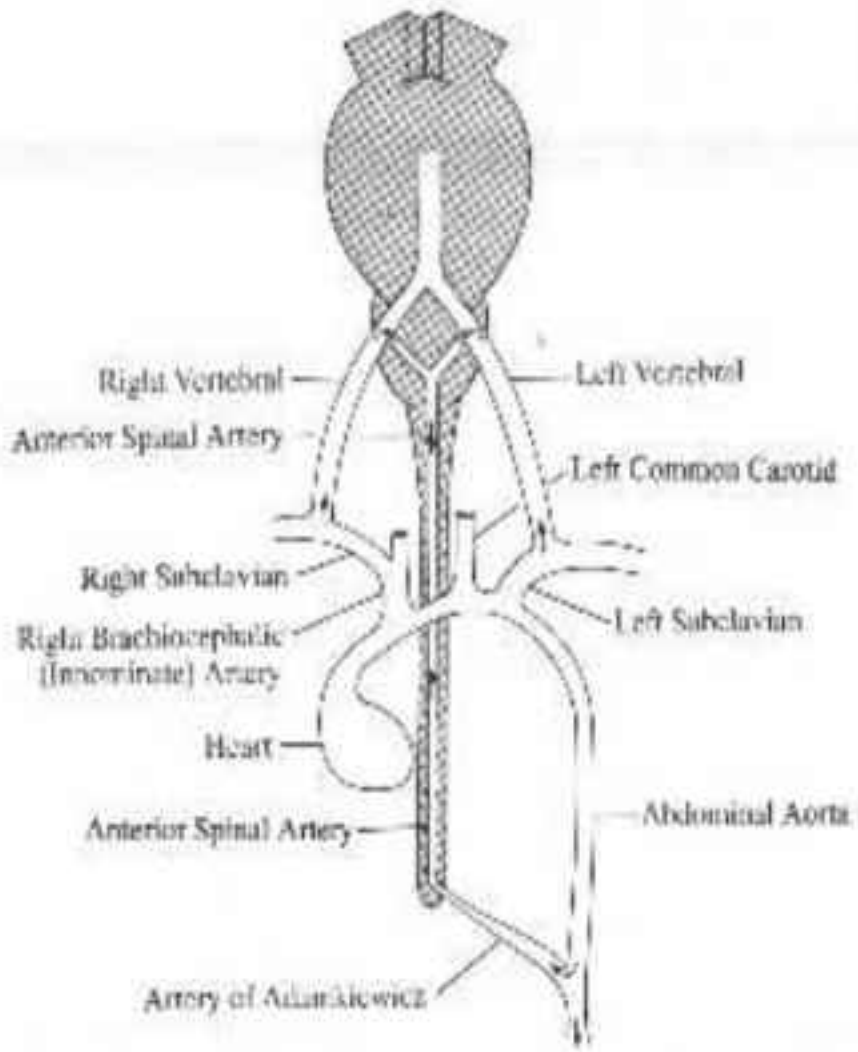
Brown-Sequard at, say, C8 on the right produces pyramidal tract signs in the right leg, flaccid atrophic weakness of the right C8 muscles, pain and temperature loss from T1–2 downward on the left, and loss of vibration and proprioception from C8 downward on the right. The pain and temperature loss is on the left side because pain and temperature fibers from the left side of the body cross to the right side of the spinal cord soon after entering the dorsal horn. And since first order pain and temperature fibers ascend several levels before synapsing onto second order neurons, the superior border of pain and temperature loss on the left side is actually a few segments below the level of the spinal cord lesion.

But what's the horizontal sign—the root or segmental sign—that proves this is a myelopathy? You have four horizontal signs to choose from: 1) the superior margin of the pain and temperature (or touch) loss on the left, called a 'sensory level'; 2) the superior margin of the vibratory or proprioceptive (or touch) loss on the right; 3) a dermatomal strip of *ipsilateral* pain and temperature loss at the exact level of the lesion, where the entering pain and temperature fibers are interrupted before they even have a chance to cross; and 4) ipsilateral lower motor neuron root signs at the level of the lesion. Since it takes several weeks for muscles to atrophy, don't expect to see atrophy and fasciculations in acute myelopathies.

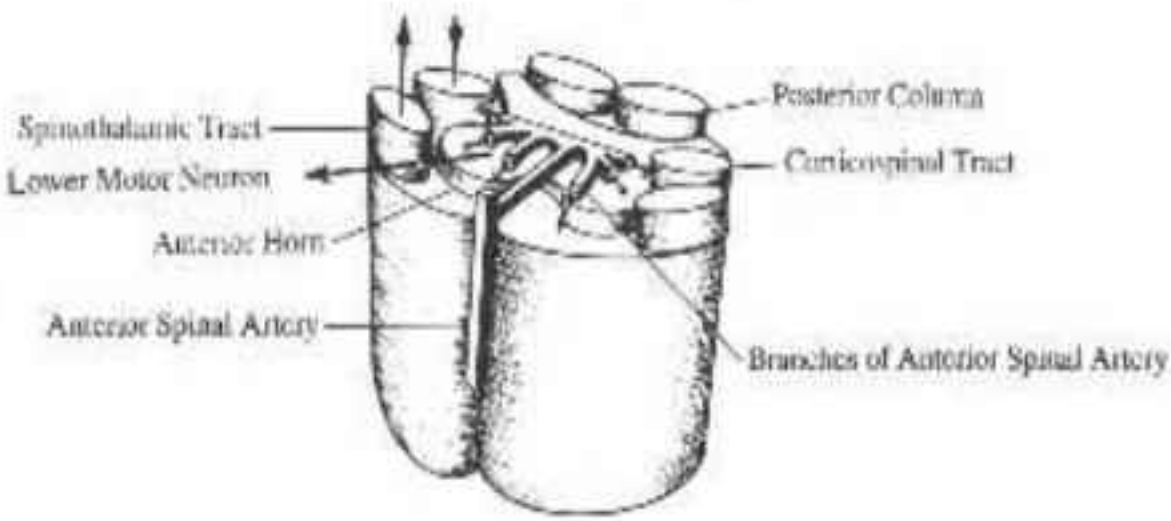
ANTERIOR SPINAL ARTERY

The anterior spinal artery, running the length of the spinal cord, supplies the anterior half of the spinal cord—ventral horns, corticospinal tracts, and spinothalamic tracts.[2] The anterior spinal artery is formed by a branch from each vertebral artery, which together provide one major source of blood for the cord. About midway down the anterior spinal artery—in the mid-thoracic region—blood descending the anterior spinal artery is met head-on by blood ascending from the cord's other major supplier, the artery of Adamkiewicz, a branch off the lower thoracic aorta.[3]

Brown Sequard: A great French neurologist of the last century who, during his peripatetic career, held positions in France, Britain, and the U.S.[1]



Anterior spinal artery ischemia translates into bilateral pain and temperature loss below the level of the lesion but no vibratory or proprioceptive loss, a sensory combination called 'dissociated sensory loss.' The infarcted corticospinal tracts produce the usual five signs of pyramidal tract dysfunction: spasticity (or flaccidity, initially), weakness, slowing of rapid alternating movements, hyperreflexia, and a Babinski. The long tract signs, then, are those of the corticospinal and spinothalamic tracts. The root, or segmental, signs are 1) the superior margin of the pain and temperature loss, and 2) hypotonia and weakness at the level of the lesion from damage to the ventral horns, followed weeks later by atrophy and fasciculations. If, for example, ischemia occurred at the lower cervical-thoracic junction, the patient would develop flaccid, atrophic weakness of both hands (C8/T1), spastic hyperreflexic weakness of both legs, and dissociated sensory loss from C8/T1 downward.

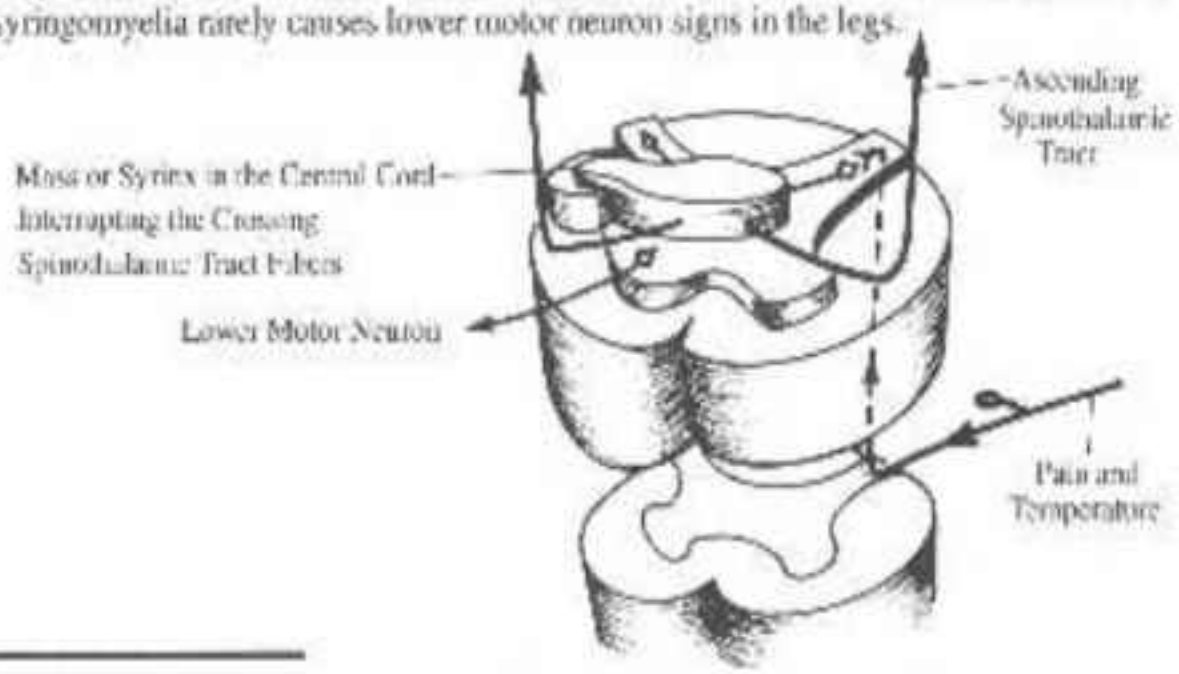


Lower motor neuron signs are less obvious if the ischemia occurs in the thoracic spinal cord, because lower motor neuron weakness of one set of intercostal* muscles is too difficult to determine clinically. Instead, we rely more on the sensory signs, like the superior margin of the pain and temperature loss (a sensory level).[4]

SYRINGOMYELIA

The anterior spinal artery syndrome is one example of dissociated sensation — severe pain and temperature loss without loss of vibration or proprioception. Here's another example. The patient has pyramidal tract signs in the right leg, loss of pain and temperature in the hands but *not* the legs, and no vibratory or proprioceptive loss anywhere. Where is the lesion? The pyramidal tract signs naturally place the lesion in the central nervous system. To explain pain and temperature loss without proprioceptive or vibratory loss, look at where pain and temperature first separate from vibration and proprioception, namely, just after the dorsal roots enter the dorsal horns. A single lesion in the center of the spinal cord would catch the crossing (second order) pain and temperature axons but not the vibratory and proprioceptive fibers. As long as the lesion remains confined to the center of the cervical cord without extending into the spinothalamic tracts (carrying pain and temperature up from the legs), the pain and temperature loss would be confined to the arms. And if the lesion extended laterally into the right corticospinal tract, the spastic right leg would also be accounted for.

Such a condition is frequently due to a congenital, slowly expanding cyst* of the spinal cord, called syringomyelia*. Centrally located spinal cord tumors, with or without an associated cyst*, interrupt the same fiber tracts as syringomyelia. Congenital syringomyelia almost always forms in the cervical region and rarely extends as far as the lumbar cord.[5] So unless the cyst results from spontaneous or traumatic hemorrhage into the lumbar cord,[6] or from a tumor in the center of the lumbosacral cord, syringomyelia rarely causes lower motor neuron signs in the legs.



Intercostal: Costa is rib in Latin. These muscles help expand the ribs on inspiration.

Cyst: A fluid-filled sac.

Syringomyelia: Syrinx is Greek for pipe or tube (like syringe). Myelo means middle or marrow (which also accounts for the term myeloproliferative — proliferation of any marrow-produced cell).

Associated Cyst: Many spinal cord tumors (and brain tumors, too) form a cyst of fluid that can, by acting as a compressive mass, cause as many symptoms as the tumor itself.

Each case of syringomyelia is different because the cysts are highly variable in shape. However, in the upper extremities, the constellation of lower motor neuron signs (atrophy, hypotonia, weakness, and hyporeflexia) and upper extremity dissociated sensory loss* (pain and temperature but not vibratory or proprioceptive loss) is virtually pathognomonic of syringomyelia in the cervical spinal cord*, regardless of any pyramidal tract signs in the legs.

Symmetrical Atrophy of Thenar and Hypothenar Eminences





Note the thumb has rotated back into the plane of the palm



Burn Scars (where he used to put out his cigarettes!)

Occasionally, the syrinx extends up into the medulla (called syringobulbia), causing atrophy, fasciculations, and weakness of the tongue and pharynx. The cyst may also cause an ipsilateral Horner's by interrupting one of the descending sympathetic tracts, a condition which, if present from the time of infancy, prevents subsequent pigmentation of the ipsilateral iris. The iris remains light blue into adult life, called heterochromia.[1]

Dissociated Sensory Loss: Though dissociated sensory loss typically extends from the shoulders (C5) into the upper thoracic dermatomes (the length of a short bolero jacket), any sensory loss may occur (including posterior column involvement), depending on the particular shape and configuration of the highly variable cyst.

Peripheral neuropathies that predominantly affect small axons (carrying pain) may also cause dissociated sensory loss. A good example is amyloid polyneuropathy.[2] Amyloid is a connective tissue protein that has only relatively recently become accessible to investigation. For many years amyloid eluded every known solvent, until a naive medical student tried distilled water.[3] Amyloidosis (deposition of amyloid throughout the body) occurs either genetically or amidst a prolonged inflammatory illness, like tuberculosis.

In the Cervical Spinal Cord: During fetal development the spinal cord is hollow but the central canal closes by birth. According to Gardner, syringomyelia develops when ventricular pulse waves—produced by pulsations of the choroid plexus—reopen the central canal into a cystic cavity. This occurs when congenital crowding around the foramen magnum by the cerebellum and downwardly displaced medulla (the Arnold-Chiari malformation) prevents ventricular pulse waves from being dissipated into the subarachnoid space.[4] (For a review of other theories, see reference 10.)

COMBINED SYSTEMS DISEASE

Another type of dissociated sensory loss occurs in vitamin* B12 deficiency. In this case, the opposite of syringomyelia occurs: vibration and proprioception are lost but pain and temperature are spared. The name for this myelopathy is combined systems disease*. The word "combined" refers to the combination of posterior column and lateral column (corticospinal tract) involvement. Lower motor neuron signs are also present, not from ventral horn involvement, but from the peripheral neuropathy of B12 deficiency. Look carefully for optic pallor, another sign of B12 deficiency*.[12] Though it's known that vitamin B12 is involved in folate and methylmalonyl CoA metabolism (chapter 35), the chemical links to combined systems disease remain a mystery*.

CENTRAL CORD SYNDROME

Suppose an elderly patient is brought in after having been found conscious but paralyzed at the bottom of a flight of stairs. On exam, you find flaccid quadriparesis (worse in the arms) with no sensory loss. Six weeks later he's much improved but you now notice mild atrophy, flaccidity, and hypoactive reflexes in the arms, and moderate spasticity and hyperreflexia in the legs. What happened to this man? This patient suffered an acute hyperextension injury when his chin hit the floor, resulting in contusion and ischemia of the central portion of his cervical cord. Injury to the ventral horns caused the lower motor signs in his arms and hands, and injury to the corticospinal tracts caused the spastic paraparesis. Sensory signs may be relatively mild if, as often happens, the spinothalamic tracts and posterior columns did not become ischemic or contused. In general, these patients make relatively good recoveries considering how severely paralyzed they were at the start.[16]

PITFALLS

Despite the relatively simple ground rules for a myelopathy (long tract and root), anatomic and physiologic pitfalls frequently make accurate localization of spinal cord lesions a real forehead slapper. For example, lower extremity pyramidal tract signs cannot possibly be due to a lumbar disc because the spinal cord terminates at the L1 vertebral body. Pyramidal tracts to the legs terminate *neurologically* at about L4 (Babinski is extensor hallucis longus: L5), *anatomically* behind about the T12 verte-

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Vitamin: Originally thought to be "vital amines," the name was altered when vitamins turned out in fact not to have the chemical structure of amines.

Combined Systems Disease: When Whipple found that he could cure anemic dogs by feeding them raw liver, dogs he had made anemic by bleeding them (making them *iron* deficient), Minot and Murphy decided to feed raw liver to hundreds of anemic patients suffering from combined systems disease. Though Minot and Murphy did the right thing for the wrong reason, it took another 20 years to identify the liver factor, cyanocobalamin (vitamin B12), which cured the anemia and the myelopathy.

B12 Deficiency: Syphilis and multiple sclerosis impersonate B12 deficiency by causing the same syndrome of myelopathy and optic neuropathy.[13]

Mystery: B12 deficiency may do its chemical damage by blocking methyl group reactions.[14] Whether another (rare) cause of combined systems disease—a genetic disease called cystinuria—has the same physiology is unknown.[15]

bral body*. So a spastic paraparesis demands a cervical or thoracic myelogram, not a lumbar myelogram.

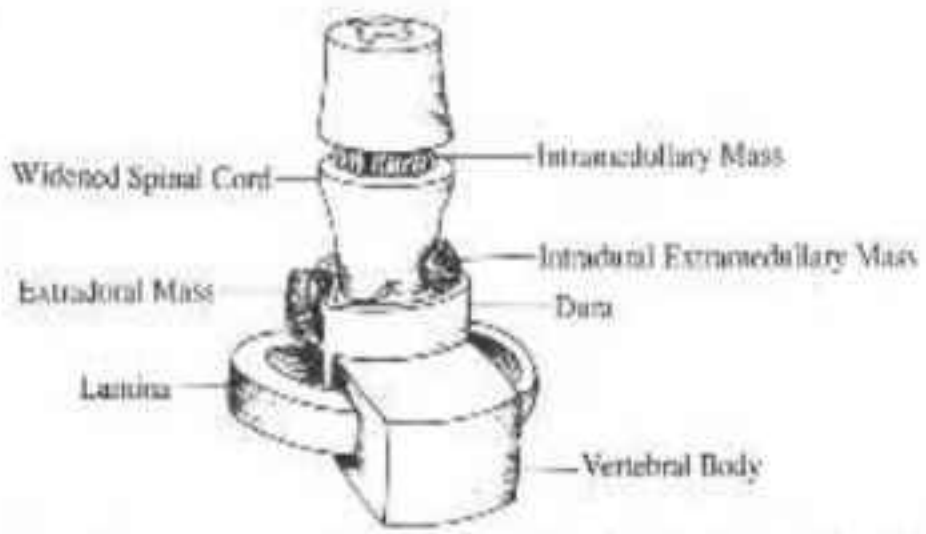
A spastic paraparesis does not automatically place the lesion between the cervical and lumbar regions. The lesion may still be—and frequently is—due to a lesion high up in the cervical region. The probable reason for this is that compressive lesions of the cord, especially anterior ones, seem to damage the cord's blood supply. The leg fibers descending in the corticospinal tracts are apparently more vulnerable to ischemia than the arm fibers.[17]

A hemiparesis sparing the face is not necessarily due to a cervical myelopathy just because the face is not involved; a pyramidal tract lesion in the internal capsule or above can also spare the face. In fact, myelopathies rarely cause a hemiparesis. The diameter of the cord is so small (a dime) that it's difficult for a cervical lesion to injure one corticospinal tract without also injuring the contralateral one.[18]

Finally, atrophy of the hands and arms (C5–8) may legitimately be due to a high cervical extramedullary mass, as high up as the foramen magnum. The party line explanation is, again, interruption of either the arterial or venous blood supply to the lower cervical ventral horns.[19]

EXTRAMEDULLARY VERSUS INTRAMEDULLARY LESIONS

An extramedullary mass is one that lies outside the spinal cord, either intradurally or extradurally.

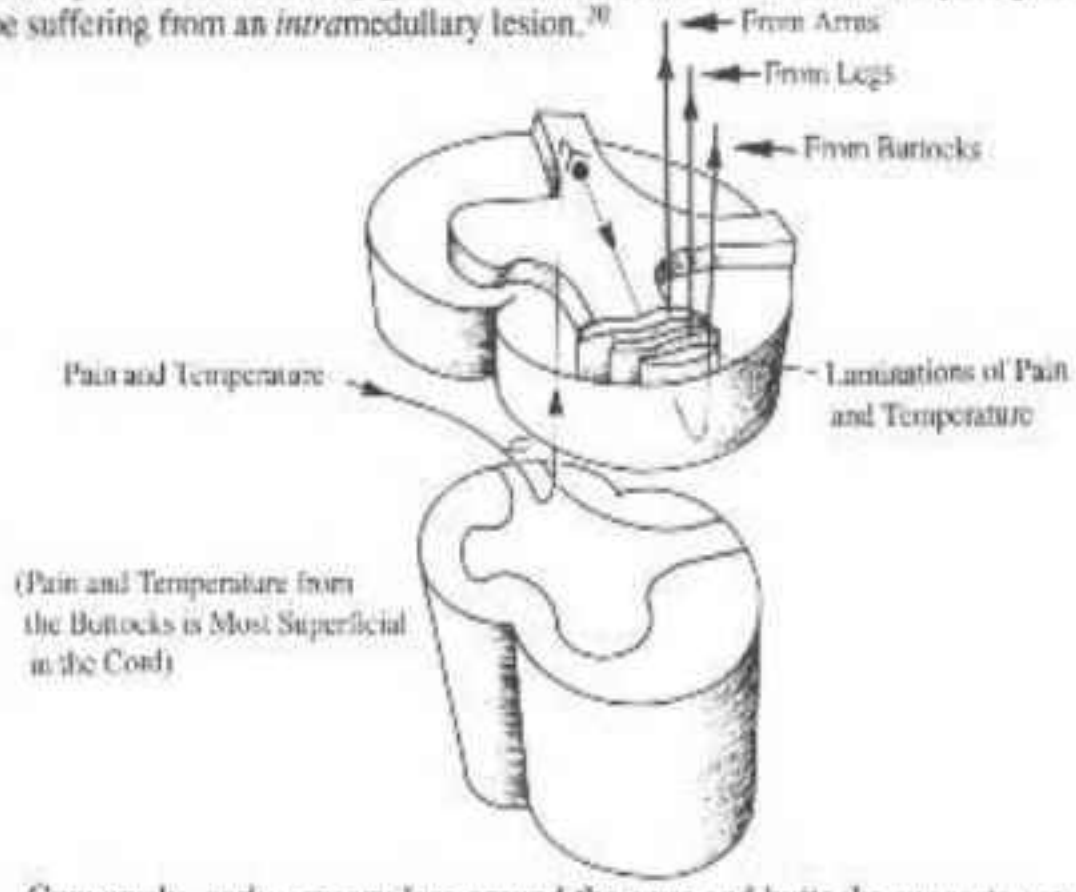


Distinguishing intra from extramedullary spinal cord lesions isn't easy, but there *are* certain clues, especially if the intramedullary lesion is a slowly evolving one. For example, extramedullary masses, which stretch sensitive nerve roots, are more painful than intramedullary masses. In addition, large extramedullary masses (tumors) characteristically cause more pain in the supine position, often forcing the patient to sleep partly upright in a reclining chair. (This is just the opposite of a herniated disc in which lying flat relieves the pain.) Pounding each spinous process and raising a straightened leg often elicit the pain necessary to localize an extramedullary, but not an intramedullary, lesion.

T12 Vertebral Body: You can identify the T12 vertebral body by feeling backward along the bottom of the rib cage (T12 rib) to the spinal column.

Intramedullary lesions, in contrast, are much more likely to produce atrophy (by damaging the ventral horn), dissociated sensory loss (by interrupting the crossing pain and temperature fibers), and early bowel and bladder problems.

Sometimes 'sacral sparing' is helpful. Because sacral sensory fibers in the spinothalamic tracts travel along the outside edge of the cord, they are particularly sensitive to extramedullary compression. Thus, a patient with a spastic paraparesis, a thoracic sensory level, but relatively good sensation around the anus (sacral sparing) may well be suffering from an *intra*medullary lesion.[30]



Conversely, early sensory loss around the anus and buttocks suggests extramedullary compression of the cord. This might be a useful clinical point when, say, a patient presents with radicular atrophy and sensory loss in the left hand, and hypesthesia to pin along the right medial buttock. These signs suggest a localized mass compressing the left C8/T1 roots *and* the outskirts of the adjacent spinothalamic tract.

MYELOPATHIES WITHOUT ROOT SIGNS

Placement of pyramidal tract lesions in the spinal cord requires an intersecting motor or sensory root sign. Often, and in fact usually, we don't find the necessary horizontal signs and are forced to diagnose the anatomic site with pyramidal tract signs alone. Fortunately, there are a number of clues to spinal cord localization even in the absence of horizontal motor or sensory root signs.

For example, an isolated paraparesis or quadriparesis is usually due to a myelopathy, a site where the pyramidal tracts, traveling close to each other, are vulnerable to a single neurologic insult. That is, by localizing the lesion to the spinal cord you can easily account for the bilateral signs with a single lesion instead of gerrymandering several statistically unlikely ones in the brainstem or hemispheres. You'll have to watch out for hydrocephalus, however, which, by stretching the leg fibers en route from the motor strip, also produces bilateral lower extremity pyramidal tract signs. But unless you find other hemispheric signs like confusion, gait apraxia, or seizures, a spinal cord site is much more common.

Another helpful clue to spinal cord localization is early bowel or bladder difficulty, though this problem, too, may occasionally be caused by hydrocephalus which stretches the sphincter fibers originating between the two cerebral hemispheres. A third tip-off to a myelopathy is that pyramidal tract lesions in the cord produce more spasticity than pyramidal tract lesions above the foramen magnum. This is a soft clue, one that leans you toward the spinal cord, but not something to bet the patient's life on. A fourth but weak clue to a myelopathy is dissociated sensory loss (even without a sensory level), as in syringomyelia and vitamin B12 deficiency. And finally, you may have to use a quasi-horizontal sign—focal tenderness of a vertebral body. Though not even a neurologic sign, don't overlook this important finding; it may be the only horizontal sign to work with.

CAUDA EQUINA SYNDROME

Two of the most commonly overlooked locations in the nervous system are the cauda equina and the conus medullaris. Lesions in either location interrupt *multiple* motor and sensory roots to the legs producing, as expected, bilateral lower extremity atrophy and weakness, depressed reflexes, downgoing toes, and a sensory level corresponding to the neurologic level of the lesion. What puts these signs squarely in the cauda equina or conus (and not in the peripheral nerves) is the sensory level and early bowel and bladder involvement: retention, incontinence, and a weak anal sphincter.

If you're unsure about the anal sphincter, check the nerves to it by asking the patient to contract his sphincter around your finger. If it feels like you're sticking your finger in his mouth, his rectal sphincter is weak. Jab the anus with a pin; if that doesn't cause an immediate 'anal wink,' the sensory or motor (and usually both) nerves to the anal sphincter are probably damaged. Same goes for an absent bulbocavernosus reflex: put one finger in the rectum and pinch the head of the penis with your other hand. You should feel the anal sphincter squeeze your finger.[21]

The cauda equina syndrome almost always involves both legs. It would be asking too much of a lesion to selectively damage only one side of the densely packed cauda equina. But when metastatic tumors compress the lower spinal cord, the paraparesis may not involve all muscles equally. Not uncommonly, the hip flexors (L1,2,3) are significantly weaker than tibialis anterior (L4,5) or the gastrocs (S1,2). One possible explanation is that masses compressing the lower spinal cord *directly* compress the ventral horn cells at L,1,2,3. The ventral horn cells may be more vulnerable to compression (or ischemia?) than the corticospinal fibers still descending to L4-S2.

How do you distinguish cauda equina from conus medullaris lesions? Cauda equina lesions are said to be more painful and more asymmetrical than conus medullaris lesions,[22] but it is often very difficult to distinguish the two.

Sphincter involvement and sensory loss are important for distinguishing the cauda equina syndrome from diabetic amyotrophy, an illness which also causes atrophy and weakness of both legs. The difference is that diabetic amyotrophy is a pure motor syndrome affecting primarily the proximal leg muscles (psoas, quads, gluteus, hamstrings) and sparing the anal and urinary sphincters.[23] Etiology remains unknown.

PERIPHERAL NERVES

LOCALIZING LESIONS TO PERIPHERAL NERVES is usually not too difficult, in part because there are only three kinds of peripheral nerve lesions, those affecting: a single peripheral nerve (mononeuropathy), multiple random individual nerves (mononeuropathy multiplex), and all peripheral nerves (polyneuropathy).

MONONEUROPATHY

Upper Extremity

A diagnosis of mononeuropathy or mononeuropathy multiplex is made by finding mixed motor/sensory loss in the distribution of individual peripheral nerves. We have already touched on the six peripheral nerves around the shoulder girdle—spinal accessory (trapezius), dorsal scapular (rhomboids), suprascapular (supraspinatus and infraspinatus), axillary (deltoid), long thoracic (serratus anterior), and musculocutaneous (biceps).

A mononeuropathy affecting the median, ulnar, or radial nerve in the arm produces mixed motor/sensory loss in the distribution of these individual nerves. For example, a median mononeuropathy, caused most commonly by compression within the carpal tunnel*, produces thenar wasting, and weakness of thumb flexion (flexor pollicis brevis), thumb abduction (abductor pollicis brevis), and opposition (opponens pollicis). Entrapment of the median nerve proximally in the antecubital fossa, besides paralyzing the thumb's intrinsic muscles, also:†

Paralyzes these clinically relevant muscles:	So that the patient cannot:
Pronator teres and Pronator quadratus	Pronate the forearm
Flexor digitorum superficialis	Flex any finger at the proximal interphalangeal joints
Median innervated half of flexor digitorum profundus*	Flex the distal interphalangeal joints of the index or long fingers
Flexor pollicis longus	Flex the thumb's interphalangeal joint

In other words, about the only way the patient with a complete median neuropathy can grip is to curl the distal interphalangeal joints of his little and ring fingers by using

---

Carpal Tunnel: A tunnel through the flexor retinaculum, a tough fibrous band at the base of the palm which keeps the tendons, arteries, and nerves anchored to the wrist when the wrist flexes.

Flexor Digitorum Profundus: The ulnar half of flexor digitorum is innervated by the ulnar nerve, and the radial half by the median nerve. So a proximal median neuropathy only affects the distal interphalangeal joint of the two radial fingers, and a proximal ulnar neuropathy only affects the distal interphalangeal joint of the ulnar two fingers.

the ulnar innervated half of flexor digitorum profundus. To test the median innervated half of flexor digitorum profundus, hold the index and long fingers in extension and ask the patient to flex the distal interphalangeal joints.

An ulnar mononeuropathy, almost always due to compression near the elbow (either in the ulnar groove or cubital tunnel*), produces:[3]

Wasting of:	Affecting these muscles:	So the patient cannot:
Palm	Abductor digiti minimi	Abduct (spread) the little finger
	Lumbricals of the ring and little fingers	Fully extend the ring or little fingers
	Interossei	Spread the fingers
Web between thumb and index finger	1st dorsal interosseous	Abduct (spread) the index finger
	Adductor pollicis	Adduct the extended thumb*
Medial forearm	Ulnar innervated half of flexor digitorum profundus	Flex the distal interphalangeal joints of the ring and little fingers
	Flexor carpi ulnaris	Adduct (ulnar deviate) the wrist

At rest, the ulnar nerve damaged hand has a characteristic posture of the Pope's benediction.



Why can't the radial nerve fully extend the ring and little fingers in the presence of an ulnar neuropathy? In order to extend the distal interphalangeal joint, the proximal interphalangeal joint must first be extended. You can demonstrate this by trying to extend your distal interphalangeal joint with a flexed proximal interphalangeal joint; you won't be able to extend the distal phalanx until you first extend the proximal interphalangeal joint. It turns out that the *lumbricals* extend the proximal interphalangeal joints by inserting into the 'extensor hood,' a thin saddle of connective tissue attached to the extensor digitorum tendon of each finger. Since the ulnar two lumbricals are controlled by the ulnar nerve, ulnar neuropathies prevent the ring and little fingers from fully extending*.[4]

Cubital Tunnel: After hooking through the ulnar groove into the medial forearm, the ulnar nerve dives into the cubital tunnel beneath the flexor carpi ulnaris muscle. The V-shaped entrance to the cubital tunnel, formed by the two heads of flexor carpi ulnaris, has relatively sharp edges that may pinch the ulnar nerve.[2]

Extended Thumb: To test adductor pollicis, the thumb must be extended to prevent flexor pollicus longus (median nerve) from adducting the thumb when the adductor pollicus is weak.

Fully Extending: Likewise, median neuropathies prevent full extension of the index and long fingers. This sign is not commonly sought, because atrophy and weakness of the thumb are almost always prominent enough to diagnose median neuropathies.

Lower Extremity

Mononeuropathies in the leg are predictable from straightforward peripheral nerve anatomy. First of all, none of the muscles that move the hip joint are controlled by the sciatic nerve. The hip has four clinically significant directions of movement: flexion (psoas muscle), extension (gluteus maximus), abduction (gluteus medius), and adduction (adductor magnus, longus, and brevis). An anonymous nerve from the lumbar plexus supplies the psoas muscle; the inferior gluteal nerve supplies gluteus maximus; the superior gluteal nerve supplies gluteus medius; and the obturator nerve supplies the thigh adductors. In addition, the pudendal nerve* supplies the perineal muscles* and skin over the privates.

Except for the quadriceps muscle and overlying skin, which are supplied by the femoral nerve, the remainder of the leg is supplied by the sciatic nerve or its divisions. The sciatic nerve descends through the deep buttock down the back of the thigh to supply the hamstrings. Just above the knee, the sciatic gives off a large nerve, the common peroneal, which circles around the head of the fibula to supply the muscles and skin in the front of the leg and top of the foot. Meanwhile, the sciatic continues down the back of the leg using a different name, the posterior tibial nerve. The posterior tibial supplies the gastrocnemius and tibialis posterior muscles, and then slips under the medial malleolus to innervate the intrinsic foot muscles. On entering the foot, the posterior tibial nerve also divides into two sensory branches to supply the skin over the sole, splitting the 'ring' toe.

POLYNEUROPATHY

Polyneuropathies are diagnosed by the constellation of 1) distal, symmetrical, stocking/glove sensory loss; 2) distal, symmetrical, lower motor neuron signs; and 3) absent distal deep tendon reflexes (ankle jerks), and later on, with more widespread involvement, loss of all the tendon reflexes.



Atrophic Gastrocnemius



Atrophic Tibialis Anterior

Pudendal Nerve: Pudendal is from Latin, 'to be ashamed.'

Perineal Muscles: Muscles controlling the rectum, penis, and vagina.

The distal distribution of weakness, stocking/glove sensory loss, and early loss of ankle jerks is explained by the vulnerability of distal nerve ends—lonely outposts dependent upon a tenuous supply line of axonal transport arriving from the cell body*.[5] Anything that disrupts axonal transport will affect the distal nerves first. But why are tendon reflexes also lost relatively early (well before the muscles become weak), and why are vibration, proprioception, and light touch lost before pain and temperature? The answer is that the large diameter, heavily myelinated axons (carrying vibration, proprioception, light touch, and the afferent limb of the tendon reflexes) are particularly vulnerable to many peripheral nerve insults.

This only begs the question: why should axons bearing vibration, proprioception, light touch, and the afferent limb of the tendon reflex be so large and so heavily myelinated? Because large diameter, heavily myelinated axons transmit electricity very rapidly, and the brain needs instantaneous and continuous reports from those sensory fibers. The brain uses sensory information to monitor what's going on inside and outside the body. Far more important, of course, is what's happening internally, information the brain needs for agile coordination. Before deciding how fast, how forcefully, and how short to contract a muscle, the brain must know a number of things. The brain must know the position of the joint that that muscle is about to move, the muscle's existing length, its tension, and—if the muscle is already being contracted—its current position and speed of contraction.[6] And during complex movements, when midstream adjustments may need to be made, the brain must know whether each individual movement was completed successfully.

Proprioception is detected in the joints. Tension is measured in the tendons by Golgi tendon organs, and muscle length is monitored by specialized slivers of muscle, called muscle spindles, buried throughout all muscles (except the eye muscles). Each spindle is composed of two separate types of muscle fibers. One type, called nuclear bag fibers, senses any rapid change in muscle length, and the other type, called nuclear chain fibers, senses the length of its parent muscle*.[8] Tapping a tendon suddenly lengthens the muscle and its spindles. The brain responds to the spindles' sudden outcry by contracting the parent muscle, which you see as the tendon reflex.

Also very important for agility is touch, especially subtle changes in touch*. Pain and temperature are no doubt useful, but how often are instantaneous decisions made

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Axonal Transport from the Cell Body: Many proteins, neurotransmitters, and lipids found in axonal boutons are actually synthesized in the cell body and transported down the axon.

Parent Muscle: Information from the spindle is immediately sent to the cerebellum. During any movement the cerebellum needs to know the moment-by-moment length of each muscle and how fast that length is changing.[7] Signals from the spindle reach the cerebellum by first synapsing in Clarke's column and then ascending up the dorsal spinocerebellar tract through the inferior cerebellar peduncle. Spindles from the arm muscles have no Clarke's column to synapse in; instead spindle axons from the arms ascend in the dorsal spinocerebellar tract to the accessory cuneate nucleus in the brainstem, and then flow into the inferior cerebellar peduncle.

Before a movement takes place, the prefrontal cortex tells the cerebellum what is going to happen. The cerebellum reports back to the motor strip with specific instructions on how to move the limb. Once the movement is in progress, the cerebellum—probably (this is speculation)—decides from its spindle input whether a muscle is lengthening too fast or too slow. The cerebellum can then inform the motor strip—via the dentate nucleus, ventrolateral thalamus, internal capsule—of any changes that need to be made.

Changes in Touch: Vibration is rapidly changing touch.

based on pain and temperature changes? Sure, touching something hot or stepping on a sharp object needs to be known immediately—and there *are* fast conducting pain and temperature fibers for that purpose—but most of the time pain and temperature changes last minutes, hours, or even days, long enough that your very survival doesn't depend on an immediate reaction. Split-second timing and coordination, though, do depend on split-second feedback of touch, proprioception, and muscle length and tension. These kinds of sensation must get to the brain and spinal cord instantaneously in such a way that each new bit of neuronal information is crisply separated from every other subsequent electrical volley, a demanding requirement that makes touch, proprioception, muscle length, and muscle tension especially vulnerable to peripheral nerve insults. Here's why.

Two separate principles are used to get proprioception, touch, muscle length, and muscle tension quickly to the spinal cord and brain. First, large diameter axons conduct faster than small diameter ones. Second (and more important), myelin—a fatty jacket of axonal insulation—hastens electrical transmission from 5 meters per second for an unmyelinated axon to 50–75 meters per second for a myelinated one. This acceleration occurs because every few millimeters there's a gap in the myelin called a node of Ranvier which allows electricity to skip from node to node in a 'saltatory' fashion. The wider apart the nodes, the faster the speed of transmission. As you'd expect, nodes along the large diameter vibratory, proprioceptive, and spindle axons are further apart than those along smaller pain and temperature axons.

By speeding up electrical transmission, myelin cleanly separates each bolus of electricity from the one in front of it and behind it. Any disruption of the myelin disperses these electrical volleys, allowing each signal to contaminate neighboring ones. The result is early blurring of afferent impulses traveling along thickly myelinated axons: vibration, proprioception, discriminative touch, sharp pain, and the afferent limb of the tendon reflexes.[7] Many peripheral nerve insults—arsenic*,[16] lead, and alcohol—select out the large diameter, myelinated axons; other peripheral nerve insults, like Guillain Barre, damage the thick myelin jackets insulating large axons.

SENSORY EXAMINATION

Vibration is assessed in the feet by holding a vibrating* tuning fork against the big toe and asking the patient to signal when the vibration stops. The patient should be able to feel it down to no vibration. So when he says the tuning fork has stopped and you can still *see* it vibrating, vibratory sensation is markedly abnormal. In the hands, simply have the patient hold the vibrating tuning fork by its stem and hand it to you when vibration stops. If you still feel the tuning fork vibrating when he hands it to you, vibration in the hands is abnormal. Loss of pain sensation in a polyneuropathy is recognized by the gradual improvement of pinprick sensation as you tap a pin up the leg or arm.

Arsenic: From the Greek, meaning strong. Arsenic was a favorite poison during the last century because its routine use as an embalming agent prevented any future confirmation of exposure to arsenic during life.

Vibrating: A tuning fork that vibrates at 128 cycles per second gives more valid responses than the smaller 256 cycle one.

Proprioception is tested by moving the big toe or distal finger phalanx and asking the patient to indicate the direction of movement. Begin with large movements to be sure the patient understands how to answer correctly, and then make the movements smaller and smaller. A normal person should be able to detect finger movements which are nearly invisible to the eye.

Severe proprioceptive loss deprives the brain of vital sensory feedback. For example, when standing, we normally depend on proprioception, visual cues, and the vestibular labyrinths to maintain our balance. Losing any two of these will make us ataxic, as demonstrated by the Romberg test: the patient with severe proprioceptive loss balances adequately when standing at attention but quickly loses his balance when he shuts his eyes, depriving the brain of its second means of maintaining balance—vision. Unless such a patient looks at his feet when walking, his brain won't know where his feet are. The brain may pick them up higher than it needs to or else slap them down too forcefully, believing the foot needed another six inches to reach the floor.[11]

A Romberg test of the hands is performed by having the patient close his eyes and hold his arms outstretched with the fingers spread apart; the fingers drift aimlessly ('pseudoathetosis') because the brain no longer knows where they are in space.

Remember that proprioceptive loss may be due to a severe polyneuropathy, posterior column dysfunction, or even parietal lobe dysfunction. What points you to a polyneuropathy is the symmetry of the stocking/glove sensory loss (including pin prick), absent distal reflexes, and, in some polyneuropathies, distal symmetrical atrophy of the hands and feet.

Sensory testing can be exasperating. Trying to map out a patient's sensory loss is often so tedious that unless it's obvious, you can get lost pursuing nuances of the patient's sensory disturbance*. Certainly the hand deserves careful attention where median and ulnar neuropathies can be confused with C6, 7, and 8 radiculopathies. Other important sensory deficits are a myelopathic sensory level; the distal, symmetrical vibratory, proprioceptive, and pin prick loss in the feet and hands from a polyneuropathy; sensory loss along the L5 dermatome (big toe) or S1 dermatome (lateral side of the foot); and meralgia* paresthetica (numbness over the lateral thigh) from compression of the purely sensory lateral femoral cutaneous nerve*.[12] And be sure that the patient's 'stroke' consisting of a hemiparesis and hemihypesthesia isn't, in reality, Brown-Sequard—check carefully for that contralateral hemihypalgesia.

Sensory Disturbance: Though numbness may be bothersome to the patient, concentrate on the patient's *motor* signs. Most of the time numbness does not impair function. A lot of people believe that surgeons can repair everything, and a lot of surgeons believe that everything needs repair. Unfortunately, doctors hurt almost as much as they help, especially when trying to repair isolated numbness. Before considering surgery, ask yourself if the patient is disabled enough by his physical findings to justify the risks of invasive tests and surgery. A motor deficit, and preferably a progressive motor deficit, is a much clearer indication for surgery.

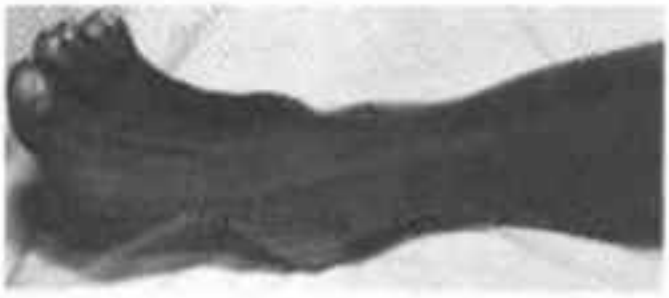
Meralgia: Meros is thigh in Greek. Algesia is pain (analgesics are pain killers).

Lateral Femoral Cutaneous Nerve: For other, rarer compression sensory neuropathies (like the superficial branch of the radial, suprascapular, genitofemoral, saphenous, sural, and T2–6 dorsal nerves), see reference 12.

MOTOR EXAMINATION

Distal symmetrical atrophy, the classical motor sign of a polyneuropathy, is more difficult to appreciate in the chunky foot than in the relatively flat hand. Look for an excessively high arch (pes cavus), evidence of intrinsic foot atrophy. Feel the individual foot muscles. Is there plenty of meat between you and the metatarsal bones? Ask the patient to dorsiflex his feet so you can check the extensor digitorum brevis muscle, a sensitive indicator of distal, polyneuropathic atrophy.[11]

Extensor Digitorum Brevis





Pes Cavus

In severe polyneuropathies long *and* short peripheral nerves are affected, so that the weakness is no longer confined to distal muscles—proximal *and* distal muscle become weak*. As you will see in the next chapter on muscles, widespread weakness is also a sign of muscle dysfunction. The signs that make widespread weakness polyneuropathic instead of myopathic are: 1) reflexes depressed far out of proportion to the weakness, 2) the presence of sensory involvement, and 3) fasciculations (if there are any).

ADDITIONAL SIGNS OF PERIPHERAL NEUROPATHY

Direct examination of individual peripheral nerves can detect three important signs of peripheral nerve pathology: nerve enlargement, Tinel's* sign, and tetany. Two good places to feel for enlarged nerves are along the extensor pollicis longus tendon and across the sternocleidomastoid muscle. You should always be able to feel a small sensory twig of the radial nerve running perpendicularly across the extensor pollicis longus tendon, but the greater auricular* nerve crossing the sternocleidomastoid is generally impalpable until it's hypertrophic. The ulnar nerve in the ulnar groove and the common peroneal nerve wrapping around the fibular head are both readily accessible, but so often subject to trauma that pathologic enlargement may be hard to judge.

Tinel's sign is produced by sharply tapping a peripheral nerve. If there is a focal lesion (usually compression) at the site of tapping, each time you tap, an electric shock should radiate in the distribution of the nerve. Focal nerve tenderness (without radiation) is a type of Tinel's sign and it, too, usually means focal nerve compression, or at least focal inflammation, at the site of tenderness. Important places to look for Tinel's sign are:

Become Weak: This is especially true in Guillain Barre, one of the few peripheral neuropathies that may begin proximally.[12] The reason for this is that, even early on, demyelination probably affects proximal and distal parts of the peripheral nerve.[16]

Tinel: A French neurologist of the early 20th century.[17]

Auricular: Auris is ear in Latin.

Site	Peripheral Nerve
carpal tunnel	median nerve
pronator teres	median nerve
ulnar groove	ulnar nerve
cubital tunnel	ulnar nerve
medial wrist	ulnar nerve
spiral groove*	radial nerve
proximal dorsal ulna	radial nerve
supraclavicular fossa	brachial plexus
ischial (sciatic) notch	sciatic nerve
femoral canal	femoral nerve
iliac crest*	lateral femoral cutaneous nerve
obturator canal	obturator nerve
medial thigh	saphenous nerve*
fibular head	common peroneal nerve
tarsal* tunnel	posterior tibial nerve

Tetany is an involuntary contraction caused by continual stimulation from a superexcitable peripheral nerve, typically made so by hypocalcemia or alkalosis. To verify nerve supersensitivity, tap the facial nerve as it emerges from under the parotid gland in front of the ear; that side of the face will involuntarily contract with each tap, called Chvostek's sign. Another way to demonstrate tetany is to make the median nerve ischemic with a blood pressure cuff inflated above systolic pressure. The hand will slowly squeeze into 'carpopedal spasm,' called Trousseau's sign, as if it were grasping a tiny pea with all five fingers.

Four other illnesses also have continuous muscle activity: tetanus, Isaac's syndrome, the stiff man syndrome, and Schwartz Jampel. Only Isaac's syndrome is due to a disturbance of peripheral nerves.

Tetanus* toxin causes diffuse, severe muscle spasms by disrupting small inhibitory cells in the spinal cord. Normally, every time a neuron fires, it shuts itself off by sending a signal to a neighboring inhibitory cell, the Renshaw cell, which returns to the neuronal cell body with an inhibitory signal. Tetanus toxin, like strychnine poisoning, paralyzes the Renshaw cell (and other inhibitory neurons); the lower motor neuron doesn't get turned off which you see as widespread sustained spasms.[16]

Spiral Groove: The radial nerve wraps around the back of the humerus in the spiral groove. You can feel the radial nerve by locating the spot where the deltoid inserts on the humerus. Inch your fingers to the back of the humerus between the deltoid and triceps muscles. As you roll your fingertips along the backside of the humerus bone, feel the radial nerve roll under your fingers.

Iliac Crest: The bony ledge of the pelvis.

Saphenous Nerve: Sometimes in removing the saphenous vein for use in cardiac bypass surgery, surgeons may inadvertently injure the saphenous nerve, a sensory branch of the femoral nerve. The patient complains of numbness, tingling, and dysesthesias along the medial side of the calf, knee, and lower thigh.

Tarsal: The instep.

Tetanus: Greek: to stretch, because patients suffer opisthotonic spasms in which the body arches backward into painful hyperextension with the head thrown back.

Isaac's syndrome ('neuromyotonia') causes its brand of muscular spasm by inexplicably stimulating distal twigs of peripheral nerves.[19] This peculiar site of pathology was decided upon after investigators terminated the spontaneous contractions by neuromuscular, but not by peripheral nerve, blockade.

The stiff-man syndrome is characterized by severe bouts of painful, widespread muscle spasms often precipitated by movement. Eventually the bouts of contractions become continual. The pathophysiology is uncertain, but (like tetanus) probably represents inadequate inhibition of lower motor neurons in the spinal cord.[20]

Schwartz-Jampel afflicts children with a characteristic puckered expression, stiff joints, and widespread muscular contractions. The pathophysiology of the abnormal muscular contractions, though still unclear, seems to lie within the muscle membrane.[21]

The final pathognomonic sign of peripheral nerve dysfunction is hyperpathic, dysesthetic, supersensitive skin. We've all experienced such a condition after sitting too long in one position and allowing a leg or arm to fall asleep from focal peripheral nerve compression. The intense, burning, at times unbearable discomfort we endure waiting for the limb to recover is the same as that elicited by slapping the skin of some patients with peripheral nerve dysfunction. In its extreme, the patient won't even allow you to get near the skin, won't allow a bedsheet to touch it, won't even allow air to blow across it. This extreme sensitivity, called causalgia*, usually results from a single, moderately traumatic injury to a peripheral nerve, not enough to transect it, but severe enough to disrupt it. Subsequent changes in the nerve (or spinal cord?—the exact pathophysiology is not known[23]) cause the patient to recoil from any stimulus—even the anticipation of being touched—with severe burning, jabbing, electric, 'neuropathic' discomfort that continues long after the stimulus has stopped. In addition, causalgia makes the skin supplied by the involved nerve dystrophic: shiny, thin, and soft.[24] Treatments for causalgia vary considerably because no one treatment is universally effective. The most consistently effective therapy is, mysteriously, blockade or severance of the sympathetic nerves to the involved area.[25]



Note Thin Atrophic Skin and Muscle Atrophy in Ulnar Nerve Distribution

Two clearly different kinds of pain have evolved in man: fast pain and a phylogenetically older slow pain. Fast pain, the sharp pain felt when you first hammer your fingernail ("ouch!"), is immediately felt, well localized, and elicits a quick withdrawal flinch. Slow pain, the terrible throbbing pain that follows ("owwwww..."), is slower in onset, poorly localized (the whole finger hurts, not just the nail), and elicits

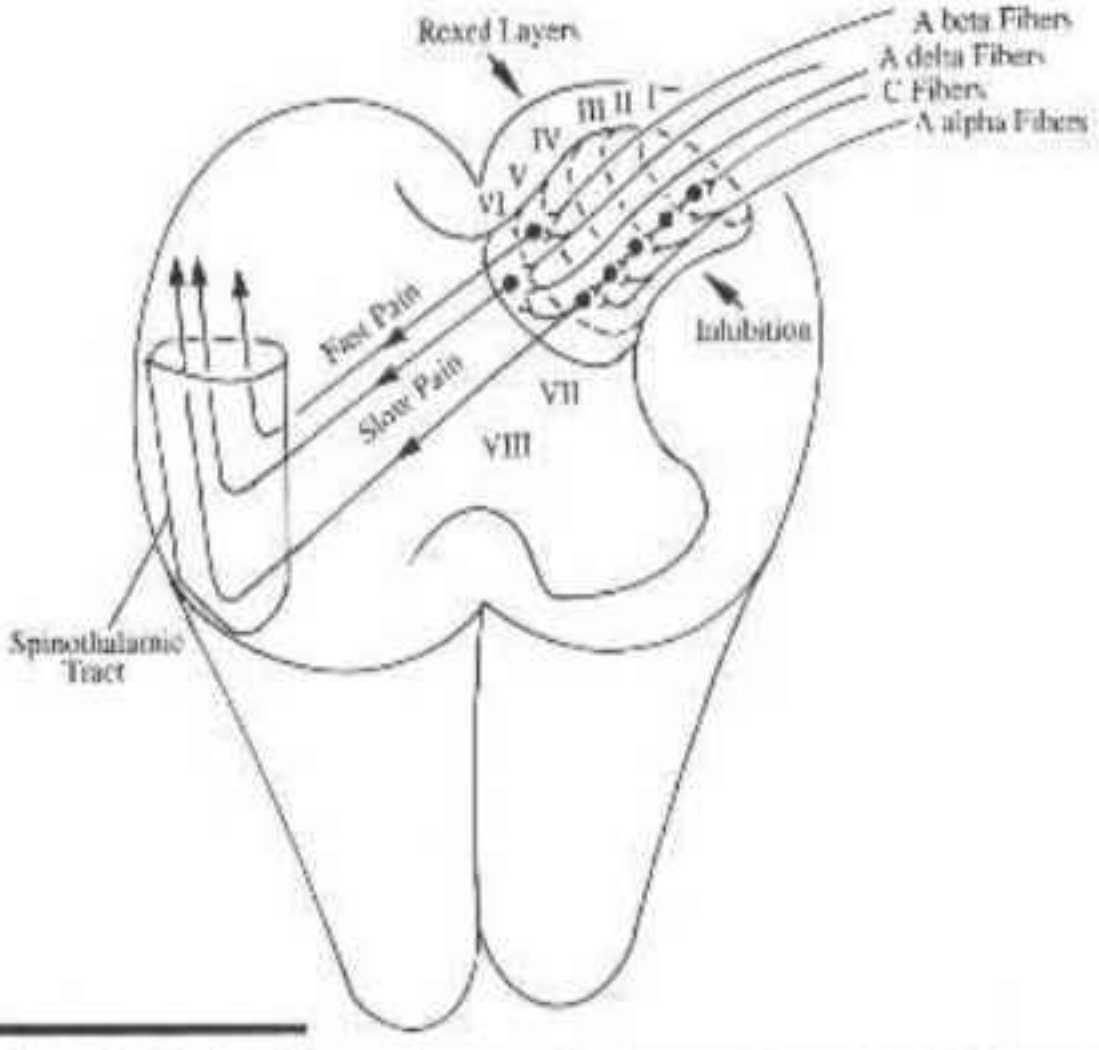
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Causalgia: Kausos means heat in Greek. Pain similar to causalgia may follow limb amputation, a condition called phantom limb pain. The pathophysiology is as baffling as that of causalgia.[22]

prolonged muscular spasm (immobilizing the painful area). Fast pain has a low threshold but then mercifully stops when the painful stimulus stops. Slow pain has a higher threshold but once that threshold is crossed, there follows a crescendo of deeply aching, emotionally charged agony accompanied by nausea, sweating, and tachycardia, all of which far outlasts the stimulus*. The type of stimulus (heat, pin, pinch, crush, knife cut) causing fast pain is accurately discerned, while slow pain all feels about the same—severe, deep, aching, tearing, throbbing, and burning—regardless of the stimulus.[27]

The uncomfortable burning and tingling after sitting on a peripheral nerve too long is probably due to compression of heavily myelinated axons.[28] As these axons recover (when you move your leg), spontaneous impulses are unleashed from the compressed segment of the nerve.[29] The diameter of the damaged axon is relatively unimportant. Painful neuropathies occur even when small diameter C fibers are selectively lost, as in diabetic polyneuropathy.[30]

Fast and slow pain are carried to the dorsal horn of the spinal cord by two kinds of nerve fibers. Fast pain travels at 5–30 m/sec along moderately myelinated A delta fibers. Slow pain takes a slower route (0.5–2 m/sec) along the far more prevalent, unmyelinated C fibers.[31] A delta fibers synapse superficially in layer I and more deeply in layver V. C fibers synapse primarily in layer II.[32]

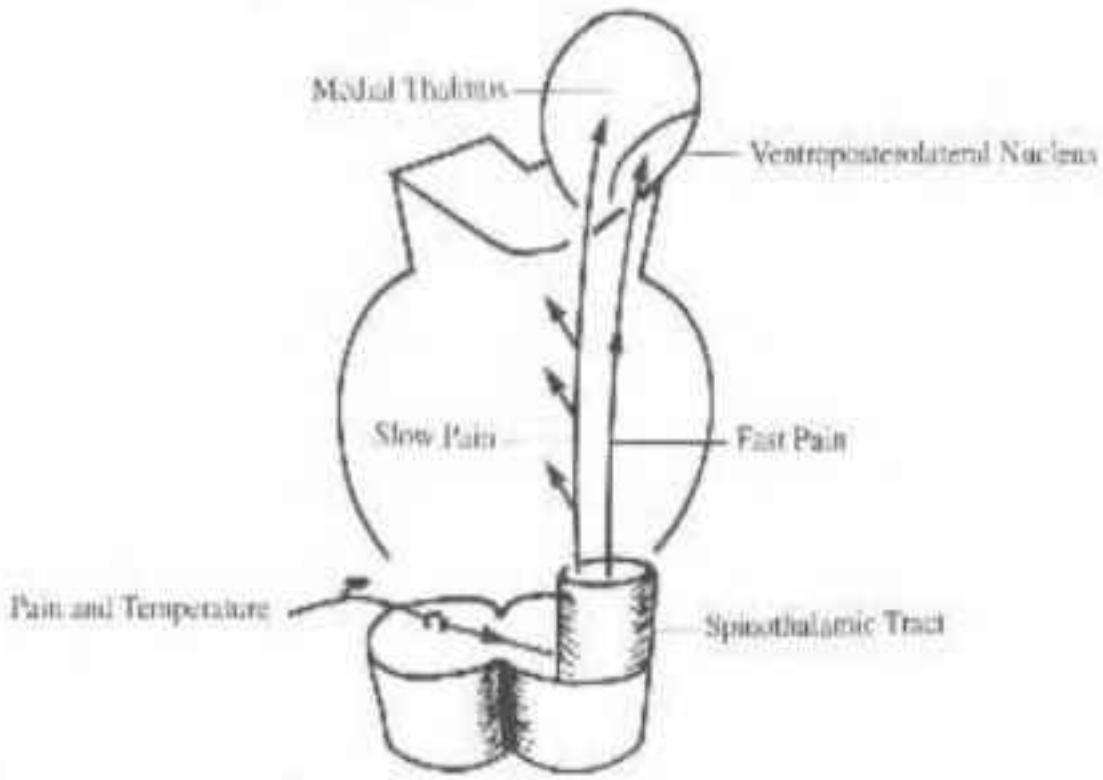


Outlasts the Stimulus: You can demonstrate this phenomenon in causalgia by lightly tapping the skin with a pin, each tap below the threshold of pain. Each tap accumulates a bit more pain, so that after four or five such taps the patient suddenly reacts as if you had delivered a single suprathreshold stimulus, a phenomenon called recruitment.[26]

Slow pain begins its passage up the spinal cord from the deepest layers of the dorsal horn, layers VI-VIII.[33] Neurons here are like sleeping dogs: they remain quiescent until a threshold of pain is crossed. Once aroused by tissue damage, however, they erupt with a vicious volley of impulses into the spinoreticular and spinothalamic tracts.[34] Painful stimulation reaches the deepest layers only after synapsing first in superficial layers and then cascading inward. Pain signals are normally prevented from cascading inward into the deepest layers by heavily myelinated vibratory and proprioceptive axons synapsing in the middle layers II-IV. Without those large, protective, inhibitory fibers, practically any trivial pain would have free access to layers VI-VIII, evoking highly uncomfortable, burning pain*.

Layer V is an interesting area because many of its neurons are quite versatile, responding not only to pain signals from the skin and viscera, but also to a variety of non-painful sensations from the skin. This physiologic arrangement makes these 'wide dynamic range' neurons a point of convergence for visceral pain and non-painful skin sensation, and explains why, for example, cardiac pain is referred down the left arm.[37]

From layers VI-VIII, slow pain ascends along two spinal pathways.[38] One, the spinoreticular tract, plugs into the brainstem's multisynaptic, central reticular system to alert the brain of impending serious tissue injury. Simultaneously, slow pain travels up the contralateral spinothalamic tract to 'nonspecific' (intralaminar) cells in the medial thalamus, cells with widespread connections to emotional and autonomic centers in the limbic system and hypothalamus.

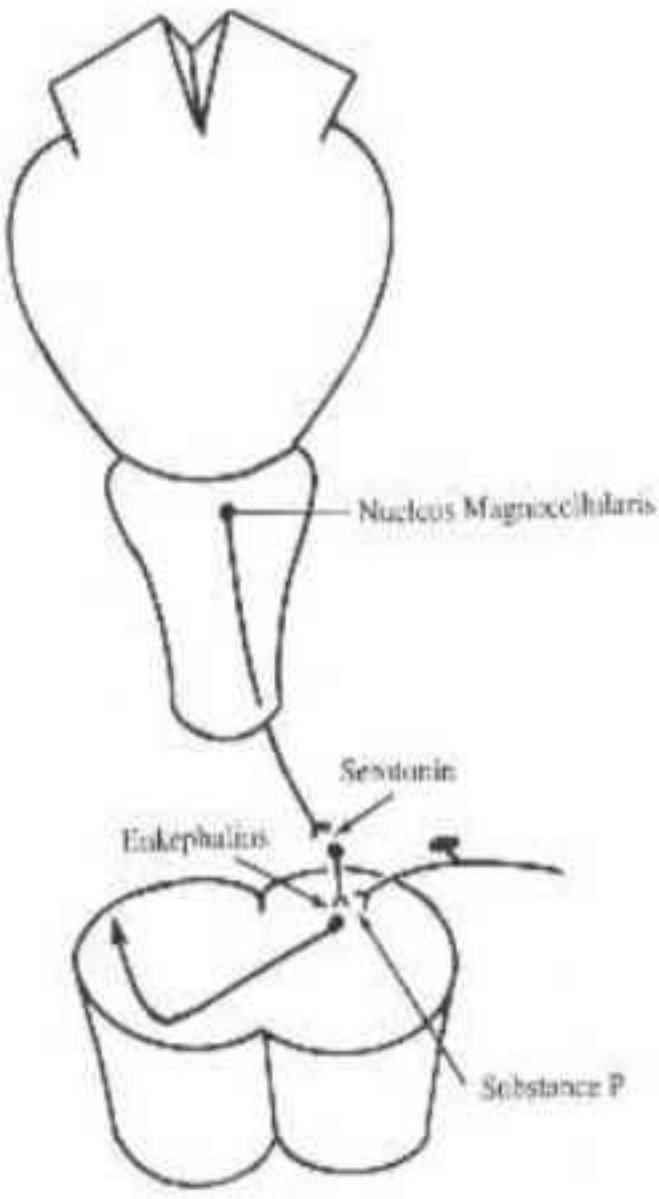


Burning Pain: You can corroborate the analgesic properties of vibratory axons the next time you bump your head. Rapidly rub the skin (vibrating it) and notice how much less intense the pain becomes. Or you can stimulate the large fiber system with a transcutaneous electrical stimulator to prevent A delta signals from reaching the deep, second order slow-pain neuron.[35]

Another way to turn on the large diameter, inhibitory fibers might be to tense our muscles, an action which activates large diameter afferent fibers from the muscle (2spindle afferents).[36] Perhaps this explains why we clench our jaws or grip something in anticipation of doctors' needles and knives.

Sharp pain, in contrast, beginning from layers I and V, leaps quickly up the contralateral spinothalamic tract to the thalamus' ventroposterolateral nucleus (VPL) and then immediately up to the sensory strip for a rapid, critical analysis of the nature of the insult, its location, and its duration to mobilize a response to the pain. Occasionally, small thalamic lesions 'unbalance' the two pain systems to produce an uncomfortable burning of the contralateral side of the body, called thalamic pain.[39]

The brain is capable of dousing pain entering the spinal cord. Inhibitory neurons in the periaqueductal gray of the midbrain and in the medulla (nucleus magnocellularis) descend to the dorsal horn to release a neurotransmitter serotonin, which stimulates another neuron to release a peptide called enkephalin. Enkephalin prevents substance P, the neurotransmitter released by pain fibers entering the cord, from stimulating second order pain fibers bound for the contralateral spinothalamic tract.[40] Acupuncture and morphine work in part by stimulating this descending inhibitory pain system[41,42] while the drug amitriptyline alleviates chronic pain in part by preventing the reuptake of serotonin released in the dorsal horn.



Inhibitory Pain System: Morphine inhibits the slow pain system, but not the fast one.[43]

MUSCLE

THE LAST SUBSYSTEM of the neuromuscular system is muscle, a subsystem with its own set of characteristic signs that include proximal weakness, pseudohypertrophy, contractures, myotonia, widespread weakness, and weakness with tenderness.[1]

PROXIMAL WEAKNESS

Proximal weakness is the most common sign of a myopathy*. Focus on the neck flexors, the deltoids, biceps, triceps, supraspinatus and infraspinatus, and—around the pelvic girdle—the psoas, glutei, quadriceps and hamstrings. Historically, the patient has trouble washing her hair, reaching for objects on the top shelf, and getting off a toilet or out of a bathtub.

On exam watch the patient get up from a chair. Does she have to lean forward and push off with both hands, signifying pelvic girdle weakness? Note any excessive lordosis in the standing position, indicative of psoas weakness. As you watch the patient walk, concentrate on her belt or hips. Patients with proximal weakness waddle, because the weak gluteus medius muscles allow the pelvis to tilt from side to side. Normally, gluteus medius elevates the hip slightly to permit the ipsilateral leg to swing forward into the next step without scraping the toe. Without gluteus medius, the hip, instead of elevating, dips with each step.

When trying to get up off the floor, children adapt to pelvic girdle weakness with a characteristic maneuver called Gower's sign: from an all fours position, they lock both knees and then push their trunk back over their legs by bracing their hands on their thighs.[2]

Myopathic muscles may atrophy over the years as individual muscle fibers gradually die off, but you shouldn't see fasciculations, a sign of neuropathic atrophy.

PSEUDOHYPERTROPHY

A pseudohypertrophic muscle is one that's surprisingly weak considering its enlarged contour. Unfortunately, only the contour is enlarged, not the muscle, because the muscle has been replaced by fat and connective tissue. This sad condition is most commonly seen in the calf muscles of young boys with Duchenne's* muscular dystrophy*.

Myopathy: Some peripheral neuropathies, most notably Guillain Barre, also cause proximal weakness. Kugelberg Welander, a congenital disease of lower motor neurons, is another example of proximal neuropathic weakness.

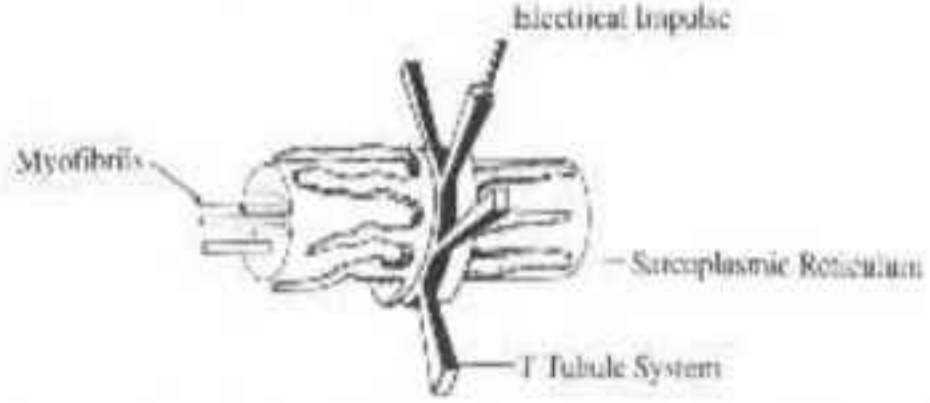
Duchenne: A mid-nineteenth century French physician who carefully examined and categorized many neuromuscular diseases with the aid of a primitive electrical stimulator. By stimulating either the nerve or muscle directly, he distinguished neuropathic from myopathic disorders.

Muscular Dystrophy: Any genetic, progressive deterioration of muscle. (Dys = mal, trophy = nourishment.)

CONTRACTURES

A contracture is a hard, contracted muscle. Contractures are not cramps. Cramps are involuntary contractions due to a disturbance in the nerve innervating the muscle—anywhere from the nerve's departure in the ventral horn to its destination in the terminal bouton. Contractions are an active, energy-consuming process. The muscle will relax as soon as the nerve quits firing.[3]

A contracture, in contrast, is locked into a shortened state. No active contracting is taking place; the muscle is electrically silent*. Normally, a muscle contracts when a nerve impulse passes into the muscle and stimulates the release of calcium from the sarcoplasmic reticulum*. This free calcium stimulates long, thin strands of interdigitating proteins, called actin and myosin, to slide past one another like the bristles of two hair brushes pressed together. The whole muscle is thereby shortened and remains so until the sarcoplasmic membrane actively (using energy from ATP*) recaptures the free calcium. Actin and myosin can then slide back again to their resting state.[4] If, because of inadequate ATP, calcium is not rebound up into the sarcoplasmic membrane, the muscle will remain in a fixed, shortened state—a contracture.



The most common reason for calcium not to get rebound into the sarcoplasmic reticulum is inadequate ATP production by the muscle*. It takes three things for mitochondria to make ATP, and if any one of them is missing, the patient may suffer painful bouts of contractures. The three ingredients for ATP production are glucose, oxygen, and fat. Glucose molecules are shaved off hunks of glycogen by an enzyme called glycogen phosphorylase. Glycogen is stored in two separate sites, liver and muscle. Consequently, there's a liver phosphorylase and a muscle phosphorylase. The glucose released from hepatic glycogen is released into the bloodstream and picked up, with the aid of insulin, by any organ needing glucose (except the brain which absorbs glucose without insulin's help). This makes the internal organs vulnerable to

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Electrically Silent: Electromyography (chapter 44) is usually necessary to distinguish an actively contracting cramp from an electrically silent contracture.

Sarcoplasmic Reticulum: The endoplasmic reticulum is a network of intracellular tunnels where proteins and other cell products are synthesized. In muscle, the endoplasmic reticulum is called the sarcoplasmic reticulum (sarco = flesh).

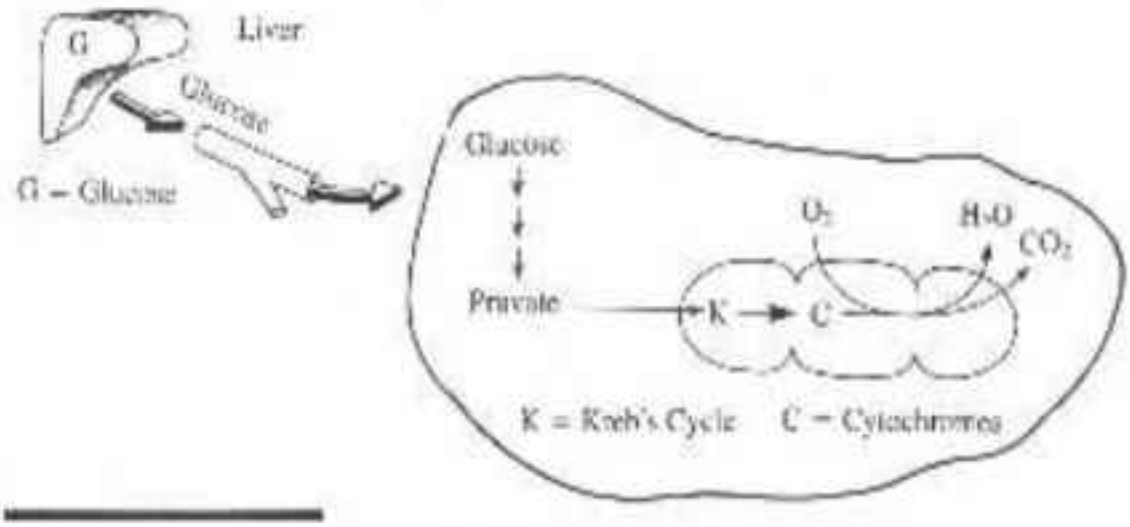
ATP: Energy for the body's thousand or so chemical reactions is stored in high energy phosphate bonds, the most common one by far being adenosine triphosphate (ATP). ATP is synthesized in subcellular structures called mitochondria—miniature power plants that take in oxygen and acetyl CoA and spew out ATP.

By the Muscle: A good example of this is rigor mortis—stiffening of a corpse.

hypoglycemia, except for muscles. By storing their own glycogen, muscles are no longer at the mercy of the blood glucose. In fact, muscles are so jealous of their private stock of glucose, that the glucose stored in muscle glycogen cannot be released into the bloodstream even during bouts of hypoglycemia; the glucose may only be used locally within the muscle*.

Glucose is metabolized down the glycolytic pathway into two pyruvate molecules. Pyruvate decarboxylase then strips pyruvate of one of its carbons and transports the resulting two carbon fragment into the mitochondrial Krebs cycle as acetyl CoA. Up to this point only two ATP molecules have been manufactured, but the Krebs cycle now takes the two pyruvates generated by a single glucose molecule and churns out an additional thirty-six ATP's. Meanwhile, DPNH, a byproduct of the Krebs cycle, is passed along to another chain of ingenious mitochondrial enzymes, the cytochromes, which strip the hydrogen off DPNH, combine it with oxygen to make water, and return DPN to the Krebs cycle.

During times of starvation, fat may substitute as a source of acetyl CoA. Fat is carried in the blood as triglycerides, a molecule of three long-chain fatty acids attached to a small glycerol molecule. In the bloodstream, fatty acids are stripped off the glycerol backbone and transported into the cell. To enter the mitochondria, the fatty acids (primarily palmitate) are first hooked up with carnitine, a molecule synthesized in the liver and delivered to the muscle. Then, carnitine-palmityl-transferase, an enzyme straddling the mitochondria membrane, transports the carnitine-palmityl couple into the mitochondrion where palmitate is immediately chopped into two carbon fragments of acetyl CoA for the Krebs cycle*.



Locally Within the Muscle: Being so dependent on glucose, the body has devised a third source of glucose besides liver and muscle glycogen—protein itself. By cleaving an ammonia group off certain amino acids, the body can convert muscle (the largest ready source of protein) into glucose during periods of starvation.

Krebs Cycle: Except for the brain, all organs require insulin to admit glucose. Without insulin (diabetes mellitus), and hence without glucose, cells must resort to lipids for the necessary acetyl CoA to make ATP. For reasons that in some way involve glucagon (the hormone that raises blood sugar), diabetics allow excess lipids to enter their mitochondria, which then churn out enormous amounts of acetyl CoA. The excess acetyl CoA is recombined into ketoacids and released into the bloodstream, producing a life threatening condition called diabetic ketoacidosis. Not only does the blood pH drop dangerously low, but hordes of excess glucose and ketoacids overflow into the kidney tubules, dragging water with them into the urine. Without fluid replenishment, the patient soon becomes dehydrated and acidotic.

The complexity of this system is both good and bad. It allows us to use fat for energy when three days of starvation deplete our liver and muscles of glycogen, but any slip-up in the delivery of acetyl CoA or oxygen can lock muscles into painful and dangerous contractures. (We'll get to the problems of glucose and fat delivery in chapter 35, Genetic Illnesses.)

Inadequate oxygen delivery usually results from ischemia, such as lying on the muscle for 12-24 hours following a coma-producing stroke or a drug overdose. Ischemic contractures are also a risk to vigorously marching soldiers. Their tight boots can prevent arteries and veins from perfusing the anterior compartment[4] at a time when their marching muscles desperately need the oxygen. The anterior compartment muscles become paralyzed in a contracture. The muscles soon begin to die and swell, and after a while the tight boots don't matter—the swollen muscles themselves compress the vascular supply, creating a vicious cycle. Ugent surgical decompression (cutting the constrictive fascia overlying the tibialis anterior muscle) may relieve the pressure in time to save the anterior compartment muscles from permanent damage.[5]

Another illness which locks muscles in their contracted state is malignant hyperthermia, a genetic illness which, upon exposure to certain general anesthetics, suddenly unleashes severe, widespread, and sustained muscular contractures*. Heat generated by these contractures may raise the body's temperature to 106° or more. How general anesthetics prevent the reuptake free calcium following muscular contractions is still unclear.[7]

MYOTONIA

Myotonia is a highly characterstic myopathic sign resulting from delayed relaxation after the muscle contracts. The reason myotonia is pathognomonic of muscle dysfunction is that the delayed relaxation can be precipitated by hitting the muscle membrane[8], unlike neuropathic types of continual contractions (tetany, tetanus, Isaac's syndrome, stiff-man syndrome, and Schwartz-Jampel).

Anterior Compartment: The compartment anterior to the tibia, containing tibialis anterior, extensor hallucis longus, and peroneus longus.

Sustained Muscular Contractures: What makes contractures (and even sustained contractions) so dangerous is myoglobinuria and subsequent renal shutdown.[6] Weakened by an inadequate supply of ATP, muscle cells release myoglobin into the bloodstream. Being small enough to filter through the kidney glomerulus, myoglobin leaks into kidney tubules and precipitates in the urine coursing through the kidney tubules. Enough precipitation can block the renal tubules, shutting down all urine production. Fortunately, since the glomeruli aren't damaged, this type of acute renal failure usually cures itself with time and medical support. More importantly, by anticipating myoglobinuria you can prevent acute tubular necrosis by administering enough fluids to flush myoglobin through the kidneys before it can sludge in the kidney tubules.

Hitting the Muscle Membrane: The physiology of myotonia is only partially understood[8]—once the muscle contracts, voluntarily or passively (after being struck), it keeps on contracting. It's as if the muscle membrane itself were irritable and once stimulated, cannot stop discharging.

In hypothyroidism, rapping a muscle may make it mound up ('myoedema') not unlike a myotonic contraction. Rapping the muscle is thought to jar calcium loose from the sarcoplasmic membrane, causing the muscle to contract. Apparently the myoedema persists because calcium reuptake is also impaired.[9]

Sharply rapping the thenar eminence causes a myopathic thumb to rotate into opposition where it sits for a few seconds and slowly, over 15 or 20 seconds, gradually returns to its resting position. Another way to elicit myotonia is to support the forearm with the wrist relaxed and rap the belly of extensor digitorium. The wrist pops up, remains up, and gradually drifts back down. If that doesn't work, ask the patient to make a tight fist. When you instruct him to quickly open the hand, his sluggish fingers open like a time-lapse nature film of a blossoming flower. Eyelid myotonia—have the patient squeeze his eyes shut and then open them quickly—looks like Stan Laurel waking up the morning after.

Myotonia occurs in three major illnesses, all of them genetic: myotonia congenita, myotonic dystrophy, and paramyotonia congenita. Myotonia congenita is an autosomal recessive illness consisting of myotonia precipitated by sudden exertion, but relieved by continued exercise. In childhood, the excessive muscular contractions create muscle-bound little dynamos known as Atlas children.

Myotonic dystrophy is a much more serious, autosomal dominant illness affecting virtually every organ system in the body: mild dementia,[10] cataracts,[11] hyperglycemia,[12] arrythmias,[13] dysphagia,[14] low serum IgG, testicular atrophy, wasting of the hands (one of the few distal myopathies), and of course, widespread myotonia. The diagnosis is usually evident before the patient even sits down—temporalis wasting, frontal balding, ptosis, masseter wasting ("hatchet face"), partially open mouth (masseter and temporalis weakness), sternocleidomastoid wasting ("swan neck"), and hand wasting*. Strangely enough, affected infants born to mothers (but not to fathers) with myotonic dystrophy frequently present at birth as floppy, weak babies with a poor suck. Affected infants given the disease by their fathers are almost always normal at birth. Apparently, some maternal factor crosses the placenta and harms the fetus.[15]



Myotonic Dystrophy

Frontal Balding

Temporalis Atrophy

Ptosis

Swan Neck

Sternocleidomastoid Atrophy



Hand Wasting: If the diagnosis of myotonic dystrophy isn't obvious when the patient enters the room, it should be obvious when he shakes your hand and, because of myotonia, can't let go. As a rule, if a patient shakes your hand and doesn't let go, palpate for testicular atrophy with your other hand. Myotonic dystrophy is easy to spot if you're prepared for it.



Sternocleidomastoid Atrophy

Paramyotonia, short for paradoxical myotonia, refers to the paradoxical worsening of myotonia with continued exercise (unlike myotonia congenita) followed by weakness during the rest period. And when exposed to cold, paramyotonic muscles first become very myotonic and then, if the temperature drops below 20° C, stiffen up into electrically silent contractures; myotonia congenita muscles are only mildly affected by cold.[16] The fundamental defect in paramyotonia is probably related to potassium movement across the muscle membrane, because occasional siblings suffer from severe bouts of widespread paralysis associated with hyperkalemia. Which leads us to the fifth characteristic myopathic sign—widespread, symmetrical weakness without sensory loss.

WIDESPREAD SYMMETRICAL WEAKNESS

In patients with widespread symmetrical weakness, pay particular attention to any sensory loss so you don't confuse myopathic weakness with Guillain Barre, an acute peripheral neuropathy which, though it resembles myopathic paralysis, usually has some distal vibratory loss. Moreover, in polyneuropathic weakness the reflexes are depressed out of proportion to the weakness. Still, it may be difficult to distinguish myopathic paralysis from Guillain Barre without a history of previous attacks. Guillain Barre virtually never strikes twice, while the muscle disease called periodic paralysis is *characterized* by recurrent bouts of quadriplegia.[17]

Fortunately, and inexplicably, these periodic attacks of paralysis do not, with rare exception, affect the muscles controlling respirations, swallowing, speaking, or eye movements. Since the periods of paralysis are accompanied by disturbances of serum potassium (usually hypokalemia, occasionally hyperkalemia), the mechanism of paralysis is connected with the flux of intramuscular potassium.[18]

WEAK AND TENDER MUSCLES

Tender, weak muscles indicate that the cause of the weakness is in the muscle, such as inflammation in the muscle, in the muscle's fascial coverings, or in the intramuscular arteries. Unfortunately, tenderness does not automatically indicate myopathic weakness, because inflammatory polyneuropathies[19] and ongoing denervation(?) may also produce weakness with muscular pain and tenderness.

When looking for muscle tenderness, be sure to squeeze the whole muscle with your palm and fingers, not just your fingertips. This avoids pinching the skin and producing a false impression of tender muscles.

NEUROMUSCULAR JUNCTION

Muscles above the shoulders are particularly susceptible to myasthenia gravis and botulism*, two illnesses which attack the neuromuscular junction. When patients present with a pure motor syndrome dominated by ophthalmoplegia*, ptosis, weakness of chewing and smiling, difficulty sucking through a straw, dysphagia, dysphonia, tongue weakness, and difficulty holding their head up, but without pyramidal tract signs in the arms and legs, think neuromuscular junction, especially if the signs improve after a night's rest (typical of myasthenia gravis).



Myopathic Smiles

Botulism: Botulos is sausage (Latin), historically a common source of the toxin. Botulinus bacteria only grow in the *absence* of oxygen. To rid our cities of sewage while producing a nutritious source of protein, it's been proposed that sewage be cheaply devoured by botulinus, and the resulting toxin be destroyed by heating the goop to 160° Fahrenheit for 30 minutes. Would need quality control.

Ophthalmoplegia: Almost any external ophthalmoplegia can be mimicked by myasthenia gravis: internuclear ophthalmoplegia, up- or downgaze palsy, VIth nerve palsy, and pupil-sparing IIIrd nerve palsy.

There is one major exception to the general rule that illnesses of the neuromuscular junction preferentially affect muscles above the shoulders. That illness is the Eaton Lambert syndrome, a blockade of neuromuscular transmission due in some way to remote cancer, usually lung cancer.[20]

Electricity reaching an axonal bouton discharges packets of acetylcholine into the neuromuscular junction. Acetylcholine then stimulates post-synaptic receptors which discharge the muscle. After stimulating the post-synaptic membrane, acetylcholine is dispensed with by an enzyme, acetylcholinesterase, lying in the post-synaptic membrane. In botulism, the acetylcholine packets cannot release their contents, and in myasthenia gravis the receptors have been damaged by immunologic attack*.[21]

Neuromuscular blockade produces 'fatigable' weakness, weakness which worsens with each contraction. The easiest place to see this is in the eyelids. Ask the patient to fix on a target above his head; after 30–60 seconds the eyelids softly droop**. You can reverse this neuromuscular fatigue acutely (but transiently) with an intravenous drug called edrophonium (Tensilon) or slowly (but for a longer period) with an oral drug called pyridostigmine (Mestinon). Both of these drugs inhibit acetylcholinesterase, thereby allowing acetylcholine to hang around longer in the neuromuscular junction to do double duty.[26]

Immunologic Attack: Though neuromuscular junctions suffer most from the immunologic attack, they probably do not instigate it. Unfortunately, investigators have still not identified the infuriating antigen to immunologic surveillance.

Droop: Four other eyelid signs indicative of myasthenia gravis are the lid twitch,[22] the peek sign,[23] transient eyelid retraction,[24] and the enhanced ptosis sign.[25]

HYSTERIA, MALINGERING, AND HYPOCHONDRIASIS

THERE ARE ONLY TWO THINGS IN THIS WORLD THAT MOTIVATE PEOPLE: love and money. Unfortunately, conflicts over them frequently end up in the doctor's office where the unsuspecting doctor accepts the patient's complaints at face value and then wanders off on a wild goose chase looking for organic illnesses. Even when the doctor does recognize hypochondriacal complaints and hysterical signs, he's reluctant to diagnose a functional* illness until all possible organic ones have been ruled out. No doctor wants to spend everyone's time and money searching needlessly for doubtful illnesses, but diagnosing functional illnesses on the basis of hysterical signs* alone can be a treacherous business.

For one thing, it's not that hard to find hysterical signs. Even patients with organic illnesses may embellish their true organic deficits with additional hysterical ones to convince you of their emotional, financial, and medical needs. Just because you find some hysterical signs does not make the patient's entire illness hysterical. It's easy to throw the baby out with the bath water without first deciding if, underneath the camouflage of hysterical signs, there exist any true, organic ones*. It's also very easy to get angry at a patient when you think he's not trying or actually faking (malingering*), but this is an absolute no-no.[1] Discipline your anger; it's too difficult to think rationally when you're angry, and as often as not you're wrong about the patient's hysterical signs.

Functional: 'Functional' originally implied the normal function of an organ, but that original meaning became sidetracked.[1] It's now used to mean no organic (chemical or structural) cause, loosely encompassing hysteria, conversion reaction, and malingering.

Hysterical Signs: Any unconsciously motivated sign that helps solve an unrecognized conflict or need, frequently a taboo one for that patient.[2] Hysterus means uterus in Greek. Seemingly confined to women, hysteria was thought by early (male) physicians to stem from an affliction of the uterus. For more on the history of hysteria, see Chodoff.[3]

Organic Ones: Sometimes the signs are organic, but surreptitiously instigated by the patient. Such professional patients are called Munchausens, after the adventures of Baron von Munchausen.[4] They may drink blood to simulate a GI hemorrhage, bleed themselves into anemia, place their thermometers in hot water, or anything else to convince the doctor of a bona fide illness.

Malingering: Consciously faking a symptom or sign to gain something, like money.

Sometimes you can get a peek at the patient's own inside knowledge of his 'deficit' by asking him what bothers him most. If his deficit is not of the utmost concern, he must know there's nothing truly to worry about, i.e., the deficit is fake. Stoic patients* also carry on without, what you consider, normal concern. But the concern is there if you ask them. Hysterical patients remain unconcerned, almost good-natured about their handicap, an attitude called 'la belle indifference.'

When you think a patient is (unconsciously) hysterical or (consciously) malingering, try to determine why the patient needs his illness. What unresolved conflict is he trying to solve with his illness?[6] Find out what specific activities are curtailed by his problem: job, sex, home responsibilities, school, friendships, etc. Does the problem interfere with activities you can assume he enjoys, like sleeping or hobbies? By knowing why the patient needs his illness, you can at least help him confront the emotionally charged conflict and begin to find new ways to manage it more effectively.

Hysterical signs present more often in the nervous system than in any other organ system. Beginning in the cortex, functional signs manifest as seizures, stuttering, amnesia, and coma.

Seizures

The most definitive test for psychogenic seizures is a normal EEG during the seizure, especially if the seizure involves loss of consciousness or any motor phenomenon*.[5] If you're not lucky enough to capture the spell on an EEG, a postictal EEG should be slow, and therefore the absence of postictal slowing suggests a psychogenic seizure.[5] Short of these EEG findings, it can be very difficult on clinical grounds to diagnose psychogenic seizures*. For example, self-injury and urinary incontinence, symptoms frequently used to diagnose organic seizures, may also occur with psychogenic seizures.[11] If you happen to witness a motor seizure, concentrate on the jerking: is there a quick and slow phase (a true jerk) or simply a tremor (probably hysterical)?[12] Are both arms jerking synchronously, or is the patient simply thrashing about?[13] (To complicate matters, even thrashing about may occur in temporal lobe seizures.[14]) Are the eyes deviated to one side*?

Probably the most reliable clinical test to confirm a psychogenic seizure would be your ability to say or do something to the patient that stops the seizure. This may include ridicule, threats, enticements, or any non-injurious maneuver. Even significantly altering a motor seizure would be very suggestive of hysteria, though admittedly during psychomotor automatisms or prolonged absence seizures patients may, like sleep walkers, follow commands or even carry on a reasonably coherent conversation.[10] And of course, one psychogenic seizure does not make all the patient's seizures hysterical.[12] Nor does improved seizure control during hospitalization mean that the patient's seizures prior to hospitalization were hysterical; many patients improve simply by being hospitalized without any change in medication.[14]

Stoic: Unmoved by emotional events. Named after a school of philosophy in ancient Greece.

Motor Phenomenon: There have been a few temporal lobe patients who, during a temporal lobe seizure, demonstrated no change in the baseline EEG.[7]

Psychogenic Seizures: Major motor convulsions raise the serum prolactin level,[15] so if you're unsure about the 'convulsion' you or the nurse just witnessed, draw a prolactin level.

Deviated to One Side: Eye deviation doesn't necessarily tell you which side the seizure focus is on, but eye deviation is at least a good indicator of ongoing seizure activity.[15]

Stuttering

Stuttering or hesitation alone, without spelling or grammatical mistakes, is not aphasia except in very rare instances. And without dysgraphia, which nearly always accompanies true aphasia, isolated stuttering from a cortical lesion must be almost unheard of.

Amnesia

Amnesia, when it includes the patient's own name, is usually hysterical. A person who forgets his own name has lost the very essence of his being, almost the soul itself. Since your name is a constantly refreshed memory, a loss of identity should be accompanied by a loss of both remote and recent memory, a distinctly rare condition without an obvious severe cerebral insult.

Try to establish the integrity of the temporal lobes by assessing the patient's ability to lay down new memories. Inability to do so, as in transient global amnesia, suggests an organic lesion, especially if the patient repeated badgers you for information just told to him. Pure retrograde amnesia without other diffuse cortical signs like loss of insight, inability to lay down new memories, confabulation, impaired reasoning, or impaired judgment must also be very rare, especially without a history of a severe cerebral event*.

Coma

Hysterical coma can be most easily diagnosed by performing cold calories. The presence of nystagmus indicates retained physiologic connections between the brainstem and cortex, and therefore no physiologic basis for the coma. Obviously voluntary reactions may be elicited by testing the corneal and gag reflexes, performing doll's eyes, painfully pinching the sternocleidomastoid muscle, and squeezing shut the nostrils and lips for thirty seconds.[19]

Blindness

Reactive pupils do not necessarily indicate hysterical blindness, because there may still be a lesion somewhere behind the midbrain, a lesion damaging the optic radiations or occipital cortex bilaterally. A normal optokinetic response in the face of blindness does indicate hysteria (or malingering), because optokinetic nystagmus requires intact connections from the retina to occipital cortex.[20] Try the Romberg test. If the patient sways when he closes his eyes, then he must have been depending on vision to help maintain his balance. If you're still uncertain, do a visual evoked response (VER)*: a normal visual evoked response also indicates structurally normal pathways.

Severe Cerebral Event: When there *is* a history of a severe cerebral consult, it may be very difficult deciding how much of the patient's 'confusion' is real. Neuropsychologists are quite perceptive with this type of clinical problem.

Visual Evoked Response: A light flashed in the eye is recorded electrically over the occipital cortex. The latency between the flash and its reception in occipital cortex should be less than about 105–115 milliseconds (depending on the laboratory). Prolongation beyond this implies a lesion in the visual pathway, almost always in the optic nerve. See chapter 44.

Visual Field Cuts

A constricted visual field, so constricted that it leaves only a central core of retained 'tunnel' vision*, is hysterical if the tunnel is not cone shaped.[21] That is, the intact field should double in diameter each time you double the distance between you and the patient. You can demonstrate the same finding by using different sized targets. Instead of holding the target further from the patient, simply use a larger target. The intact central field should expand with each larger target.

Spiral visual fields are ones that progressively constrict as you move the target around the perimeter of the visual field. Begin along the 1 o'clock radial and move the target toward central fixation until the patient says, "I see it." Then slide the target down to the 2 o'clock radial, but instead of moving the target back out to beyond the visual perimeter, begin presenting the target from the point at which the 1 o'clock radial was noted. As you work your way around the visual field this way, the perimeter of the visual field will spiral inward. When you eventually reach the 1 o'clock radial again, the patient will deny seeing your target even though the target is well inside the range of the original visual field.

VIth Nerve Palsy

Some patients can mimic a VIth nerve palsy by converging their eyes while looking to the side. The tip-off is that convergence also constricts the pupil.[22]

Weakness

Uncovering hysterical weakness can be done in a number of ways as long as you're careful not to call antalgic weakness hysterical. One way is to elicit collapsing or ratchety* weakness: in true weakness the muscle gradually gives way. Ratchety weakness is easiest to find in those muscles not normally used in a gradual, graded fashion, like the wrist extensors, extensor hallucis longus, tibialis anterior, and peroneus longus.

The second way to detect hysterical weakness is, while vigorously testing the strength of an individual muscle, to suddenly let go. If the muscle fails to spring back to its contracted position, the patient wasn't trying. Sometimes it helps to test both limbs at the same time. Ask the patient to abduct both deltoids. Now yank one elbow down, then the other, and then both simultaneously. The hysterical patient either won't be able to keep things straight, i.e., keep the strong arm strong and the 'weak' arm weak, or the weakness will be so collapsible as to be obviously voluntary.

When testing grip strength, watch the thumb. If flexor pollicus longus doesn't flex the distal interphalangeal joint, the patient wasn't really trying.

The Hoover maneuver is another popular method of detecting insufficient effort by the patient.[23] After placing one of your palms under his heel, ask the patient to lift his other leg against your other hand. If you don't feel his heel digging into your palm, he's not really trying to lift his leg.

Tunnel Vision: The patient complains that he can only see exactly what he's looking at, as if looking through a tunnel. True tunnel vision—i.e., isolated macular vision—may easily result from central retinal artery occlusion, the macula having been rescued by a cilioretinal artery. Bilateral occipital lobe infarctions commonly produce macular sparing because of collateral flow to the occipital tips via the anterior cerebral artery.

Ratchety: Like a ratchet wrench, the muscle demonstrates sudden 'give and catch' weakness.

Hysterical weakness may also be diagnosed by finding marked weakness on individual muscle testing, but only mild weakness on tests of function. For example, marked weakness in a gastrocnemius with the patient supine is discredited by retained ability to stand on the toes of that foot. Same for marked weakness of both gluteus maximus muscles but retained ability to rise normally from a squatting or sitting position. Or poor gluteus strength when asked to dig his heel into the bed, but good gluteus strength when asked to raise the other leg forcefully against your hand in the Hoover maneuver. Hysterically hemiparetic patients also forget that pyramidal lesions selectively weaken tibialis anterior. Though they drag the leg, there's no circumduction; in fact, they purposely elevate the toe to keep it from scraping the floor.

Total paralysis which disappears when you painfully jab the skin with a pin is one, admittedly cruel, way to penetrate the psychologic defense barrier.

Sensory Loss

Withdrawal of a limb to pin also belies another common hysterical complaint: marked sensory loss. It's easier to uncover hysterical hemihypesthesia, though, by demonstrating non-organic splitting of vibration at the midline. This works best over midline bony structures like the forehead, nasal bridge, sternum, and pubis*. Since vibration is transmitted well through bone, a major discrepancy between the right and left sides of these bony structures is unphysiologic. Try holding the vibrating tuning fork in the midline and simply leaning the tuning fork to the left or right. Then ask, "If this is worth a dollar, how much is it worth over here?" It's surprising how many hysterics fall for this rather obvious ploy and report, "25 cents."

Hysterical patients know that severe sensory loss should include proprioception. What they don't know is that severe proprioceptive loss makes the limb ataxic, especially with the eyes closed (pseudoathetosis). As long as you have the patient's eyes closed, hold one of his hands in mid-air and ask him to touch the tip of his thumb with his free hand. If he's *really* lost proprioception in one arm, he shouldn't be able to find it with his good hand, because he won't know where his 'bad' hand is. Most hysterical patients will do the opposite: they'll grope for their good hand with their (non-ataxic) 'bad' hand, but quickly locate their 'bad' hand with their good hand.

Ataxia

If a patient is 'ataxic,' watch for normal coordination when his attention is distracted. For example, if he's ataxic performing finger-nose-finger, ask him to write something and watch for any ataxia when he reaches for the pen.

Pubis: The bone palpable through the pubic hair.

Pain

Many low back pain patients, including (especially) malingerers, know that the straight leg raise test should increase the pain of bona fide sciatica. But with the patient seated on the edge of the examining table, you may discover no pain at all when lifting the leg 'to check the Babinski.' Likewise, exquisite pain on straight leg raising in the supine position miraculously disappears when performed in reverse. Instead of lifting the leg, have the patient sit up on the pretense of listening to his chest for rales. When he sits up with his legs now stretched out 90 degrees in front of him, the absence of leg pain belies the previously bitter complaints on routine straight leg raising. It's also difficult to believe patients who complain of excruciating back pain when asked to forceably contract small, distal muscles like the toe flexors which don't strain the back muscles. And who can believe patients who wince in pain when you gently pinch a roll of lumbar skin or gently tap their lower back?[24]

Hysteria is the hardest of all diagnoses to make because there's no gold standard—no pathognomonic clinical or laboratory test—for hysteria. And hysterical signs do not make a patient hysterical—the patient may simply be elaborating a subtle, but very real organic illness.[25] Until you've had a chance to examine the patient a few times, to explore possible psychological or financial problems, and perhaps do a few screening tests, reserve judgment. By making a diagnosis of hysteria too early, you trap yourself into defending that opinion instead of watching for new signs and alternative organic diagnoses. Sure it's important to get hysterical patients into therapy, but just keep an open mind to avoid ending up with egg on your face. It's too easy to assume that because you can't figure out the patient's problem, he must be crazy. To give you some examples: a patient who claims he sees double when he covers one eye should be hysterical, but monocular diplopia happens to be a well understood phenomenon caused by a number of (primarily intraocular) illnesses.[26] And surely the patient who claims that his visual world is standing on its ear must be hysterical, but visual tilting can unquestionably occur with brainstem ischemia.[27]

ORGANIZING THE NEUROLOGIC EXAM

WELL, WE'RE FINISHED WITH THE SIGNS OF THE NEUROMUSCULAR SYSTEM. It may seem like we've discussed a hundred signs but rest assured that each and every sign is not sought in every patient. An experienced neurologist first determines from his history and from his own observations of the patient during the history-taking what part of the neuromuscular system is probably malfunctioning. He then focuses his exam on whatever signs are necessary to confirm the postulated site of the lesion. The neurologic exam is not a mindless fishing trip throughout the entire neuromuscular system. Each neurologic exam is tailored to elucidate that patient's complaints. Think before you exam the patient. Propose that his neurologic problem is due to a malfunctioning neuromuscular *sub*system whose signs you will now demonstrate. The site of the lesion is postulated *before* you examine the patient, not after.

This is not to say, don't examine the entire nervous system. It *is* important to do a whole neurologic exam, but linger over those areas that are likely to yield fruitful signs, signs that will explain your patient's neurologic problem. Naturally, if you think of another anatomic site to explain the lesion, expand the neurologic exam to spotlight that area of the neuromuscular system, too.

Unfortunately, when you're just beginning to learn neurologic physical diagnosis, the fear of missing abnormal signs and the uncertainty of anatomic localization will prompt you to do a complete neurologic exam. Understandable. But we've just reviewed a swirling cauldron of neurologic signs, and you now need to organize a systematic approach.

Just as in the general physical exam, two approaches are possible. One is to examine the neuromuscular system by subsystems, analogous to examining the body by organ systems. The other way is to examine the neuromuscular system traditionally, geographically, analogous to head, eyes, ears, neck, chest, abdomen, and extremities in the general physical exam. In the neuromuscular system this geographical approach is organized into: mental status, cranial nerves, motor system, sensory system, and reflexes. But, even if you do elicit the signs geographically, it's important that you *think* anatomically, by neuromuscular subsystems.

To help you think anatomically when examining the nervous system, get small, small enough that you can stand on a cranial nerve or inside a ventricle and identify all the nearby nuclei, all the bypassing fiber tracts, and all the adjacent bony structures. The brain is not a series of two dimensional anatomic plates; it's a beautifully laid out three-dimensional sculpture with enough interior and exterior crevices for you to sit down and take in the panorama. So whether you exam geographically or by neuromuscular subsystems, at any moment you should know exactly where you are in the brain and be able to describe your position three dimensionally.

GEOGRAPHIC NEUROLOGIC EXAM

Mental Status

Begin the mental status by establishing what kind of patient you're dealing with: his level of consciousness, attention span, and orientation. Next, look for focal cortical signs, beginning in the left temporal lobe with aphasia which simultaneously checks Broca's area in the left frontal lobe. Slip across the Sylvian fissure to screen Gerstmann's area for right-left confusion, finger agnosia, acalculia, and if necessary, dysgraphia. If you really suspect focal left hemispheric dysfunction, expand your search by seeking object dysnomia, color dysnomia, cortical sensory loss of the right hand, apraxia of the right hand, and any suspicious twitching of the right face or hand to suggest focal seizures. To get to the right frontal lobe you need to cross the corpus callosum, checked by asking the patient to read (alexia without agraphia) and to salute with his left hand (left hand apraxia). The right frontal lobe is relatively silent, so move back to the right parietal lobe for focal disturbances—figure copying, clock drawing, dressing apraxia, and spatial disorientation (without a widespread disruption of higher intellect). The occipital lobes (visual agnosia, cortical blindness) are not routinely checked.

After focal cortical signs, look for signs of bihemispheric cortical dysfunction: confusion (memory loss, impaired reasoning and judgment, and loss of insight), psychotic thinking (hallucinations, delusions, paranoia), and mood disturbances (mania or depression).

As discussed in chapter 15, memory consists of 1) immediate memory ("Repeat this telephone number. . . . Repeat these numbers backwards"); 2) recent memory ("What time did you arrive in the hospital? What roads did you take to get here? What tests have you had so far?"); 3) anterograde memory ("I want you to remember these three items which I'll ask you for again in a few minutes: red rose, New York Times, and 35 Oak Street"); and 4) general knowledge ("Who's the President of the United States? Vice President? Who was the President before this one? Before him? What's been going on in the Middle East these days?"), and any other recent news event or general knowledge item you think he should know.

Though many neurologists rely on the performance of serial sevens ("100 . . . 93 . . . 86 . . . 79 . . ."[1]) to assess general knowledge, I have found serial sevens too educationally dependent to be very helpful.[1] Instead, I assess calculations and general knowledge in one step, by asking how much a pack of cigarettes costs. If he doesn't know, I tell him it costs 65 cents and then ask him how much change he would get if he gave the cashier a dollar. This type of question is less threatening to the patient than serial sevens, and more accurately assesses a patient's ability to function in society. You begin to appreciate the family's problem better when you discover the patient can't purchase a package of cigarettes correctly than discovering he can't do serial sevens.

Reasoning and judgment are tested by asking how and why questions tailored for each patient. For example, "Why did you vote for Reagan in the last election? Why did you only have two kids? What do you like about Baltimore? How will you support your family if you remain off work?" Lack of insight doesn't ordinarily need a direct question, since it should already have been obvious when taking the history. I tend to avoid asking the meaning of proverbs unless, suspecting schizophrenia, I want to see

how concrete* a patient thinks. Otherwise, I find proverbs too culturally dependent.

Psychotic thinking and affect disturbances are sought next if that area looks fertile, especially if there's been a recent disruption of job and home life. Ask straightforward questions about depression, vegetative symptoms, mania, delusions, and hallucinations. Trace any psychotic confusion to its source keeping an eye out for a clear sensorium and good memory.

Cranial Nerves

If you suspect cranial nerve dysfunction, expand your exam to include all the signs described in chapter 20. But in a routine patient whom you are only screening for neurologic signs, you can do the following:

II.	Visual acuity with glasses*
	Hand comparison or double simultaneous finger counting
	Ophthalmoscopy of discs and fundi
III,IV,VI.	Extraocular movements (EOM's)
	Nystagmus
	Ptosis
	Pupillary reaction to light
V.	Cheek sensation to light stroking ("Feel the same?")
VII.	Eye closure (buries eyelashes symmetrically)
	Symmetrical nasolabial fold
	Same number of teeth on each side of midline
VIII.	Able to hear whisper bilaterally
IX,X,XII.	Dysarthria*

Concrete: Schizophrenic patients think concretely. They think the proverb 'A rolling stone gathers no moss' means that a stone rolling downhill gathers no moss.

Glasses: Some neurologists and ophthalmologists use a pinhole as a substitute for reading glasses. However you examine visual acuity, if the visual acuity is not 20/20, be sure to recheck it in a month or two. Far more important than a single instance of diminished visual acuity is *progressive* visual loss, a sign that until proven otherwise indicates an enlarging mass compressing the optic nerve.

Dysarthria: Dysarthria, like difficulty walking, has a wide anatomic differential diagnosis. You must postulate each anatomic site and seek the necessary signs to confirm or refute each site.[2]

This subsystem:	Makes the patient's speech sound:
Bilateral Pyramidal Tracts (pseudobulbar palsy)	Stiff and slow (look for a hyperactive jaw jerk)
Basal Ganglia	Soft and twittery or slow and awkward (rigid)
Cerebellum	Ataxic (scanning)
Lower Brainstem (bulbar palsy)	Thick, slow, and guttural (like he has a mouthful of mashed potatoes)
Vagus Nerve	Hoarse (recurrent laryngeal nerve to the vocal cord)
	Nasal (cannot close off the soft palate)
Hypoglossal Nerve	Thick and slow (as if the dentist had just anesthetized one side of his tongue)
Pharyngeal Muscles	Depends on involvement of the soft palate, pharynx, and tongue

Motor System

The motor system is the most confusing and frustrating part of the neurologic exam because there are so many things to look for. Approach the motor system by breaking it down into three general areas of increasing complexity: Observation, Feel, and Test.

Observation: Gait, dystonia, involuntary movements, bradykinesia, atrophy, fasciculations
Feel: Muscle consistency, tone, straight leg raise, peripheral nerve size, Tinel's sign, myotonia
Test: Individual muscle strength
Groups of muscle strength
Rapid alternating movements
Cerebellar signs

Begin by observing the gait. If the patient is too unsteady to walk unassisted*, stand next to him on his left side, wrap your right arm around his waist, and let him balance his left hand in yours. Your right arm around his waist prevents him from falling away from you, and your body provides support when he lists toward you. This position also allows you to test retropulsion without fear of making the patient fall.

By observing the gait first, you can often solve the patient's problem before you even lay a hand on him. At the very least the gait focuses your thinking. If it's abnormal, you'll seek signs in the rest of the motor exam to help explain why it's abnormal. For example, if one arm doesn't swing, what's the anatomic cause: pyramidal, extrapyramidal, cerebellar, lower motor neuron, or muscle? Also, the gait will immediately tell you about the patient's ability to function independently at home.

After the gait, look for relevant physical signs. By that I mean, don't spend a lot of time looking for fasciculations in a seizure patient; the yield will be too low. Do look for such significant signs as dystonic posturing or asymmetric use of one hand.

After observation, 'feel' the patient: poke, probe, palpate, pound, and bend the patient while he remains passive. Use these techniques to: 1) bring out fasciculations, 2) check for softened muscles (atrophy), cramps, and contractures, 3) assess the tone, and 4) elicit a positive straight leg raise, a Tinel's sign, or percussion myotonia.

After feeling the patient, 'test' him. In this more complex category you need the patient's cooperation. And, just as you have progressed from simple observation to more complex techniques of feeling and then testing, arrange testing from simple to complex: 'Observation. Feel. Test. . . . simple-to-complex.' Begin by testing the strength of individual muscles, then groups of muscles, then rapid alternating movements, ending up with the most complex of all, cerebellar movements. Keeping this simple to complex approach in mind will not only standardize your exam, hence facilitating it and making it easier to remember, but will also help you avoid overlooking pertinent motor signs.

Too Unsteady to Walk Unassisted: You can easily wrench your back hauling bedridden patients to the head of the bed or lifting them out of bed. To get a patient into a chair, sit him on the edge of the bed and ask him to wrap his arms around your neck. Keeping your back as straight and vertical as possible, arch backward and stand him up into a slow-dance stance. Rotate together to the chair and set him down. To move a patient higher in bed, hook your anterior fossa into his axilla, keep your back straight, and then push with your legs.

To make the description of weakness more objective, a standard, quantitative grading system was devised. The standard grades of weakness are as follows: grade 5—normal strength; grade 4—able to resist both gravity and an unspecified (!) amount of effort by the examiner; grade 3—only able to overcome gravity (but not gravity and the examiner too); grade 2—able to slide the limb across a bed or table (unable to overcome gravity); grade 1—flicker of movement; grade 0—totally paralyzed.

The obvious inadequacy of this system is that it distinguishes between nuances of severe weakness, but fails to sort out mild to modest weakness where accurate descriptions really count. It's a bit like skewing your car's gas gauge to tell you whether the tank is ⅜ or ⅞ full (who cares?!), but failing to distinguish ⅛ from empty. In addition, there are too many muscles that have nothing to do with gravity. What, for example, would qualify for grade 3 weakness of the finger flexors, adductor pollicis, supinator, rhomboids, peroneus longus, tibialis posterior, and many others? How would you position the limb to assess the ability of the triceps, pectoralis, thigh adductors, gastrocnemius, and others to overcome gravity? How would you use the numbers to describe an arm drift?

The numbers have their use, but I think it's preferable to use common English adjectives for describing weakness (or for that matter, describing any other abnormality, like tremor, chorea, aphasia, confusion, etc). Five M's—Minimal, Mild, Modest, Moderate, and Marked—evenly cover the full range of most neurologic abnormalities, though 'completely paralyzed' should be added for describing weakness. These terms are relatively clear to all physicians and are easy to remember; besides most physicians don't even know the numerical system for grading weakness*.

If subtle changes in strength are that important—say you're watching for progression of a mild stroke—it's sometimes easier to be sure of progression (or improvement) if you also describe the weakness in functional terms instead of relying on a single number or term. How many inches can he lift his heel (or knee) off the bed? How long can he keep his hands lifted above his head? Can he stand on one foot? Can he stand on the toes of one foot? How many of *your* fingers can overcome each of his muscles?

Sensory System

The routine sensory exam consists of checking vibration at the toes for a polyneuropathy, and double simultaneous stimulation to look for subtle hypesthesia of one side of the body. If you really suspect abnormal sensation, check pain and temperature, vibration and proprioception, touch and directional kinesthesia*, 2-point discrimina-

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Grading Weakness: Minimal weakness corresponds roughly to grade 5−, mild weakness to 4−, modest weakness to 4, moderate weakness to 4−, marked weakness to 3, 2, or 1, and completely paralyzed to 0.

Directional Kinesthesia: The ability to tell which direction the skin is pulled. An indicator of posterior column function.[3]

tion* and double simultaneous stimulation*, and graphesthesia and stereognosis, all while asking yourself if the sensory loss is in the distribution of a polyneuropathy, mononeuropathy, root, long tract, or cortical sensory lesion*. My bias is not to get too wrapped up in the sensory system unless I need the sensory exam to explain a motor deficit. Patient uncertainty and unreliability is often exasperating.

Reflexes

The reflexes are the biceps, triceps, brachioradialis, knee and ankle jerks, and the Babinski signs. Superficial abdominals, Hoffman, grasp, snout, and glabellar reflexes may also be sought depending on the clinical problem.

Geographic Neurologic Exam

Below is a checklist for the geographic neurologic exam. If something wasn't examined, the item is left blank.

MENTAL STATUS

	R - L
Level of Consciousness:	
Alert_____	Localizes Pain _____-_____
Eye Contact_____	Thrashes to Pain _____-_____
Follows Commands _____	Decorticate_____-_____
	Decerebrate_____-_____

Orientation: Person_____ Place_____ Time_____

2-Point Discrimination: Briefly touch one of the patient's finger pads with two safety pins about 2mm apart. If he only feels one pin, keep retouching the finger while creeping the safety pins further apart until he feels both pins. The distance between the pins at this point is his 2-point discrimination. Really fine 2-point discrimination is the ability to feel the year on a coin, or better still, the ability to pull out a five dollar bill from a pocketful of assorted greenbacks.

2-point discrimination, graphesthesia, and stereognosis are specific for parietal cortex when all other sensations—touch, vibration, proprioception, pain, and temperature—are relatively intact. Otherwise, 2-point discrimination, graphesthesia, and stereognosis may be absent, for example, in large fiber polyneuropathies and posterior column dysfunction.[4]

Double Simultaneous Stimulation: If the primary modalities of sensation (touch, vibration, proprioception, pain, and temperature) are intact, simultaneously touch both of the patient's hands. If he consistently extinguishes one side, something is wrong with the contralateral cerebral hemisphere.[5]

Cortical Sensory Lesion: Cortical sensory loss consists of: 1) graphesthesia (identification of letters or numbers traced on the patient's hand); 2) stereognosis (identification of objects—keys, coins, pencils, paper clips—placed in the patient's hand; 3) identification of types of material—wood, cloth, fur, metal—rubbed across the patient's skin.

Normal

_____Aphasia:
- Comprehension_____
- Repetition_____
- Fluency_____
- Naming_____
- Reading_____

_____Gerstmann's Syndrome:
- Finger Agnosia_____
- R-L Confusion_____
- Acalculia_____
- Dysgraphia_____

_____Color Agnosia_____
_____Left Hand Apraxia_____
_____Left Sided Neglect_____
_____Constructional Apraxia_____
_____Dressing Apraxia_____
_____Spatial Disorientation_____

Normal

_____Attention Span_____
_____Memory
- Immediate_____
- Anterograde_____
- Recent_____
- General Info_____

_____Reasoning_____
_____Judgment_____
_____Insight_____
_____Affect_____
_____Delusions_____
_____Myoclonus_____
_____Asterixis_____
_____Seizures_____
_____Alcoholic Breath_____
_____Gait Apraxia_____

CRANIAL NERVES

Normal	R	L
_____Smell		
_____VA		
_____VF*		
_____Red Washout		
_____Marcus Gunn		
_____Discs		
_____Fundi		
_____EOM's:		
INO		
Upgaze Palsy		
Downgaze Palsy		
Gaze Palsy		
LR Weakness		
SR Weakness		
SO Weakness		
Skew Deviation		
_____Convergence		
_____Doll's Eyes		
_____Calorics		
_____Pupil Size		
_____Pupil React		
_____Pupil Shape		
_____Horizontal Nystagmus		
_____Rotary Nystagmus		
_____Up/Downbeat Nystagmus		
_____Optokinetic Nystagmus		
_____Ptosis		

VFs:

Normal	R	L
_____Corneal Reflex		
_____Facial Sensation		
_____Temporalis		
_____Masseters		
_____Pterygoids		
_____Nasolabial Fold		
_____Lower Facial Weakness		
_____Orb Oculi Weakness		
_____Forehead Weakness		
_____Lacrimation		
_____Hyperacusis		
_____Whisper		
_____Weber		
_____Rinne		
_____Dysarthria		
_____Dysphonia		
_____Gag Reflex		
_____Pharyngeal Sensation		
_____Soft Palate Weakness		
_____Pharyngeal Curtain		
_____Sternocleidomastoid		
_____Trapezius		
_____Tongue Bulk		
_____Tongue Fascics		
_____Tongue Weakness		
_____Tongue Movements		

MOTOR EXAM

Normal

_____Posture: Stooped _____
Loss of Lumbar Lordosis _____
Kyphotic _____
Scoliotic _____
Dystonic _____

_____Gait: Diminished Arm Swing _____
Circumduction _____
Spastic (Both Legs) _____
Wide-Based _____
Antalgic _____
Waddling _____
Steppage _____
Festinating _____
Unable to Heel Walk _____
Unable to Toe Walk _____

_____Stance: Positive Romberg _____
Unable to Balance On One Foot _____
Unable to Hop On One Foot _____

Normal	Hands R · L	Arms R · L	Legs R · L	Trunk	Neck	Face
__At Rest: Tremor	__ · __	__ · __	__ · __		____	
__ Chorea	__ · __	__ · __	__ · __			____
__ Ballismus		__ · __	__ · __			
__ Athetosis			· __	____	____	
__ Bradykinesia		__ · __	__ · __			____
__ Diminished Blink						____
__Tone:						
__ Spastic		__ · __	__ · __			
__ Rigid		__ · __	__ · __	____	____	
__ Flaccid		__ · __	__ · __			

Normal	Individual Muscles:	Atrophy R · L	Fasciculations R · L	Weakness R · L	Myokymia R · L	Tenderness R · L
__ C234	Diaphragm (Phr*)			__ · __		
__ C234	Sternocleido (SpA)	__ · __	__ · __	__ · __		
__ C5T1	Pectoralis (Pec)	__ · __	__ · __	__ · __		
__ C567	Serratus Anterior (LoT)	__ · __	__ · __	__ · __		

Phr:

Phr = Phrenic Nerve
SpA = Spinal Accessory Nerve
Pec = Pectoral Nerves
Ax = Axillary Nerve
SuS = Suprascapular Nerve
DoS = Dorsal Scapular Nerve
MCS = Musculocutaneous Nerve
Rad = Radial Nerve
Uln = Ulnar Nerve
Med = Median Nerve

Psn = Nerve to the Psoas
Fem = Femoral Nerve
Obt = Obturator Nerve
CoP = Common Peroneal
PoT = Posterior Tibial
Sci = Sciatic
InG = Inferior Gluteal
SuG = Superior Gluteal
Pud = Pudendal

Normal	Individual Muscles:	Atrophy R · L	Fascics R · L	Weakness R · L	Myotonia R · L	Tenderness R · L
___	C5 Deltoid (Ax)	___ · ___	___ · ___	___ · ___		___ · ___
___	C5 Supraspinatus (SuS)	___ · ___	___ · ___	___ · ___		
___	C5 Infraspinatus (SuS)	___ · ___	___ · ___	___ · ___		
___	C5 Rhomboids (DrS)	___ · ___	___ · ___	___ · ___		
___	C6 Biceps (MC)	___ · ___	___ · ___	___ · ___		___ · ___
___	C6 Brachioradialis (Rad)	___ · ___	___ · ___	___ · ___		
___	C6 Supinator (Rad)	___ · ___	___ · ___	___ · ___		
___	C7 Triceps (Rad)	___ · ___	___ · ___	___ · ___		___ · ___
___	C7 Wrist Extensors (Rad)	___ · ___	___ · ___	___ · ___	___ · ___	
___	C8 Exten Digitorum (Rad)	___ · ___	___ · ___	___ · ___		
___	C8 Ext Pol Longus (Rad)	___ · ___	___ · ___	___ · ___		
___	C8 Flex Carpi Uln (Uln)	___ · ___	___ · ___	___ · ___		
___	C8 Flex Dig Prof (Med/Uln)	___ · ___	___ · ___	___ · ___		
___	C8 Flex Pol Longus (Med)	___ · ___	___ · ___	___ · ___		
___	C8T1 1st Dor Interos (Uln)	___ · ___	___ · ___	___ · ___		
___	C8T1 Hand Intrinsics (Uln)	___ · ___	___ · ___	___ · ___		
___	C8T1 Abduct Dig Quint (Uln)	___ · ___	___ · ___	___ · ___		
___	C8T1 Opponens (Med)	___ · ___	___ · ___	___ · ___	___ · ___	
___	C8T1 Flexor Poll Brev (Med)	___ · ___	___ · ___	___ · ___		
___	C8T1 Abduct Pol Brev (Med)	___ · ___	___ · ___	___ · ___		
___	L123 Psoas (Pso)			___ · ___		
___	L234 Quads (Fem)	___ · ___	___ · ___	___ · ___		___ · ___
___	L234 Thigh Adductors (Obt)	___ · ___	___ · ___	___ · ___		
___	L45 Tibial Anterior (CoP)	___ · ___	___ · ___	___ · ___		
___	L45 Peroneus Longus (CoP)	___ · ___	___ · ___	___ · ___		
___	L5 Ext Hall Long (CoP)	___ · ___	___ · ___	___ · ___		
___	L5 Ext Digit Brevis (SuP)	___ · ___		___ · ___		
___	L5 Tibialis Post (PoT)			___ · ___		
___	S12 Foot Intrinsics (PoT)	___ · ___	___ · ___	___ · ___		
___	S12 Gastrocs (PoT)	___ · ___	___ · ___	___ · ___		___ · ___
___	L5S1 Hamstrings (SciI)	___ · ___	___ · ___	___ · ___		
___	L5S2 Gluteus Maximus (InG)	___ · ___	___ · ___	___ · ___		
___	L5S1 Gluteus Medius (SuG)			___ · ___		
___	S345 Rectal Sphincter (Pud)			___ · ___		

Normal Grouped Strength:

	R · L
_____ Weak Grip	___ · ___
_____ Arm Drift	___ · ___
_____ Unable to Stand on One Leg	___ · ___
_____ Unable to Hop	___ · ___
_____ Pushes Off from Chair	
_____ Unable to Squat	

_____ Rapid Alternating Movements:

		R · L
Slow but Accurate	Hands	___ · ___
	Feet	___ · ___
Fast but Inaccurate	Hands	___ · ___
	Feet	___ · ___

Normal

Cerebellar Testing:

	R	L
Intention Tremor: Finger-Nose-Finger		
Heel-Shin		
Ataxic Tandem Gait		

SENSORY EXAM

Upper Extremity:

Normal	Glove L	Glove R	Mononeuropathy L	Mononeuropathy R	Root L	Root R	Long Tract* L	Long Tract* R
Pain								
Temperature								
Touch								
Vibration								
Proprioception								
Directional Kinesthesia								

Lower Extremity:

Normal	Stocking L	Stocking R	Mononeuropathy L	Mononeuropathy R	Root L	Root R	Long Tract L	Long Tract R
Pain								
Temperature								
Touch								
Vibration								
Proprioception								
Directional Kinesthesia								

Cortical Sensory Loss:

Normal	Hands L	Hands R	Feet L	Feet R
2-Point Discrimination				
Double Simultaneous Stimulation				
Graphesthesia				
Stereognosis				

REFLEXES

	R	L
Biceps		
Triceps		
Brachioradialis		
Knee		
Ankle		
Babinski		
Jaw Jerk		
Hoffmann		

	R	L
Supraspinatus		
Pectoralis		
Hamstring		
Crossed Adductor		
Supinator		
Superficial Abdominal		
Cremasteric		
Cervical Compression		

	R	L
Straight Leg Raise		
Cross Str Leg Raise		
Chvostek		
Trousseau		
Anal Wink		
Bulbocavernosus		
Grasp		
Snout		

Long Tracts: In the space provided, write the superior level of the sensory loss.

Abbreviated Geographical Neurologic Exam:

1. MENTAL STATUS:

Level of Consciousness
Orientation
Aphasia
Gerstmann's
Dyspraxia
Color Agnosia
L Hand Apraxia
L Sided Neglect
Constructional Apraxia
Dressing Apraxia
Spatial Disorientation
Seizures
Attention Span
7 #'s
3 Item 3'
Recent
Remote
General Info
Insight
Judgment
Delusions
Affect
Gait Apraxia
Myoclonus
Asterixis

2. CRANIAL NERVES:

I. Smell

II. VA
VF
Macula Glare
Rel Weakness
Discs

III. EOM's
IV. Ptosis
VI. Pupils
Nystagmus

V. Corneal Reflex
Facial Sensation
Temporalis/Masseters

VII. Lower Face
Orb Oculi
Forehead

VIII. Whisper

IX. Pharynx
X. Soft Palate
Pharyngeal Contr
Dysarthria
Dysphagia

XI. SCM

XII. Tongue

3. MOTOR:

Bulk
Atrophy
Fasciculations
Masked Face
Bradykinesia
Movement Disorder
Tone
Tri Dr
Opponens
Grip
Wrist Extensors
Brachioradialis
Biceps
Triceps
Deltoid
Supra/Infraspin
Rhomboids
Serratus Ant
Psoas
Quads
Tib Ant
Gastroc
Tib Post
Hams
G Max
G Medius
Adductors
Arm Drift
Squat
Stork stance
Toe Walk
Heel Walk
Rapid Alt Moves
P N F
Heel Shin
Tandem Walk

4. SENSORY:

Vibration
Proprioception
Pin
Touch
2-Point Discrim
Graphesthesia
Stereognosis

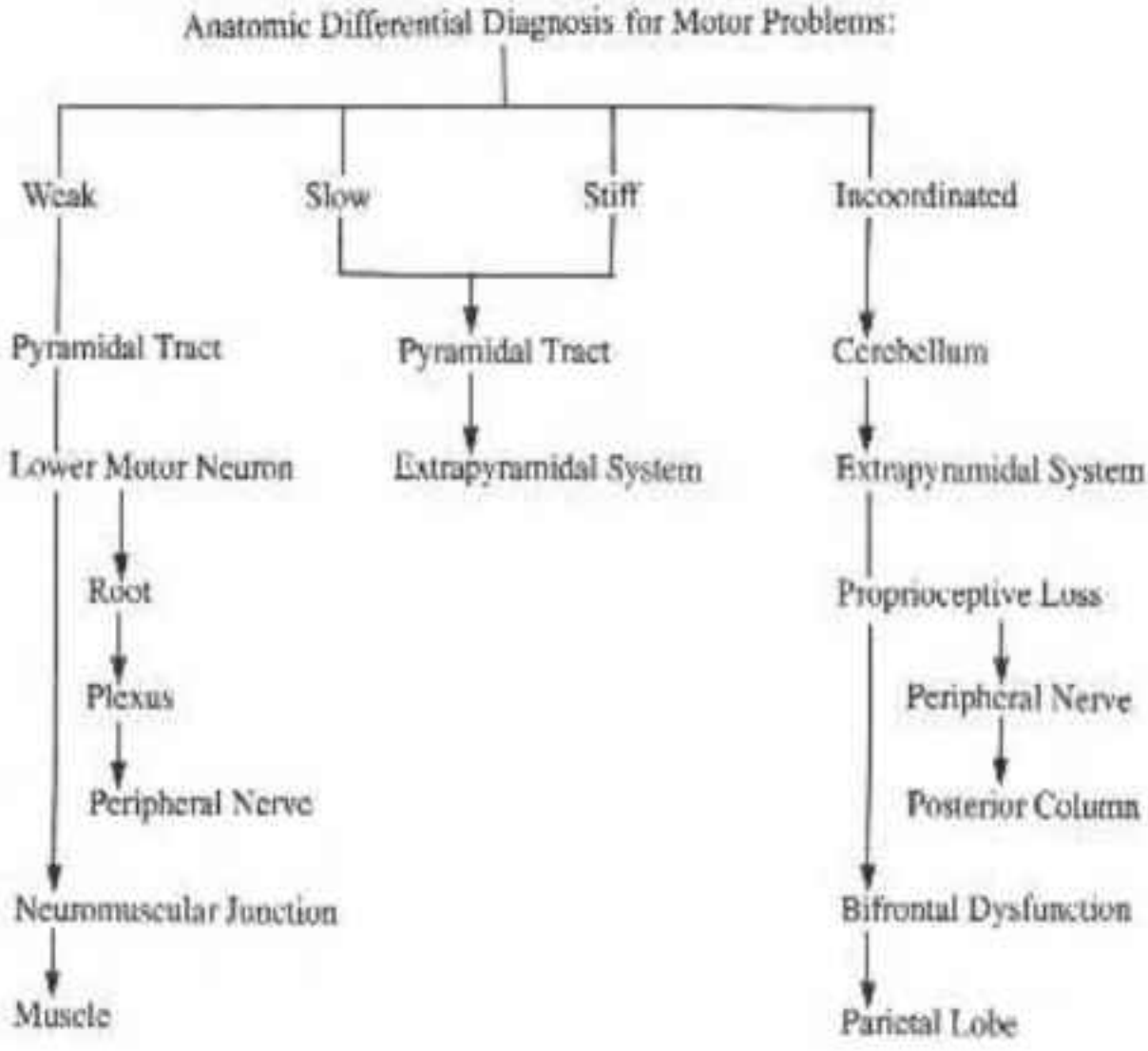
5. REFLEXES:

Biceps
Triceps
Brachiorad
Knee
Ankle
Jaw Jerk
Babinski

SUBSYSTEM EXAM

AS YOU GAIN CONFIDENCE IN YOUR EXAM, in your history taking, in neuroanatomy, and in the signs of each neurologic subsystem, you will begin to examine the nervous system to match the way you think—anatomically by subsystems. Instead of examining all the neuromuscular systems equally, you will focus on the subsystem that the patient (or his family) complains about. Examining a demented patient, for example, will not only include the routine mental status listed above, but also a greatly expanded search of his cortex for apraxia, spatial disorientation, cortical sensory signs, grasp, snout, etc.

Examining by subsystems makes the neurologic exam much more interesting because it allows you to organize your thoughts and test hypotheses. For example, the vast majority of motor complaints are due to either weakness, stiffness, slowness, or incoordination (or pain). Each of these symptoms has an anatomic differential diagnosis, and you can use the subsystem exam to 'test' each anatomic site.



By thinking anatomically you can adjust the exam to search for signs of a neighboring subsystem. For example, if your patient (or his family) complains of difficulty walking which you attribute on examination to cerebellar ataxia, you will then carefully focus on neighboring brainstem signs—ophthalmoplegia, coarse nystagmus, absent corneal reflex, jaw weakness, facial weakness, unilateral hearing loss, and dysarthria—*as well as* signs of fourth ventricular obstruction (noncommunicating hydrocephalus) like lethargy, confusion, papilledema, and bilateral pyramidal tract signs worse in the legs than the arms.

The subsystem exam is a simpler, more efficient exam with a higher yield than the geographical one. Instead of letting you simply rake in a large pile of signs to be sorted out later, the subsystem forces you to think during the exam. You may have to take a minute to consider the anatomic differential diagnosis, but by the end of the exam you will have made up your mind where the lesion is.

Know the signs of each subsystem, know how to elicit them, and you'll know neurology because anatomic localization is the heart and soul of neurology. The etiologic differential diagnosis is relatively straightforward once you've established the anatomic site of the lesion.

Below is the neurologic exam organized according to subsystems. The total number of signs is the same as the geographical exam, but they're consolidated into subsystems. The subsystem exam appears longer than the geographic exam, but only because I've spelled out the motor system in all its glorious detail. In fact, the subsystem exam is actually shorter than the geographical one, because you'll be focusing on perhaps two or three subsystems while only screening the other ones.

Moreoever, the subsystem exam more accurately reflects the way you think than the geographical exam. Notice, for example, that the peripheral nervous system is not organized by muscles as it is in the geographical exam. This is because you don't (usually) examine individual muscles; you examine roots or peripheral nerves or groups of muscles (like proximal muscles).

Admittedly, if you do not do a complete medical student's neurologic examination, you will be vulnerable to criticism at some future date when someone asks if a particular sign (which you did not look for) was present. In actual practice, however, you've already 'examined' most areas of the nervous system by observing the patient as he walks into your office, relates his history, and moves about the room. If something looks suspicious, besides what the history tells you is suspicious, direct your neurologic examination to that subsystem as well. Fortunately, with most neurologic problems, symptoms precede signs. It's relatively uncommon to discover asymptomatic neurologic signs*. The only neurologic signs I consistently look for in every patient regardless of symptoms are the visual acuity, the discs, and hearing — areas that cannot be readily observed during the interview.

Asymptomatic Neurologic Signs: The one disease *characterized* by asymptomatic signs is multiple sclerosis. The patient may think only one leg is stiff and weak, and be completely unaware that he has, in fact, a moderately severe paraparesis.

1. **CORTEX**

LEVEL OF CONSCIOUSNESS

- Alert
- Eye contact
- Follows commands
- Appropriate to pain
- Thrashes or grimaces to pain
- Decorticate
- Decerebrate
- No response

FOCAL CORTICAL SIGNS

Left Temporal Lobe:

- Wernicke's aphasia
- Right pie in the sky field cut
- Temporal Lobe Seizure
- Dysacusia (also indicative of parietal and frontal lobes)

Left Parietal Lobe:

- Gerstmann's syndrome
  - Finger agnosia
  - Right/left confusion
  - Acalculia
  - Dysgraphia
- Color agnosia (parieto-occipital)
- Cortical sensory loss right hand
  - Graphesthesia
  - Astereognosis
  - 2 Point discrimination (with relatively normal touch)

Left Frontal Lobe:

- Broca's aphasia
- Focal seizure right face/hand/Leg

Corpus Callosum:

- Apraxia left hand

Right Parietal Lobe:

- Constructional apraxia (block design, figure copying)
- Dressing apraxia
- Left sided neglect (of the body, of a clock)
- Spatial disorientation (on the ward)
- Cortical sensory loss left hand
- Severe proprioceptive loss left hand

Right Temporal Lobe:

- Left pie in the sky field cut

BIHEMISPHERIC CORTICAL SIGNS
Orientation (person, place, time)
Shortened attention span
  Agitated
  Not agitated
Memory Loss
  Anterograde
  Immediate
  Recent
  Remote
  General information
Loss of insight
Impaired reasoning
Impaired judgment
Apathy
Impulsiveness
Affect
Delusions
Gait apraxia
Frontal release signs (snout, grasp, paratonia)
Truncal myoclonus
Asterixis

2. **BASAL GANGLIA**
Dystonic posture
Gait
  Dystonic
  Choreic
  Parkinsonian (retropulsion, en bloc turns, festination, difficulty starting and stopping)
Masked face
Diminished blinking
Soft voice
Bradykinesia
Resting tremor
Chorea
Athetosis
Ballismus
Rigidity (cogwheel)
Glabellar reflex

3. **CEREBELLUM**
Truncal ataxia (wide based gait, impaired tandem gait)
Intention tremor (finger nose finger, heel-shin)
Dysmetric finger tapping or toe tapping
Scanning speech
Titubation
Ocular fixation deficit
Saccadic overshoot

4. LONG TRACTS

PYRAMIDAL TRACTS

- Gait
  - Diminished arm swing
  - Circumduction
- Spasticity (wrist, supinator, biceps, quadriceps)
- Weakness
  - Individual muscles
    - Hand intrinsics
    - Opponens
    - Wrist extensors
    - Biceps
    - Triceps
    - Deltoid
    - Psoas
    - Quadriceps
    - Tibialis anterior
    - Extensor hallucis longus
    - Peroneus longus
    - Gastrocnemius
    - Hamstrings
    - Gluteus maximus
  - Groups of Muscles
    - Grip
    - Arm drift
    - Squat
    - Stork leg
    - Hopping
    - Toe walk
    - Heel walk
  - Slowing of rapid alternating movements
  - Hyperreflexia (threshold, latency, speed, amplitude, spread)
  - Babinski
  - Loss of abdominal reflexes
  - Pseudobulbar palsy (bilateral pyramidal tracts)
    - Spastic dysarthria
    - Emotional incontinence
    - Hyperactive jaw jerk

SPINOTHALAMIC TRACTS

- Hemihypalgesia (pain)
- Hemihypesthermia (temperature)
- Hemihypesthesia (light touch)

POSTERIOR COLUMNS

- Unilateral vibratory Loss
- Unilateral propioceptive loss
- Unilateral hypesthesia (hemihypesthesia)
- Unilateral loss of directional kinesthesia
- Positive Romberg
- Lhermitte's sign

5. **THALAMUS**
   Homolateral*:
      Hemiparesis
      Limb ataxia
      Hemianalgesia (not just hypalgesia)

6. **CRANIAL NERVES**
   I. Smell
   II. Visual acuity (corrected)
      Visual fields (hand waving, comparing hands, finger wiggle, finger adding, red desaturation)
        Prechiasmal (uniocular: central, centrocecal, paracentral, arcuate, altitudinal, binocular: junctional, no respect for vertical)
        Chiasmal
        Retrochiasmal
      Marcus Gunn pupil
      Red desaturation
      Papilledema (hyperemia, vessel obscuration at disc margins, disc hemorrhages)
      Optic disc atrophy (plus loss of nerve fiber layer)
      Fundi (splinter hemorrhages, dot and blot hemorrhages, emboli)
   III,IV,VI Extraocular movements
      Nystagmus
      Ptosis
      Pupil size/reaction (to light and accommodation)
   V. Corneal reflex
      Facial hypesthesia
      Atrophy and weakness of chewing muscles
   VII. Facial weakness
      Orbicularis oculi weakness
      Forehead weakness
   VIII. Hearing loss
   IX. Pharyngeal hypesthesia
   X. Soft palate weakness
      Pharyngeal curtain weakness
      Dysarthria
      Dysphagia
   XI. Sternocleidomastoid (atrophy, weakness)
      Trapezius (atrophy, weakness)
   XII. Tongue (atrophy, fasciculations, weakness)

7. **BRAINSTEM**
CRANIAL NERVE AND **CONTRALATERAL** LONG TRACT
   IIIrd nerve & contralateral hemiparesis
   VIth nerve & contralateral hemiparesis
   VIth and VIIth & contralateral hemiparesis
   Gaze paresis & contralateral hemiparesis
   Vth, ipsilateral Horner's, & contralateral hemihypalgesia

Homolateral: These three signs are homolateral to each other and contralateral to the thalamic lesion.

INDIVIDUAL SIGNS
- Internuclear ophthalmoplegia (with or without coma)
- INO and ipsilateral gaze palsy ('one and a half')
- Skew deviation
- Upbeat nystagmus (especially primary position)
- Downbeat nystagmus (especially primary position)
- Coarse horizontal nystagmus (cerebellar-brainstem connections)
- Upgaze palsy*
- Downgaze palsy

INTERSECTING HORIZONTAL SIGNS
- Parinaud's syndrome:
  - Generous sized pupils fixed to light
  - Upgaze palsy
  - Nystagmus retractorius
  - Convergence insufficiency
  - Collier's sign
- Vertical (up *and* down) Gaze Palsy

8. **ROOTS**

MOTOR: *atrophy, fasciculations, and weakness* (with hypotonia and hyporeflexia):

C3,4	Trapezius
C3,4,5	Diaphragm
C5	Rhomboids
	Supraspinatus
	Infraspinatus
	Deltoid
C6	Biceps
	Brachioradialis
	Supinator
	Wrist extensors
C7	Triceps
	Finger extensors
	Flexor carpi radialis
C5,6,7	Serratus anterior
C8/T1	Flexor carpi ulnaris
	Flexor digitorum superficialis
	Flexor digitorum profundus
	Opponens
	1st dorsal interosseous
	Intrinsics
	Abductor digiti minimi
L1,2,3	Psoas
L2,3,4	Quadriceps
	Thigh adductors
L4,5	Tibialis anterior
	Peroneus longus

Upgaze Palsy: Sometimes up and downgaze palsy are due to lesions above the brainstem. But such lesions won't prevent the eyes from looking up or down in response to doll's eyes maneuver (rocking the head forward and backward) or in response to cold or warm water injected into the ears.

L5	Extensor hallucis longus
	Tibialis posterior
	Gluteus medius
L5,S1	Hamstrings
L5,S1,S2	Gluteus maximus
S1,2	Gastrocnemius
	Flexor hallucis longus
	Foot intrinsics
S3-5	Rectal tone

SENSORY: (DERMATOMES)

C5	Shoulder
C6	Thumb, index finger
C7	Long finger
C8	Ring/little finger, medial forearm
T1	Medial arm, axilla
T4	Nipple
T10	Umbilicus
L2,3	Anterior thigh
L4	Knee
L5	Anterior shin, dorsum foot, lateral heel
S1	Lateral sole, lateral half posterior leg
S2	Medial heel, medial half posterior leg
S3-5	Perianal

REFLEXES:

C6	Biceps, Brachioradialis
C7	Triceps
L4	Knee jerk
S1	Ankle jerk
S2-4	Bulbocavernosus

MECHANICAL ROOT SIGNS:
Pain on lateral neck flexion
Pain on vertical compression
Loss of lumbar lordosis
Positive straight leg raise
  Positive ankle dorsiflexion sign
  Positive bowstring sign
Positive crossed straight leg raise

9. **SPINAL CORD**
Root and Long Tract (preferably bilateral long tracts)
Early Loss of Sphincters

SYNDROMES:
Anterior Spinal Artery Syndrome (anterior half)
Brown-Sequard (lateral half)
Combined Systems Disease (posterior half)
Syringomyelia (dissociated sensation)
Central Cord

10. CAUDA EQUINA/CONUS MEDULLARIS

Bilateral multiple motor roots to legs
Bilateral multiple sensory roots to legs
Rectal incontinence/retention; sphincter weakness
Urinary incontinence/retention
Absent bulbocavernosus reflex

11. PERIPHERAL NERVES

MONONEUROPATHY

Atrophy And Weakness (with hypotonia and hyporeflexia)

Dorsal Scapular	Rhomboids
Suprascapular	Supraspinatus
	Infraspinatus
Axillary	Deltoid
Long Thoracic	Serratus anterior
Musculocutaneous	Biceps
Radial	Triceps
	Supinator
	Brachioradialis
	Wrist extensors
	Finger extensors
Median	Opponens
	Abductor pollicis brevis
	Flexor pollicis brevis
	Flexor pollicis longus
	Flexor digitorum superficialis
	Radial half flexor digitorum profundus
	Pronator Teres
	Pronator Quadratus
Ulnar	1st dorsal interosseous
	Interossei
	Abductor digiti minimi
	Adductor pollicis
	Flexor carpi ulnaris
	Ulnar half flexor digitorum profundus
Nerve to Psoas	Psoas
Femoral	Quadriceps
Obturator	Thigh adductors
Superior Gluteal	Gluteus medius
Inferior Gluteal	Gluteus maximus
Sciatic	Hamstrings
Superficial Peroneal	Peroneus longus
Deep Peroneal	Tibialis anterior
	Extensor hallucis longus
Tibial	Gastrocnemius
	Tibialis posterior
	Flexor hallucis longus
	Foot intrinsics

Sensory Loss:

Radial—crotch between thumb/index finger, posterior thumb
Median—splits ring finger, below wrist
Ulnar—splits ring finger, below wrist
Femoral—anterior thigh
Lateral Femoral Cutaneous—lateral thigh
Saphenous—medial thigh, medial calf
Sciatic—posterior thigh
Common peroneal—anterior shin, dorsum foot
Posterior tibial—posterior calf, sole foot

Tinel's Sign or Focal Tenderness:

Adson's maneuver—inferior brachial plexus
Spiral groove—radial
Dorsal proximal ulna—radial
Ulnar groove—ulnar
Cubital tunnel—ulnar
Medial wrist—ulnar
Carpal tunnel—median
Pronator teres—median
Supraclavicular fossa—brachial plexus
Femoral canal—femoral
Iliac crest—lateral femoral cutaneous
Ischial notch—sciatic
Obturator canal—obturator
Medial thigh—saphenous
Fibular head—common peroneal
Tarsal tunnel—tibial

POLYNEUROPATHY

Distal, symmetrical atrophy and weakness
Distal, symmetrical (stocking/glove) hypesthesia to vibration, proprioception, touch, and pin
Absent distal reflexes
Hyperpathia
Enlarged nerves

12. **AUTONOMIC NERVOUS SYSTEM**[†]

No change in heart rate on standing
Orthostatic hypotension
No valsalva overshoot*
Fixed pupils
No sweating
No tearing
No salivation

13. **MUSCLE**

Proximal, symmetrical weakness/atrophy
Widespread weakness without sensory loss
Enlarged, weak muscles (pseudohypertrophy)
Indurated, weak muscles (contracture)
Tender, weak muscles
Myotonia

14. **NEUROMUSCULAR JUNCTION**

Pure Motor Syndrome
Predominantly Above the Shoulders (Below in Older Patients):
Ophthalmoplegia, Ptosis, Jaw and Neck Weakness, Myopathic Stable Dysphagia, Dysarthria
Often Waxes and Wanes

Valsalva Overshoot: A 10–15 second grunt normally raises intrathoracic pressure high enough to drop the blood pressure (by preventing venous return to the heart). After the patient relaxes, the blood pressure briefly rises *above* (overshoots) its baseline pressure.

SYNCHRONIZING THE NEUROLOGIC HISTORY AND PHYSICAL

THE BULK OF OUR ATTENTION has been focused on the signs of neurologic dysfunction, not its symptoms. The reason for this is that neurologic symptoms are obvious once you know the signs. In fact, neurologic symptoms are so allied to neurologic signs that a thoughtful history alone will often lead you to within an inch of the lesion. The old adage that 'the neurologic exam localizes the lesion, and the history reveals the etiology' can be expanded to 'the neurologic exam localizes the lesion, and so does the history while *also* revealing the etiology.'

You need only be cautioned about certain complaints which may sound unambiguous to you but which, in fact, have an entirely different meaning to the patient. Dizziness, to some, may mean vertigo, giddiness, near syncope, ataxia, incoordination, or confusion. Similarly, numbness means hypesthesia to you, but paralysis, incoordination, or even confusion to others. Blindness may actually be diplopia, and confusion, aphasia. Fatigue (normal initial strength, but early exhaustion) may be misconstrued as weakness*. Imbalance—is it ataxia, hemiparesis, or inability to correct a brief imbalance because of frontal lobe or basal ganglia disturbance?

With thoughtfully elicited questions and attentive observation of the patient during the interview, before ever touching the patient, you may very well know where the lesion is and the differential diagnosis causing it. Neurologic symptoms are approached no differently than any other symptom of internal medicine. The first step is anatomic diagnosis; only in the case of the nervous system the site will be a subsystem of the neuromuscular system. The patient's complaints will suggest a particular neurologic subsystem and you'll ask the necessary questions to confirm dysfunction of that subsystem. If no responsive chords are struck, choose another site (subsystem) and seek those symptoms. For example:

A 55 year-old man comes to the emergency room because of sudden right hemihypesthesia. Take him back to the very moment he noticed something was wrong:

Weakness: Fatigue is a systemic symptom which may be due to true muscular weakness, but is usually due to internal organ failure, drugs, infections, or other blood-borne insults.

Doctor: When did you first notice the right-sided numbness?
Patient: This morning.
Doctor: What time?
Patient: When I got up to go to work.
Doctor: Did you notice it before you got out of bed?
Patient: No.
Doctor: Did you feel anything was wrong before you got out of bed?
Patient: No.
Doctor: So you got up to go to work. When was the first moment you felt anything wrong?
Patient: When I stood up out of bed, I fell backwards into the bed.
Doctor: Then what?
Patient: I tried getting up again but I couldn't.
Doctor: Why not?
Patient: Because I couldn't stand.

At this point you should have two sites in mind. The numbness of his right side (his chief complaint) is either hemispheric (cortical or internal capsule) or brainstem. If the trouble standing was due to a hemiparesis, the numbness is hemispheric; if due to ataxia, a brainstem site is more likely. Etiologically, the abruptness of onset suggests a stroke.

Doctor: Was this because you were weak on one side or because your balance was off?
Patient: I couldn't balance myself.
Doctor: You're sure you weren't weak on one side?
Patient: Well, I was numb on my right side.
Doctor: By numb, do you mean the skin felt funny or that it was weak?
Patient: No, it felt numb and tingly. I could use it okay.

The imbalance suggests a brainstem lesion, and for practical purposes the only brainstem stroke that causes hemihypesthesia without hemiparesis is the lateral medullary (Wallenberg) stroke. So propose the lateral medulla as the site of the lesion.

Doctor: Was your face numb?
Patient: Yeah, it was.
Doctor: Which side?
Patient: The left side of my face.

There's your answer. There is no other place but the lateral medulla that can cause ipsilateral facial numbness and contralateral body numbness. Finish him off with a few confirmatory symptoms.

Doctor: Did you have any hiccups?
Patient: I did for about a half hour.
Doctor: How about nausea or vomiting?
Patient: No.
Doctor: Any headache?
Patient: Just a little in the back of my head.
Doctor: Has your left eyelid always drooped a little? (Horner's)
Patient: I don't know, I never looked.
Doctor: Is your left hand perfectly okay? (Ipsilateral cerebellar ataxia)
Patient: No, it feels a little clumsy.

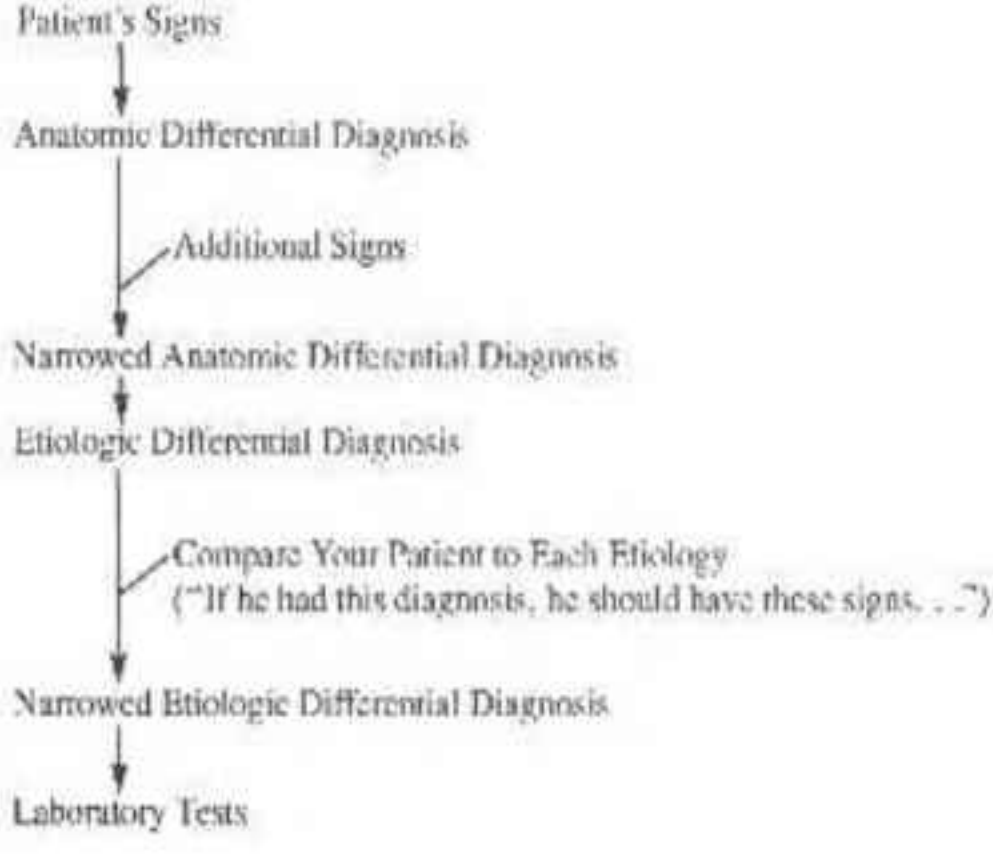
Within two minutes you've localized the lesion to the lateral medulla and ipsilateral cerebellar hemisphere; what could be easier? Now all you have to do is confirm ipsilateral facial hypalgesia, contralateral body hypalgesia, a left Horner's, and left arm dysmetria. If you want to do an entire detailed neurologic exam, fine, but if you have six more consults to see, a ward to look after, or a husband or wife who would like to see you once in a while, simply check a few other signs in the distribution of the basilar artery like no hemianopia, dysconjugate gaze, or arm drift, and rule out a few asymptomatic but potentially catastrophic signs like papilledema.

In considering etiologies for this man's stroke, look carefully for hypertension, focal arterial stenosis (subclavian or vertebral artery bruit in the supraclavicular fossa), a source of emboli (heart murmur or atrial fibrillation), polycythemia (facial plethora), and temporal arteritis (large, tender, non-pulsatile superficial temporal arteries).

This type of limited, but directed physical exam allows you to focus on critical areas of the body that might otherwise be overlooked on the so-called complete physical exam.

As you'll see in chapter 43 (Emergency Room Case Histories), the etiologic differential diagnosis is begun by taking your patient's signs and constructing an anatomic differential diagnosis. If the anatomic differential diagnosis is too broad, return to the patient to find whatever signs are necessary to narrow the anatomic differential diagnosis. From the narrowed anatomic differential diagnosis, construct an etiologic differential diagnosis. Then consider each etiology and compare it to your patient's signs: do your patient's signs fit the postulated etiology? (Thumbnail sketches of treatable etiologies are described in chapter 34.) Once you've narrowed the etiologic differential diagnosis in this way, you're ready to order tests (or treat even before you have the diagnosis).

Which etiologies you decide to rule out first (or treat on a presumptive basis) will depend on a number of things: 1) the likelihood of the diagnosis, 2) the danger that diagnosis poses if therepy is delayed minutes or hours, 3) the ease of making the diagnosis, 4) the ease of therapy, and 5) the risk of therapy.



VASCULAR ANATOMY

FOCAL SIGNS ARE AS SIGNIFICANT IN NEUROLOGY as they are in internal medicine. Focal dysfunction of the cerebellum is as significant as focal dysfunction of the heart. And just as the differential diagnosis in internal medicine is heavily weighted by whether the illness affects a single organ system or multiple ones, likewise in neurology, the differential diagnosis is strongly modified by whether the illness affects a single subsystem or multiple ones.

There's one additional twist in the cerebral cortex. Focal areas of cortex are each a subsystem of a subsystem! It is not enough to diagnose a cortical lesion. You must distinguish between a focal cortical lesion, a bihemispheric cortical lesion, or the combination of a focal and bihemispheric cortical lesion. Each of these three categories greatly alters your thinking about the differential diagnosis. For example, a patient with Broca's aphasia alone is vastly different from a patient with Broca's and confusion, and both these patients are a far cry from the patient with simple confusion without aphasia. So, whenever you encounter a patient with any neurologic problem, determine whether the problem is affecting one neurologic subsystem, more than one neurologic subsystem, and if it involves the cortex, whether the cortical signs are focal, focal and bihemispheric, or bihemispheric only.

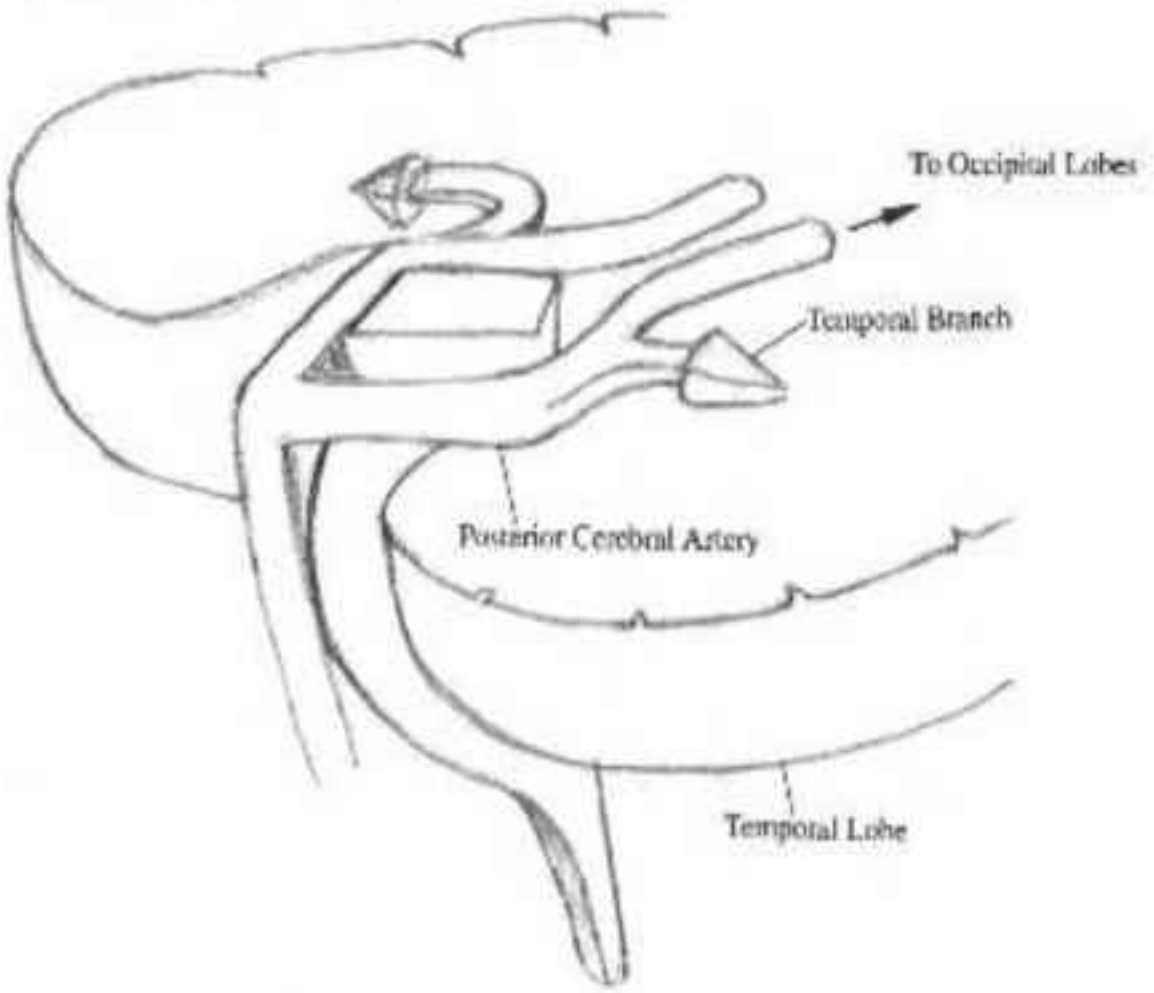
What makes the diagnosis of focal neurologic signs so difficult is that widely separated subsystems often share a common vascular supply. So when you propose a vascular (ischemic) etiology for a patient's symptoms, you have to be sure that all the signs lie in a single vascular territory. This becomes especially important when faced with a patient who has had two separate ischemic insults. If both events occurred in the same vascular territory, you should probably arteriogram the artery supplying that area. If, however, the two ischemic events occurred in two different vascular territories, either the patient has focal disease in each artery or he is throwing emboli from a more proximal source like the heart. That's if he has vascular disease. Once you recognize two separate arterial distributions, you can also begin to think of other diagnoses, like multiple sclerosis, a diagnosis of which requires two neurologic events separated in time and occurring in two different vascular distributions*.[2]

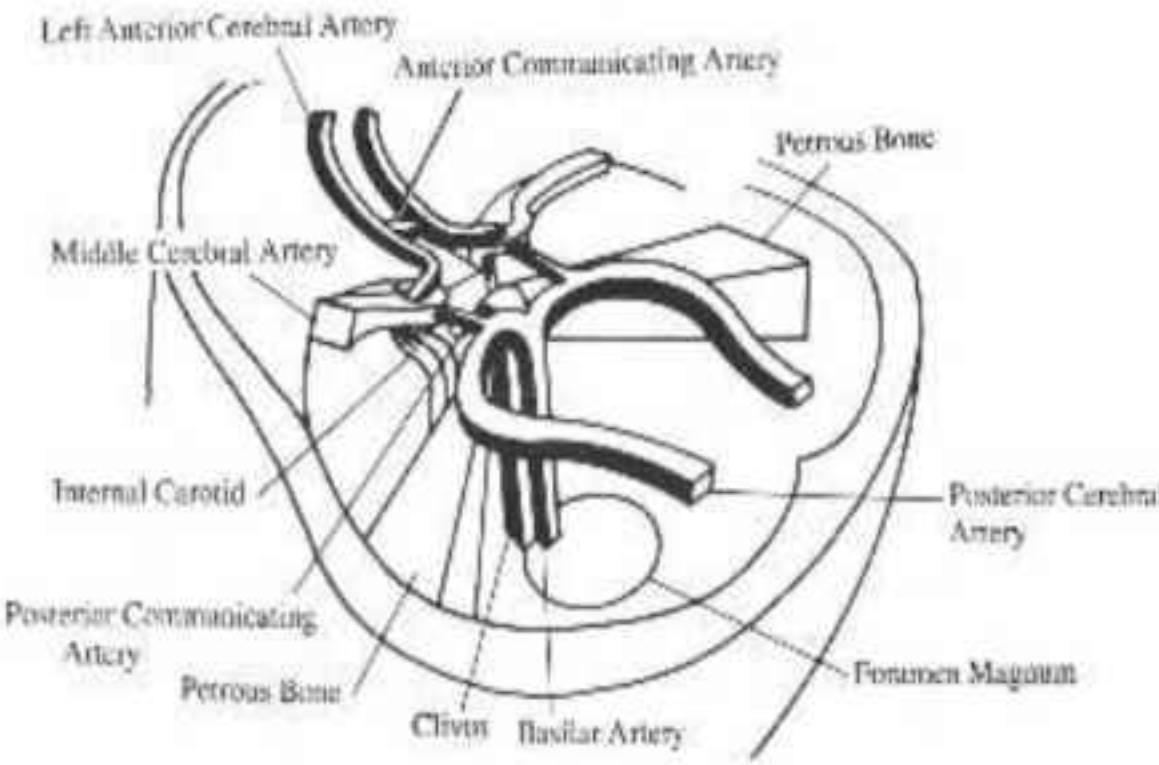
Two Different Vascular Distributions: A good example would be optic neuritis (ophthalmic artery) on one occasion and Brown-Sequard (anterior spinal artery) on another. Or internuclear ophthalmoplegia (basilar artery) and spastic paraparesis (anterior spinal artery). Be cautious about diagnosing multiple sclerosis when the two neurologic events fall within the same arterial distribution; you may be missing a vascular malformation.[1] If the patient has had only one neurologic insult, you can be at least suspicious of multiple sclerosis by finding abnormal signs or laboratory abnormalities in another area of the nervous system.

Even finding two neurologic events separated in time and vascular distributions won't prove multiple sclerosis. Infections, metastatic tumors, and arteritis may also be separated in time and vascular distribution.

Arteries

The blood supply to the brain is divided into an anterior (internal carotid) and a posterior (vertebrobasilar) circulation. The vertebrals, through the posterior inferior cerebellar arteries, supply the lateral medulla; the basilar supplies the pons, midbrain, and cerebellum. At the top end of the brainstem in front of the midbrain the basilar divides into two posterior cerebral arteries each of which wraps around the midbrain and gently inclines over the free edge of the tentorium to supply the ipsilateral occipital lobe and medial temporal lobe.[3]





Vertebrobasilar ischemia, then, would encompass occipital, medial temporal, midbrain, pontine, cerebellar, and medullary symptoms. For patients in whom you suspect posterior circulation ischemia, begin your questions at the posterior cerebrals and work your way down the brainstem:

(1) Did you have any blindness? Was it total blindness (occlusion of the top end of the basilar before it bifurcates into the two posterior cerebrals) or blindness in the same field of each eye? (One posterior cerebral*)[3]
(2) Were you confused? (Medial temporal lobes*)
(3) Did you have any double vision? (III, IV, VI, medial longitudinal fasciculus)
(4) Did your eyelids droop? (Oculomotor nucleus*)
(5) How about facial numbness?
(6) Did your face feel weak?
(7) Ringing in your ears?
(8) Nausea? Hiccups?
(9) Difficulty swallowing?
(10) Slurred speech?
(11) Did your tongue feel numb or thick?
(12) Difficulty walking—staggering? (Cerebellum)
(13) Clumsiness of one or both hands? (Cerebellum)
(14) Any drop attacks?[4] (Bilateral pyramidal tracts)
(15) Weakness of one side of your body? (Unilateral pyramidal tract)
(16) Weakness on both sides? (Bilateral pyramidal tracts)

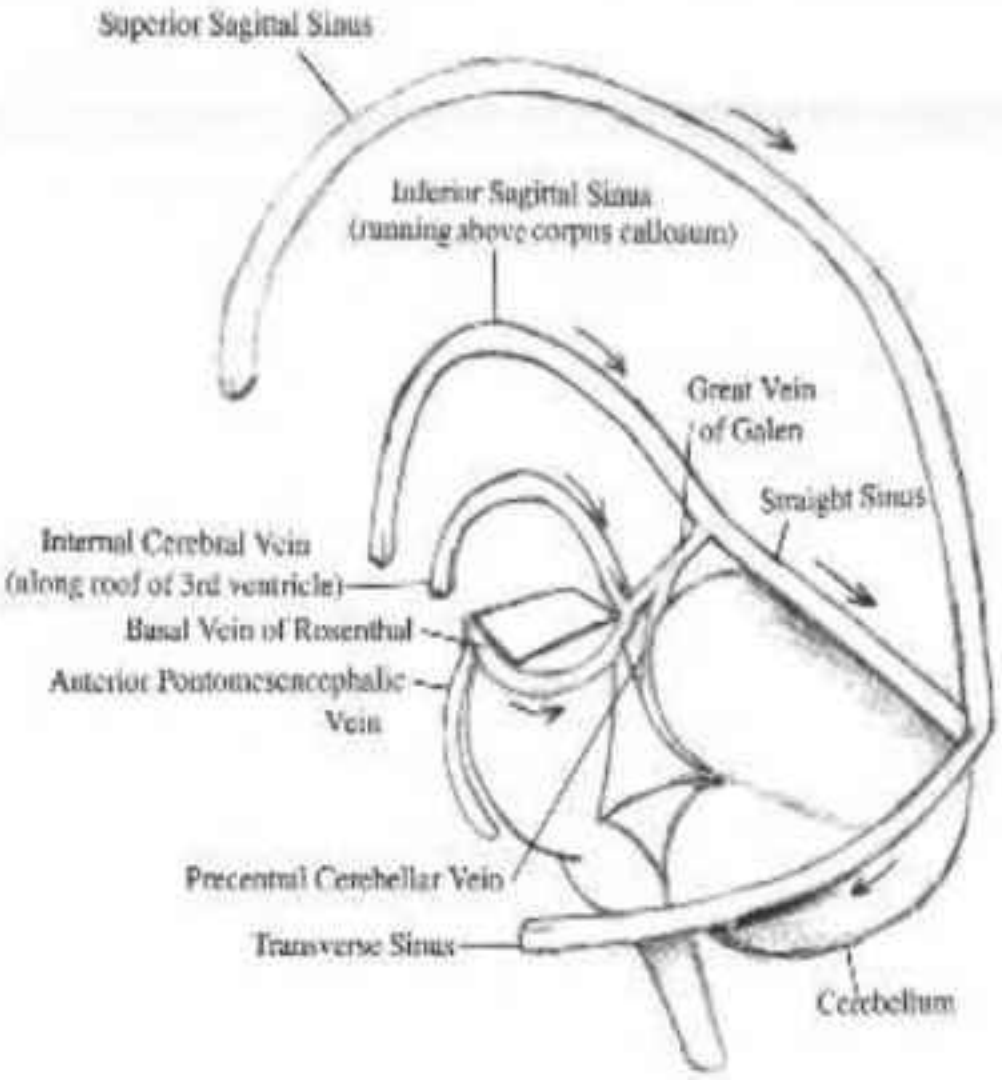
Basilar artery atherosclerosis often extends throughout the entire length of the basilar artery. It's not uncommon for basilar artery strokes to involve simultaneously a patch of medulla, pons, midbrain, and even occipital lobes. Don't be misled by your inability to place the lesion in one particular spot within the basilar artery distribution. If all the abnormal sites are irrigated by the basilar artery, your patient has likely had a basilar artery stroke.

The internal carotid begins at the common carotid bifurcation in the neck, and has no major branches until it penetrates the skull through foramen lacerum. And even then, the internal carotid waits a full inch before reluctantly giving up its first sizeable branch, the ophthalmic artery. During that first inch inside the skull, the internal carotid shares a berth with cranial nerves III, IV, VI, V^1 and V^2 in the cavernous sinus just lateral to the pituitary fossa. Once through the cavernous sinus the internal carotid rapidly splinters into the ophthalmic, anterior cerebral, middle cerebral, and posterior communicating arteries.

One Posterior Cerebral: A dense homonymous hemianopia alone—without a hemiparesis or aphasia—is almost certainly a posterior cerebral artery stroke,[4] because the occipital lobe, where all the visual fibers converge, is far from either the motor strip or Wernicke's area.

Medial Temporal Lobes: Besides giving off two posterior cerebral arteries, the tip of the basilar also supplies the medial aspects of both temporal lobes where new memories are incorporated. Patients lose immediate and recent memory during the period of ischemia.[5]

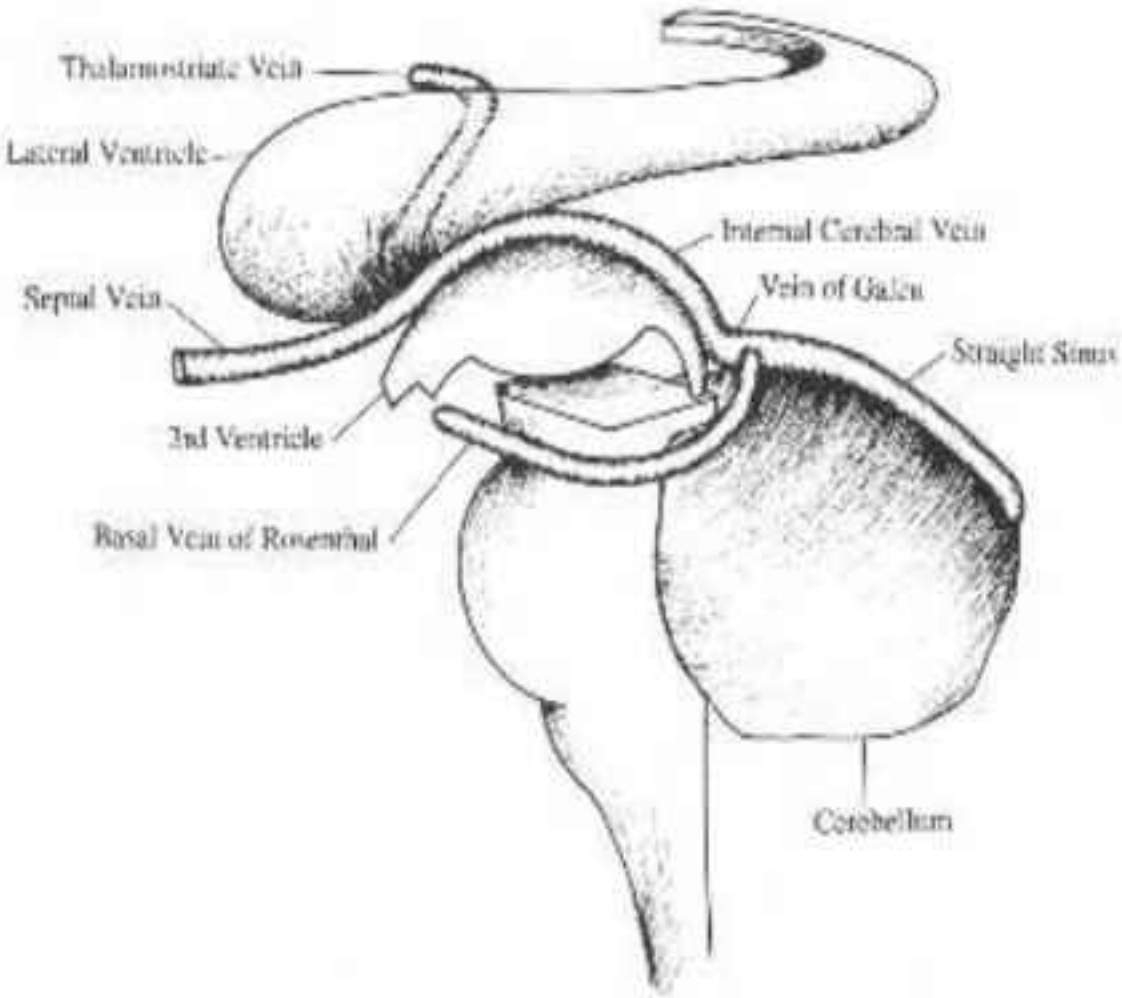
Oculomotor Nucleus: Both the right and left levator palpebrae superioris muscles are controlled by a single subdivision of the midbrain oculomotor nucleus.[7]



The anterior cerebral artery courses along the medial aspect of the frontal lobe in the interhemispheric fissure to supply the leg and genital areas draping from the medial ends of the motor and sensory strips. The remainder of the motor and sensory strips, the internal capsule, and Wernicke's area are all supplied by branches of the middle cerebral artery. The two anterior cerebral arteries are linked together by the short and stubby anterior communicating artery.

The left and right posterior communicating arteries provide supplemental blood to the posterior circulation by anastomosing* the internal carotid artery to the ipsilateral posterior cerebral artery. The midline anterior communicating artery completes the Circle of Willis, a vital arterial arrangement by which focal areas of brain can be provided with collateral blood during times of ischemia. One ischemic hemisphere can be quickly supplemented with blood from the other hemisphere across the anterior communicating artery or from the posterior circulation via the posterior communicating artery. Similarly, the posterior circulation can depend on both internal carotids for extra blood through the posterior communicating arteries.

Anastomosing: Ana = through stoma = mouth; joining of one structure to another.



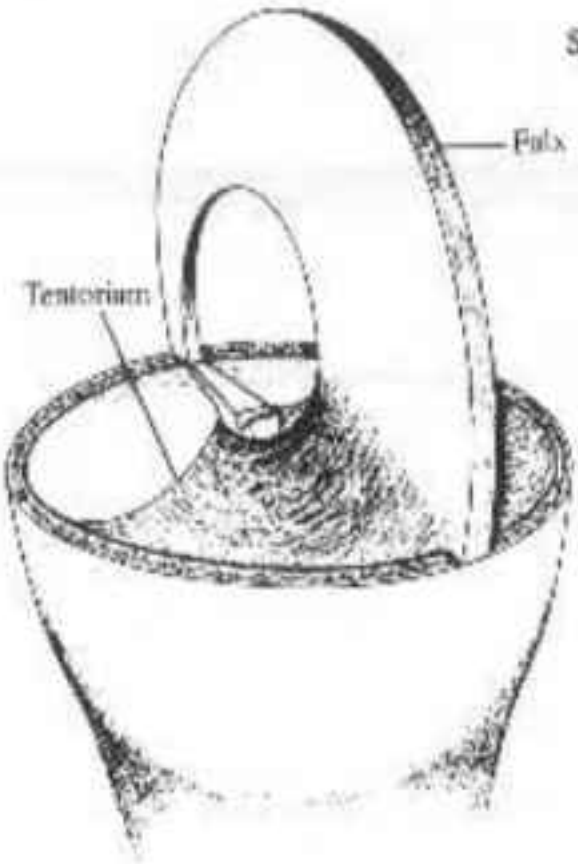
Just by knowing this simple arterial anatomy, you can often localize arterial ischemia to a particular arterial branch. For example, monocular blindness or an altitudinal scotoma would implicate the ophthalmic artery, while leg weakness, or a hemiparesis worse in the leg, suggests ischemia of the medial motor strip from the anterior cerebral artery. Combined aphasia and hemiparesis are due to ischemia of a cortical branch of the middle cerebral artery, while a dense hemiplegia without aphasia or alteration in consciousness is probably due to a deep white matter lesion (internal capsule) from lateral striate branches of the middle cerebral artery.

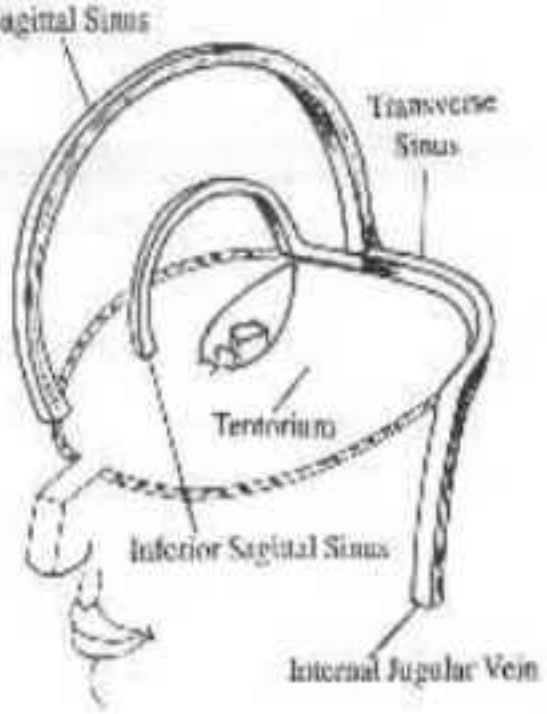
Conversely, aphasia without a hemiparesis suggests a superficial cortical lesion, like an embolus lodging in a small terminal branch of the middle cerebral artery.[9] Partial homonymous hemianopias often accompany the hemiparesis of middle cerebral artery ischemia, but an isolated, dense homonymous hemianopia is more likely due to posterior circulation ischemia which interrupts all visual fibers converging on the occipital lobe.

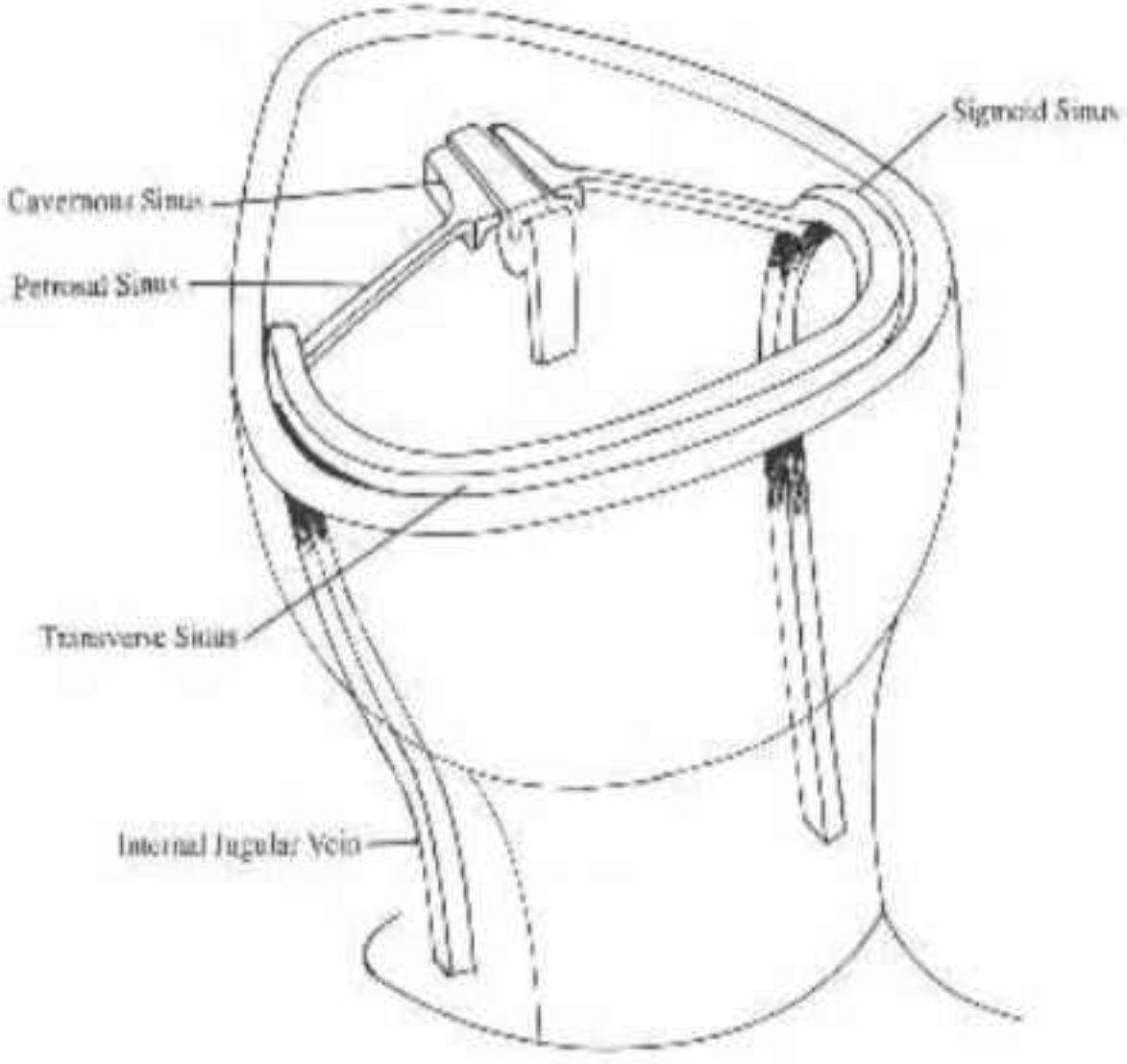
Veins

Some of the brain's major veins we have already touched on. The superior sagittal sinus, draining most of both cerebral hemispheres, meets three other major sinuses—the straight sinus and the two transverse sinuses—at the torcula, a point corresponding to the bony nubbin palpable on your own occiput. While the superior sagittal sinus empties the central bulk of brain, the transverse sinuses drain the lateral and posterior cerebral hemispheres. In addition, the transverse sinuses indirectly drain the eye and triangle of death through the cavernous sinus via the petrosal sinus.

The straight sinus coursing along the apex of the tentorium drains the midbrain and deep hemispheric structures like the lateral and 3rd ventricles, thalamus, and deep white matter.


Falx
Tentorium


Superior Sagittal Sinus
Transverse Sinus
Tentorium
Inferior Sagittal Sinus
Internal Jugular Vein


Sigmoid Sinus
Cavernous Sinus
Petrosal Sinus
Transverse Sinus
Internal Jugular Vein

CHILDHOOD MILESTONES

ALTHOUGH ABNORMAL NEUROLOGIC SIGNS ARE IMPORTANT TO RECOGNIZE IN ADULTS (so that steps can be taken to prevent further neurologic damage), they are doubly important to recognize in early childhood. Seventy years of anguish may hang in the balance if you miss a treatable childhood neurologic illness. You must, at the very least, recognize when a child's neurologic development is lagging.

Milestones for the first seven or eight months progress in a rostral-caudal direction at monthly intervals: one month—eyes, two months—mouth, three months—neck, four months—shoulder, five months—hand, six months—hips, seven months—knees. By one month a baby should be visually tracking his mother's face. By two months he should be smiling socially. If, by three months, the mother walks into your office still supporting the infant's head, the infant is developing too slowly. At four months he should be reaching (actually swiping) for objects (shoulder and proximal arm control), and by five months picking things up with his hands. Sitting unsupported should take place by six or seven months, and most, but not all, infants stand with support by seven or eight months.

From six months to one year the child improves his ability to grasp small objects, beginning at six months with thumb and all four fingers, progressing by eight months to thumb and two fingers, and by ten-twelve months to thumb and index finger alone.[1]

By one year a child should be taking a few independent steps and saying a few words, at least mama and dada. By 18 months he should be saying single words and by 24 months putting them together into phrases. By three years he should be talking to you. At no time before 18 months should the child show hand preference, a sign that strongly suggests something is wrong with the opposite hand (like a hemiparesis).

Head circumference at birth should be about 35 cm. By one year it should have reached 45 cm, and by the teenage years, 55 cm. More importantly, head circumference should grow along the same percentile it began at. If head circumference crosses percentiles, there's something in the head that doesn't belong there: hydrocephalus, subdural hematoma, brain tumor, etc.[2]

SLEEP

THE ONLY SURE THINGS KNOWN ABOUT SLEEP are that it's universal in the animal kingdom and controlled by the brainstem. The trigger for sleep, the reasons for it, the specific cerebral housecleaning that goes on during sleep are all still part of the brain's quiet mystery.

*Narcolepsy**

The intense midnight urge to fall asleep strikes some unfortunate victims during the day, sometimes in embarrassing but rarely dangerous situations. These narcoleptic attacks are related in some way to incoordinated dream cycles. Soon after pounding the pillow we descend from drowsiness (stage 1) into deep sleep (stage 4) over a matter of 30–40 minutes, ascending back to light drowsiness (stage 1 again) over another half hour. At this point—during the second episode of light sleep—begins the first dream of the night. The entire body becomes suddenly limp except for the eyes which dance in all directions (viewing the dream?). After about 5–10 minutes of these rapid eye movements (REM) we descend again into stage 4 sleep, and back up to stage 1 for another dream. With each succeeding cycle (perhaps 8–10 during the night) the descent becomes shallower and the dreams shorter until we awaken, often stepping right out of a dream.

Narcoleptic patients begin REM as soon as they drift off into stage 1 sleep instead of waiting until they ascend from the depths of stage 4 sleep. Narcoleptics may recall these initial dreams as vivid hypnagogic* 'hallucinations.' Or in the morning they may find themselves unable to snap out of the flaccid quadriplegia that normally accompanies REM sleep. Yet, a spouse's mere touch ends this almost magical spell of 'sleep paralysis.'

Even stranger is cataplexy*. When suddenly startled or struck by something funny, narcoleptic patients may instantly collapse into the flaccid quadriplegia of normal REM sleep but without losing consciousness or dreaming. Fortunately, a cataplectic attack lasts only seconds or minutes before the patient is able to resume his usual activities.

This, then, is the full blown tetrad of narcolepsy: daytime sleep attacks, hypnopompic (or hypnogogic) hallucinations, sleep paralysis, and cataplexy.[1] The most straightforward test for narcolepsy is EEG monitoring of the brain waves and eye movements to detect rapid eye movements at the onset of sleep.[2]

Narcolepsy: Narcosis is a state of stupor; lepsy means seizure.

Hypnagogic: On descending into sleep. Hypnopompic, ascending from sleep.

Cataplexy: Not to be confused with catalepsy (waxy flexibility), a strange type of akinesia most commonly seen in certain schizophrenics. When placed in literally any position, cataleptic limbs will remain in that position for hours at a time.

Sleep Apnea

Naturally not everyone who nods off during the day has narcolepsy.[3] Some patients just don't sleep well at night because while sleeping they periodically stop breathing! and the resulting hypoxia awakens them. There are two major reasons for 'sleep apnea.' In one case, soft tissues in the pharynx collapse and obstruct the airway.[4] In the other type of sleep apnea, the patient stops breathing for no apparent reason, called central apnea.[5]

Sleep apnea can be suspected by a history of thrashing about during sleep (in response to the hypoxia), morning headaches, or an attentive spouse who recognizes long periods of apnea during sleep. A history of loud snoring should make you suspicious of partial airway obstruction. Confirmation of sleep apnea requires the nocturnal monitoring of respirations, arterial oxygen, and intrathoracic pressure* (to distinguish airway obstruction from central apnea.)

Though the mainstays of treatment for narcolepsy are psychic energizers (amphetamines), obstructive sleep apnea usually requires a tracheostomy* to bypass the obstruction, or else surgical removal of pharyngeal soft tissue to relieve the obstruction.[6]

Central sleep apnea has been more difficult to treat, because it requires a medication selective enough to stimulate the medullary respiratory center. After noting that pregnant women breath rapidly, even in early pregnancy before the fetus has had time to press up against the diaphragm, investigators have tried treating central sleep apnea with the placental hormone, progesterone, but with only modest success.[7]

Pavor Nocturnus

One of the most striking disturbances of sleep is a childhood condition called pavor nocturnis (night terrors).* Youngsters awaken an hour or so after going to sleep with blood curdling shrieks, only to be forgotten by morning. EEG monitoring has revealed that these children become temporarily stuck in stage 4 sleep. Valium, which prevents us from entering stage 4 sleep, tides these children over until their brains mature enough to spontaneously lift them out of stage 4 sleep.

Intrathoracic Pressure: Forceful attempts to expand the chest in the face of airway obstruction result in highly negative intrathoracic pressures which can be measured with a pressure transducer sounded into the esophagus.

Tracheostomy: A hole is made in the trachea just below the thyroid cartilage. The hole is kept open by a plastic or metal tube inserted through the tracheostomy hole.

NEUROLOGIC DIFFERENTIAL DIAGNOSIS

MOST PHYSICIANS WANT NOTHING TO DO WITH NEUROLOGIC PATIENTS. Because of the complexity of neuroanatomy and the complexity of the neurologic exam, the first step in physical diagnosis, anatomic localization, is simply too frustrating an obstacle. Moreover, since many neurologic illnesses do not have laboratory tests to confirm them (though this has changed with the CAT scan), the etiologic diagnosis often rests precariously on your clinical impression and judgment. Physicians are understandably afraid of misdiagnosing neurologic illnesses and allowing the true diagnosis to work its irreparable damage on the rather unforgiving nervous system.

Besides learning how to analyze neurologic problems, this fear can be minimized by concentrating your differential diagnosis on treatable diagnoses. Unlike internal medicine where an untreatable illness is a rarity, neurology has a sizeable number of illnesses stubbornly unresponsive to treatment*. This may be understandably discouraging to many physicians, particularly ones who want to defeat life-threatening diseases a la Arrowsmith.

The large number of untreatable neurologic illnesses only emphasizes that you *must* recognize the treatable ones. Though it is important to diagnose untreatable conditions (because it stops unnecessary time, money, and effort looking for incorrect diagnoses), understand that once you attach a diagnostic label to a patient, everyone stops questioning that patient's diagnosis, especially if you're a specialist. After all, who's going to challenge a specialist's opinion? Make sure you're not staring at a treatable disease before condemning your patient to an untreatable condition. Make them drag you kicking and screaming to an untreatable one. I don't care how astute you are in diagnosing striatonigral degeneration* or Unverricht's myoclonic epilepsy*, just be

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Unresponsive to Treatment: Many young doctors berate neurology because so little can be done to reverse a neurologic insult. And indeed, following some patients in neurology clinic is a lot like walking the dog. But so is obstetrics clinic where notes may be as brief as 'she okay' or 'she not okay.' It is true that you can cure anything you can get a clamp on and that you can tell more with a needle than you can with a stethoscope, but the reason to enter a specialty should not rest solely on doing something. Each specialty helps people in its own way. If you decide to specialize, just remember that you're going to have to read about the organ you specialize in for the next forty years. So choose an organ that can sustain your interest, one that you actually look forward to reading about.

Striatonigral Degeneration: An illness which resembles Parkinson's disease without the tremor. Striatonigral degeneration does not respond to L-Dopa, presumably because dopamine receptors in the striatum have also degenerated.

Unverricht's Myoclonic Epilepsy: A ruthlessly progressive dementing illness associated with myoclonic seizures of the limbs and trunk. Diagnosis is confirmed by finding pathognomonic Lafora bodies on brain or muscle biopsy.*

sure you don't miss fungal meningitis, hyperthyroid myopathy, subdural hematoma, etc, etc.

In constructing an etiologic differential diagnosis, you need to have a thumbnail sketch of each diagnosis so that after considering each one, you can return to the patient to seek the symptoms and signs that confirm or refute each diagnosis you considered.

Below is a general working list of treatable neurologic insults, ones you must constantly keep in mind simply because they're treatable. If you don't already know which neurologic subsystems or which internal organ systems they affect, if you don't know what signs—neurologic or otherwise—to expect for each of these illnesses, then your work is cut out for you. For any disease you should be able to fill out the following chart.

Disease: _____

Organ System:	Clinical Manifestations:
Systemic	
Skin	
Neuromuscular	
Eyes	
Ears	
Endocrine	
Respiratory	
Cardiac	
GI	
RE	
Urologic	
Genital	
Vascular	
Hematologic	
Bone & Joint	
Coverings & Connective Tissue	

	PRESENTING ORGAN SYSTEM:	TROJAN HORSE ORGAN SYSTEMS:		
	Neuromuscular	Vascular	Hematologic	Coverings & Connective Tissue
DRUG				
A. Drug	Almost any drug in excess Drug withdrawal Drug side effects, especially anticancer drugs,[3] Antabuse*, phenothiazines* Heavy metals* Methyl alcohol* Hypothermia* Drug-induced myasthenia gravis*	IV Amphetamine	Oral contraceptives	Pantopaque*

	PRESENTING ORGAN SYSTEM:	TROJAN HORSE ORGAN SYSTEMS:		
	Neuromuscular	Vascular	Hematologic	Coverings & Connective Tissue
B. Vitamins[12]	Thiamine[*] deficiency Pyridoxine[*] deficiency Pyridoxine excess[13] B12 deficiency Folate[*] deficiency[3] Vitamin A[*] toxicity Biotin[*] deficiency Vitamin E deficiency[*]			
C. Toxin	Tick paralysis[*]			
D. Radiation	Radiation necrosis[*]			
INFECTION				
A. Bacterial[23]	Sepsis[*] Diphtheria[*] Brain abscess[*] Botulism[*] Subacute bacterial endocarditis[*] Tetanus Whipple's disease[*] Leprosy[*] Mycoplasma[*]	Cavernous sinus thrombophlebitis Mycotic aneurysm[77]		Bacterial meningitis[*] Tb meningitis[*] Epidural abscess Subdural empyema[*]
B. Fungal[26]	Fungal brain abscess[26] Mucormycosis[*]			Fungal meningitis[78]
C. Spirochetal	Syphilis[79] Lyme Disease[*]			
D. Rickettsial	Rocky Mountain Spotted Fever[*]			
E. Viral	Herpes Simplex encephalitis Herpes Zoster[*] (Shingles)			
F. Parasitic	Cysticercosis[*] Trichinosis[*] Toxoplasmosis[*]			
GENETIC/DEGENERATIVE				
Vitamin Dependent Inborn Errors (see chart on page 438)		Unruptured Cerebral AVM	Sickle Cell Anemia	Arachnoid cyst[*]
Arnold Chiari Malformation[*]		Unruptured spinal AVM[*]	Hyperlipidemia	Subarachnoid cyst
Klippel-Feil[*]		Unruptured aneurysm		Anterior sacral meningocele[*]
Syringomyelia[*]		Fibromuscular Dysplasia[*]		Dermal sinus tract[*]
Parkinson's Disease[*]				
Wilson's Disease[*]				
Dystonia Musculorum Deformans[*]				
Gilles de la Tourette[*]				
Adrenoleukodystrophy[*]				
Porphyria[*]				
Narcolepsy				
Leigh's Encephalopathy[*]				
Refsum's Disease[*]				
Neurofibromatosis[*]				
Periodic Paralysis[*]				

PRESENTING ORGAN SYSTEM:	TROJAN HORSE ORGAN SYSTEMS:		
Neuromuscular	Vascular	Hematologic	Coverings & Connective Tissue
IMMUNOLOGIC			
Multiple Sclerosis*	Systemic Lupus Erythematosus*	Thrombotic thrombocytopenic purpura*	Arachnoiditis*
Sydenham's Chorea*	Polyarteritis*	Hemolytic anemia syndrome*	
Postinfectious demyelination*	Temporal arteritis*		
Sarcoid*	Granulomatous arteritis*		
Behcet's Disease*	Takayasu's disease*		
Vogt Koyanagi Harada*			
Cogan's syndrome*			
Tolosa Hunt*			
Bell's Palsy			
Sjogren's syndrome*			
Rheumatoid Arthritis*			
Guillain Barre*			
Scleroderma*			
Myasthenia Gravis*			
Polymyositis/Dermatomyositis*			
Polymyalgia Rheumatica*			
TUMOR			
Malignant Glioma*	Atrial myxoma*	Polycythemia vera*	Meningioma*
Ependymoma*	Marantic endocarditis	Leukemia	
Medulloblastoma*		Lymphoma*	
Cerebellar astrocytoma*			
Cerebellar Hemangioblastoma		Waldenstrom's Macroglobulinemia*	
Teratoma*			
Neuroblastoma			
Dermoid/Epidermoid*			
Chordoma*		Thrombocytosis	
Pinealoma*		Hand-Schuller-Christian Disease*	
Histiocytosis*			
Metastatic Tumor			
3rd Ventricular colloid cyst*			
Choroid plexus papilloma*			
Craniopharyngioma*			
Pituitary tumor*			
Optic nerve glioma			
Nasopharyngeal carcinoma*			
Mucocele*			
Accoustic neuroma			
Glomus tumor*			
Morton's neuroma*			
Eaton Lambert syndrome*			
Opsoclonus			
Other remote effects of carcinoma*			
TRAUMA			
Traumatic syringomyelia	Carotid cavernous fistula*		CSF leak*
Depressed skull fracture*	Aortic dissection		Subdural hematoma
Cervical fracture			

PRESENTING ORGAN SYSTEM:	TROJAN HORSE ORGAN SYSTEMS:		
			Coverings & Connective
Neuromuscular	Vascular	Hematologic	Tissue
Causalgia	Carotid dissection*		Epidural hematoma
			Leptomeningeal cyst*
MECHANICAL			
Hydrocephalus*	Atherosclerosis* (& aortic thrombosis)		
Pseudotumor cerebri*			
Premature suture closure*			
Cerebral herniation	Embolic arterial occlusion		
Giant aneurysm*			
Tic Douloureux*	Vertebral artery compression by osteophyte*		
Hemifacial spasm			
Atlanto-Axial dislocation*			
Diastematomyelia*	Carotid sinus syncope*		
Spinal stenosis*			
Herniated disc			
Compression Neuropathy[13]			
Thoracic outlet			
Saturday night (radial) palsy*			
Tardy ulnar nerve palsy*			
Cubital tunnel syndrome*			
Anterior interosseous nerve*			
Carpal tunnel syndrome*			
Lateral femoral cutaneous			
Sciatic			
Common peroneal			
Tarsal tunnel*			
ORGAN DYSFUNCTION			
Systemic: Orthostatic hypotension*			
Vasovagal hypotension*			
Hypertension*			
Fever*			
Neurologic: Subclinical status epilepticus*			
Hysteria			
Psychosis			
Depression			
Ear: Meniere's disease*			
Endocrine[17]: Inappropriate ADH*			
Diabetes mellitus			
Diabetes insipidus			
Panhypopituitarism*			
Hyper/Hypo thyroidism*			
Hyper/Hypo calcemia*			
Hypophosphatemia*			
Hypomagnesemia*			
Hyper/Hypo glycemia*			
Hyper/Hypo cortisol*			
Pheochromocytoma*			

PRESENTING ORGAN SYSTEM:	TROJAN HORSE ORGAN SYSTEMS:			
	Neuromuscular	Vascular	Hematologic	Coverings & Connective Tissue
Respiratory	Hypoxia* (including pulmonary emboli)			
	Hypercapnia*			
	Hyperventilation syndrome*			
	Neurogenic pulmonary edema*			
Cardiac	Tachy/Brady syndrome*			
	Ventricular tachycardia[165]			
	Sinus bradycardia			
	Aortic stenosis*			
	Valve emboli*			
	Mitral valve stenosis			
	Mitral valve prolapse			
	Mural thrombi			
	Left atrial myxoma[167]			
	Idiopathic hypertrophic subaortic stenosis*			
Gastrointestinal	Liver failure*			
Urologic	Uremia*			
	Hyper/Hyponatremia*			
	Hyper/Hypokalemia*			
	Polycystic kidneys*			
Genital	Pregnancy*			
Vascular	Migraine*			
	TIA/Light stroke*			
	Retinal emboli*			
	Subarachnoid hemorrhage*			
	Intracerebral hemorrhage			
	Cerebellar hemorrhage*			
	Pituitary apoplexy*			
	Hypertensive encephalopathy*			
	Superior sagital sinus thrombosis*			
	Subclavian steal*			
	Aortic coarctation*			
Hematologic	Polycythemia			
	Anemia*			
	Thrombocytosis*			
	Thrombocytopenia*			
	Hyperproteinemia*			
	Hyperlipidemia			
	Prolonged prothrombin time*			
	Prolonged partial thromboplastin time*			
	Disseminated intravascular coagulation[166]			
Bone & Joint	Ankylosing spondylitis*			
	Fibrous dysplasia*			
Coverings & Connective Tissue	Cardiac tamponade			

DRUGS

Antabuse (disulfuram): A drug which interrupts the metabolism of alcohol at a step that accumulates acetaldehyde, a lethal chemical. The patient who drinks while taking Antabuse develops headache, vomiting, dyspnea, hypotension, and even stupor, coma, and death. Antabuse is a stiff reminder to alcoholics not to drink. Antabuse can also cause a motor polyneuropathy.[4]

Phenothiazines: Besides producing Parkinsonian signs, phenothiazines also lower the seizure threshold somewhat.[5] Rarely, patients taking phenothiazines may suddenly develop altered consciousness, rigidity, and dramatic fever, called the neuroleptic malignant syndrome.[6]

Heavy Metals: Lead,[7] arsenic,[8] mercury,[9] thallium[10].

Methyl Alcohol (Methanol): 'Wood alcohol.' Accidental poisoning can quickly result in severe bilateral optic neuropathy with characteristic centrocecal scotomas. Treatment is to dilute out the methyl alcohol with intravenous ethyl alcohol (what we normally drink), or else hemodialysis.[11]

Hypothermia: Extreme cold may damage the large axons in peripheral nerves causing painful dysesthesias.[12]

Drug Induced Myasthenia: Certain drugs like penicillamine (used to treat rheumatoid arthritis and Wilson's disease) and some antibiotics may partially block neuromuscular transmission causing a weakness that resembles myasthenia gravis.[13]

Pantopaque: The oily dye used in myelography. There's also a water-soluble dye called Metrizamide. Some patients react to the dye with meningeal inflammation, a potentially serious condition called arachnoiditis. The risk is much higher if the myelogram is performed when there's blood in the CSF, so if a radiologist nicks a blood vessel with the LP^3 needle, he may very well cancel the myelogram. The risk of arachnoiditis is probably lower with the water soluble dye, Metrizamide.[14]

Thiamine: Vitamin B1. Besides Wernicke's encephalopathy, thiamine deficiency causes beri-beri: heart failure and polyneuropathy. Wernicke's encephalopathy can occur in anyone on prolonged IV's without vitamin supplements.[15]

Pyridoxine: Vitamin B6. An important cofactor in many enzymatic reactions, especially GABA synthesis. Because GABA is a critical inhibitory neurotransmitter, infants born with genetically low GABA levels may seize shortly after birth. The seizures usually respond to high dose vitamin B6.[17] (See vitamin responsive amino acidopathies in chapter 35.)

Folate: A water soluble vitamin central to many important metabolic pathways—see amino acid chart in chapter 35.

Vitamin A: A fat-soluble vitamin used by the eye for normal vision. Daily ingestion of more than 25–50,000 units runs the risk of pseudotumor cerebri.

Biotin: Another coenzyme (see amino acid chart in chapter 35).

Vitamin E Deficiency: Results from chronic malabsorption (as occurs in Bassen-Kornzweig disease). Causes a sensory/motor polyneuropathy.[20]

Tick Paralysis: Certain ticks contain a paralyzing poison which works by preventing electrical transmission along terminal axonal twigs.[21]

Radiation Necrosis: Months to years after excessive radiation, the brain or spinal cord suffer progressive vascular occlusions and resulting infarctions.[22]

INFECTION

Sepsis: Fever, chills, prostration, and delirium due to bacteria (and occasionally fungi) in the bloodstream.[24]

Diphtheria: Diphtheria is now virtually nonexistent in developed countries because of the near universal DPT innoculations against Diphtheria, Pertussis (whooping cough), and Tetanus. Diphtheria begins as a pharyngitis covered by an adherent exudative membrane which, when peeled off, leaves the underlying mucosa bleeding. Diphtheria releases a toxin that demyelinates cranial and peripheral nerves.

Brain Abscess: Don't wait for fever to diagnose brain abscesses. Perhaps 50% of patients with brain abscesses are afebrile.[25] The brain itself is immunologically "privileged"; unless inflammatory cells reach the blood or meninges, the body may be unaware of an abscess forming in the brain. Somewhat surprising is that brain abscesses rarely develop in the midst of meningitis.

Amazingly enough, the best record to date for the surgical treatment of brain abscesses is over a hundred years old, held by the Scotsman, Dr. William Macewen. To keep pus draining from the abscess, he often sewed—don't laugh—a chicken bone into the abscess cavity.[26]

Botulism: There are four varieties of botulism that produce disease in man: type A, B, E and rarely F.[27] Types A and B, which account for almost 90% of the outbreaks, are more likely to involve the respiratory muscles than type E.[28] Besides eating the toxin, you can contract botulism by letting it contaminate devitalized areas of a wound.[29]

Subacute Bacterial Endocarditis: A smoldering heart valve infection. Because there's no blood supply to the valve itself, white cells can't reach the bacteria to kill them. The friable vegetations which form on the valve may embolize to any artery of the body. At times, bacteria from the infected valve embolize to small distal arterioles in the brain. The bacteria infect and weaken the arteriolar wall, causing a 'mycotic' aneurysm. (Mycotic, a term denoting fungal infections, is a misnomer.)

Whipple's Disease: A low grade bacterial infection of the gut producing abdominal pain, diarrhea, malabsorption, low grade fevers, arthralgias, and occasionally neurologic signs resembling Wernicke's encephalopathy.[30] Very rare condition.

Leprosy: From scaly or rough in Greek. Leprosy is an infection which damages peripheral nerves either by direct infection (lepromatous leprosy) or by allergic inflammation (tuberculous leprosy). Patches of skin become completely anesthetic to any stimulus. Eventually the insensitive skin suffers repeated unrecognized trauma resulting in unsettling disfigurement.[31]

Mycoplasma: Normally, bacteria have a rigid outer wall lined on the inside by a thin plasma membrane. Mycoplasma are bacteria without the rigid outer wall. Mycoplasma usually causes a mild type of pneumonia called atypical pneumonia, but may rarely cause infections of the brain.[32]

Bacterial Meningitis: Infants less than two months of age are particularly susceptible gram negative meningitis and listeria (gram positive) meningitis. From two months to five years of age, children are particularly vulnerable to Hemophilus influenza meningitis.

Partially treated meningitis may obliterate bacteria on both the gram stain and culture without curing the infection, which then roars back in a day or so without continued, proper antibiotic therapy.[34]

Tb Meningitis: Tuberculous meningitis is relatively common in childhood. Do an acid fast stain on the CSF in any child with suspected meningitis if the routine gram stain does not readily reveal gram positive or gram negative bacteria.

Empyema: A collection of pus outside the parenchyma of an organ in a preexisting space, like the pulmonary pleural space, subdural space, or subphrenic space (between the liver and diaphragm).

Mucormycosis: A highly invasive fungal infection of the nasopharynx and orbit, usually seen in diabetics who have suffered bouts of ketoacidosis.[37]

Lyme Disease: A tick-borne, spirochetal, summertime disease beginning with a rash, fatigue, myalgias, headache, and fever. Within a month or two, patients develop a variety of peripheral nerve, root, and cranial nerve signs (especially facial weakness). Inflammatory CSF.[40]

Rocky Mountain Spotted Fever: A rickettsial disease transmitted by certain ticks. The disease begins with fever, headache, and abdominal pain, and develops a characteristic rash that begins—unusual for rashes—on the palms and soles. Neurologic signs occur when the vasculitis accompanying this disease produces cerebral ischemia.[41]

Herpes Zoster: The chicken pox virus (herpes zoster) doesn't die; it merely hibernates in dorsal root (or cranial nerve) ganglia. Later, in adult life the virus reemerges as painful pustules in the

distribution of a root or cranial nerve (more commonly in patients with cancer). The pain may then persist long after the pustules have healed. Zoster affecting V^1 is called herpes ophthalmicus, an illness that may scar the cornea.[42]

Cysticercosis: Eating uncooked pork infested with the pork tapeworm, cysticercus, may allow the parasite to encyst (hibernate) in the brain (especially cortex) or form grape-like clusters in the fourth ventricle. Common in Mexico.[43]

Trichinosis: Another pork parasite which encysts in muscle (including the heart) causing tender myopathic weakness.

Toxoplasmosis: A common parasite which most people contract without overt infection. Fetuses and patients on anticancer drugs or otherwise immunosuppressed are susceptible to this multisystem infection.[44]

GENETIC/DEGENERATIVE

Arnold Chiari: A multifaceted malformation of the central nervous system whose trademark is herniation of the medulla, 4th ventricle, and cerebellar tonsils downward through the foramen magnum.[45] Cerebellar ataxia, bilateral pyramidal tract signs, and lower brainstem signs (downbeat nystagmus, dysarthria, dysphagia, tongue atrophy) may not appear until adolescence or even middle life.[46]

More severe forms of Arnold Chiari include aqueductal stenosis (causing noncommunicating hydrocephalus) and heterotopias (islands of cortex deep within the white matter resulting in retardation and/or seizures). In the spinal column Arnold Chiari may be associated with syringomyelia, spina bifida (asymptomatic splitting of the vertebral lamina ring) or worse, congenital lumbar myelomeningocele: herniation of the lumbosacral cord and roots through the spina bifida causing paraplegia and absent bowel or bladder control.[47] A skull xray may make the diagnosis of Arnold Chiari by showing upward displacement of the dens.[48]

Klippel Feil: A malformation of cervical vertebrae, primarily fusion of two or more adjacent vertebrae. The underlying cervical spinal cord is also malformed, often causing a curious childhood disturbance called mirror movements—movements of one hand are mirrored by the other hand. The explanation for mirror movements may lie in rerouted messages through the cervical cord or in recruitment of motors centers outside the motor strip (basal ganglia, supplementary motor area?), centers which normally use bilateral pathways into the spinal cord.[49]

Syringomyelia: These patients frequently have Arnold Chiari malformation, too, and surgery for the associated Arnold Chiari malformation sometimes helps the syringomyelia.[50]

Parkinson's Disease: Three other degenerative illnesses mimic the bradykinesia of Parkinson's disease: Striatonigral Degeneration, Shy Drager, and Progressive Supranuclear Palsy.[51] Shy Drager's most characteristic sign is blatant orthostatic hypotension due to autonomic insufficiency. Progressive Supranuclear Palsy's signpost is a remarkable inability to look up and down voluntarily, but retained ability to do so passively! Have the patient stare at an object while you stimulate his labyrinths by rocking his head forward and backward (vertical doll's eyes). The eyes now rotate up and down in their sockets surprisingly well because the up and down gaze centers in the midbrain are being stimulated from *infranuclear* centers in the vestibular nucleus.

Wilson's Disease: This disease results from an autosomal recessive absence of ceruloplasmin, the serum protein which transports dietary copper from the gut. Without ceruloplasmin to attach to, copper attaches loosely to albumin and gets deposited in the liver, kidney, and brain, causing cirrhosis, Fanconi's syndrome (urinary loss of bicarbonate, amino acids, and glucose), and extrapyramidal signs. In children, Wilson's disease also causes hemolytic anemia and acute hepatitis.[52]

Dystonia Musculorum Deformans: A cruel disease of childhood which bends and twists children into shockingly contorted dystonia. A thalamotomy may help. No known pathology.[53]

Gilles de la Tourette: Another childhood illness without microscopic pathology, presumably affecting the extrapyramidal system. Thought for a long time to be psychiatric, this disease causes

involuntary outbursts of barking, grunting, and swearing with tics of the limbs and face.[54]

Adrenoleukodystrophy: A sex-linked illness causing adrenal failure and myelin breakdown (leuko = white matter).[55]

Porphyria: An autosomal dominant overproduction of heme (heme is part of the hemoglobin molecule). Accumulated intermediates turn the urine purple when the urine is exposed to sunlight (porphyria means purple in Greek). Symptoms include abdominal pain, convulsions, psychosis, and acute peripheral neuropathy.[56] Treatment is hematin, a chemical that inhibits one of the upstream enzymes, delta-aminolevulinic acid synthetase.[57]

Leigh's Encephalopathy: A recurrent brainstem illness of childhood caused by an uncertain disturbance of thiamine metabolism. Exact pathophysiology is unknown.[58]

Refsum's Disease: An enzymatic block of phytanic acid degradation (a fatty acid). Patients suffer from ichthyosis (severe scaly skin), retinitis pigmentosa, deafness, peripheral neuropathy, and posterior column damage.[59] The constellation of retinitis pigmentosa, ataxia, peripheral neuropathy, and deafness is also seen in two other genetic (but untreatable) diseases: Kearns Sayre syndrome, and Bassen Kornzweig (abetalipoproteinemia.)

Neurofibromatosis (Von Recklinghausen's Disease): An autosomal dominant multisystem disease with two relatively separate neurologic targets: the central nervous system and the peripheral nervous system. The CNS form causes malignant brain tumors and acoustic neuromas; the peripheral form causes tumors on peripheral nerves. Eventually these peripheral nerve tumors degenerate into malignancy.[60]

Periodic Paralysis: Relatively acute episodes of quadriparesis lasting hours to days precipitated by sudden shifts of serum potassium (into and out of muscle?). Probably due to an abnormality of the muscle membrane.

Unruptured Spinal AVM: Spinal arteriovenous malformations cause myelopathic signs in two ways: by shunting blood away from normal spinal cord tissue, and by slowly enlarging over years into a mass large enough to compress the cord.[61]

Fibromuscular Dysplasia: An idiopathic thickening of arterial walls resulting in narrowing of the lumen, sometimes severe enough to impair blood flow through the artery (renal and carotid arteries especially). More common in women.[62]

Arachnoid Cyst: A congenital collection of CSF within the arachnoid indenting the brain.[63] If the cyst is completely within the parenchyma of the brain, it's called a subarachnoid cyst. If the cyst communicates with the lateral ventricle, it's called a porencephalic cyst. Any of these bubbles can cause focal disturbances like seizures or hemiparesis.

Anterior Sacral Meningocele: A dural outpouching from the lumbar spinal canal into the pelvis, dragging the cauda equina with it.[64]

Dermal Sinus Tract: An innocent looking dimple over the lumbosacral region or occiput may actually be the opening of a thin channel leading bacteria directly into the subarachnoid space. For this reason, dermal sinus tracts should be surgically repaired to prevent meningitis.[65] Frequently associated with a lipoma in the cauda equina at the point where lumbar dermal sinus tracts terminate.[66]

IMMUNOLOGIC

Multiple Sclerosis: Roughly speaking, multiple sclerosis progresses in two ways: as recurrent bouts above and below the foramen magnum, or as a slowly progressive myelopathy.[67] As immunologic evidence gathers, neurologists are beginning to use aggressive immunologic therapy.[68]

Sydenham's Chorea: In mounting an attack against a streptococcal throat infection, the body presumably mistakes the basal ganglia for streptococcus. A similar mistaken attack against the patient's own heart valves is called rheumatic fever.[69]

Postinfectious Demyelination: An allergic attack against a patient's own central nervous system myelin, presumably directed against an antigenic site on the virus which resembles one in the patient's myelin.[20]

Sarcoid: A poorly understood, usually low grade inflammatory illness directed against an unknown agent. Typically attacks the lungs, lymph nodes, cranial nerves (mainly II and VII), hypothalamus, and peripheral nerves.[21] More frequent in blacks.

Behcet's Disease: A low grade, multisystem venulitis/arteritis, more commonly seen in the Far East. Causes recurrent small (aphthous) ulcers in the mouth and genitalia, uveitis, and not uncommonly, arthritis, colonic ulcers, thrombophlebitis, and a multitude of CNS signs.[22]

Vogt-Koyonagi-Harada: An idiopathic inflammatory illness affecting the eye, skin (depigmentation of hair and skin), and multiple cranial nerves; inflammatory CSF.[23]

Cogan's Syndrome: Bilateral deafness associated with inflammation in the anterior chamber of the eye (keratitis). Etiology unknown.[24]

Tolosa Hunt Syndrome: A painful inflammatory condition along the cavernous sinus intercepting III, IV, VI, and V^1. Etiology also unknown.[25]

Sjogren's Syndrome: Idiopathic inflammation in the salivary and lacrimal glands. Classically causes dry eyes and dry mouth. Neurologic complications, mainly vasculitis, may also occur.[26]

Rheumatoid Arthritis: An inflammatory joint disease which begins in joint synovia and destroys the underlying joints, particularly the wrists, knees, and ankles. Neurological involvement results from an associated arteritis causing cerebral and peripheral nerve infarctions. Also, inflammatory destruction of the ligaments binding C1 to C2 allows the dens to repeatedly bump the cord resulting in a cervical myelopathy.[27]

Guillain Barre: An inflammatory attack against peripheral nerve myelin. It's not clear if the demyelination begins in the roots and proximal nerves and over days to weeks spreads centripetally into more distal peripheral nerves, or if the demyelination begins simultaneously in the roots and peripheral nerve.[28] Without intact myelin, patients become quickly paralyzed, often requiring a ventilator for life support until the myelin can be repaired—usually weeks to months. Guillain Barre usually, but not always, spares the bowels, bladder, and extraocular muscles, and may occasionally begin at the cranial nerves and progress caudally.[29] The two characteristically abnormal tests—elevated CSF protein and slowed nerve conduction velocity—do not turn positive until at least a week after the onset of symptoms.

In contrast to the acute steroid *resistant* demyelinative neuropathy of Guillain Barre is the more chronic, slowly progressive (or fluctuating) demyelinative neuropathy that *does* respond to steroids.[30]

A rare subvariant of Guillain Barre, the Fisher variant, begins with cerebellar ataxia and ophthalmoplegia (including the pupils) with only mild to moderate progression below the neck. The ataxia is thought by some to result from demyelination of heavily myelinated axons en route from the muscle spindle to the cerebellum.[9]

Scleroderma: Slowly progressive scarring and stiffness in the skin, heart (?), GI tract, and kidneys. Major damage occurs in the kidneys. May also cause a peripheral or trigeminal neuropathy.[31]

Myasthenia Gravis: Fluctuating (improves after a night's rest) weakness (usually worse above the shoulders, but in older patients may be worse below the shoulders) resulting from antibodies against acetylcholine receptors in the neuromuscular membrane. Removal of the thymus gland, the source of cell mediated immunity, seems to improve the patient's clinical state over the long haul. Some 15% of myasthenics harbor a (usually benign) thymoma.[32]

Polymyositis/Dermatomyositis: Widespread inflammation in muscles directed against some, as yet, unrecognized muscular antigen.[34] If associated with a skin rash, the myopathy is called dermatomyositis. In adults, the rash is typically seen over the upper chest; in children, over the knees and knuckles with a bluish discoloration around the eyes.[35]

Polymyalgia Rheumatica: An inflammatory arteritis of older people (over 60 years) which looks under the microscope like temporal arteritis, but differs from temporal arteritis by generally confining itself to arteries below the neck.[86] Patients suffer from low grade fever, anorexia, fatigue, stiffness, and tender (but not weak) muscles.

Systemic Lupus Erythematosus: The patient, usually young, is mysteriously stimulated to make antibodies against her own DNA. The resulting antigen-antibody complex deposits in arteries, especially those in the kidney, eliciting a frequently life threatening arteritis. Cerebral involvement causes strokes, seizures, chorea, pseudotumor cerebri, and myelopathy.[87] May occasionally cause an isolated trigeminal neuropathy.[88] Some patients manufacture coagulation inhibitors, making them vulnerable to subdural hematomas.[89]

Polyarteritis: A more obscure arteritis than lupus, but equally life threatening, polyarteritis may obstruct or perforate any artery in the body, and thereby produce virtually any symptom or sign. Common ones, though, are hypertension, mononeuropathy multiplex, pulmonary hemorrhage, GI tract necrosis, and renal failure.

Temporal Arteritis: An affliction of older people which preferentially occludes cranial arteries, especially branches of the ophthalmic artery. Patients suffer from headaches, swollen and tender superficial temporal arteries, infarctions of the optic nerve and retina, ophthalmoplegia, and strokes.[90]

Granulomatous Arteritis: A granuloma is a slow, grumbling inflammatory reaction in which a posse of chronic inflammatory cells (lymphocytes and macrophages) encircles the antigen. Frequently included in the attack are multinucleated Langerhans giant cells (multiple inflammatory cells fused together) indicating chronic inflammation. TB and sarcoid are two common granulomatous diseases.

Takayasu's Disease: An arteritis involving the large vessels in and around the aortic arch.[91]

Thrombotic Thrombocytopenic Purpura: Idiopathic, life-threatening hemolysis and thrombocytopenia. Therapy includes anti-inflammatory drugs (steroids, anticancer drugs), splenectomy, and plasmapheresis.[92]

Hemolytic Uremia Syndrome: A malicious, idiopathic childhood illness that strikes from nowhere with sudden intravascular hemolysis and renal failure.

Arachnoiditis: A slowly progressive inflammatory scarring of the spinal meninges and subarachnoid space. The dense adhesions trap the cauda equina and strangle the cord, resulting in slowly progressive sensory and motor paralysis (upper *and* lower motor neuron signs).[93]

TUMOR

Glioma: A tumor of glial cells: oligodendrocytes (CNS myelin) and astrocytes (the brain's inflammatory and support cells).

Ependymoma: A tumor of ependymal cells, the cells which line the ventricular walls and central spinal canal. Since the central spinal canal collapses before birth, ependymal cells in the spinal cord constitute a central column of cells extending into the filum terminale, a filament that tethers the conus medullaris to the bottom tip of the spinal canal.

Medulloblastoma: Blast is a general term for any primitive cell before it differentiates into an adult cell line. A medulloblast is a primitive cerebellar neuron. The vast majority of medulloblastomas occur in early childhood, almost always beginning in the cerebellar vermis with truncal ataxia. Friable bits of the tumor metastasize throughout the subarachnoid space, commonly gravitating down the spinal canal. Medulloblastomas always melt away with radiotherapy, but usually return.[94]

Cerebellar Astrocytoma: Unlike medulloblastomas, cerebellar astrocytomas are frequently cystic, begin in a cerebellar hemisphere (limb ataxia), do not metastasize, strike slightly older children (6-12 years), and despite resistence to radiation, usually disappear after surgical resection.[95]

Cerebellar Hemangioblastoma: A small, vascular angioma attached to the wall of a large associated cyst. A chemical released from this tumor often stimulates the bone marrow to make extra blood (polycythemia).[96]

Teratoma: A tumor consisting of tissue which doesn't belong in that region, like a tooth in an ovarian tumor.

Dermoid/Epidermoid: A tumor which resembles dermal or epidermal tissue, presumably arising from dermal or epidermal cells caught during fetal development within deeper structures.

Chordoma: A locally invasive tumor commonly found along the clivus or in the sacral region. Chordomas arise from primitive cells that in early embryonic life transiently formed a notochord. As a cartilaginous-like column extending down the back, the notochord was once very important to our phylogenetic ancestors; our transient embryonic notochord acknowledges this heritage.[97]

Pinealoma: A pineal tumor consisting of many subtypes depending on the predominant cell. Frequently causes premature puberty. Metastasizes early across the third ventricle to the hypothalamus and optic chiasm.[98]

Colloid Cyst: A slowly growing cyst of thick gooey protein, most commonly found suspended from a short stalk in the third ventricle. When the patient bends over, the cyst may swing into and acutely obstruct the foramen of Monro, causing acute unilateral hydrocephalus; clinically the patient develops a severe headache and sudden unconsciousness.[99]

Choroid Plexus Papilloma: A tumor of the choroid plexus. Usually occurs in the atrium of the lateral ventricle where the tumor can attain a surprisingly large size before becoming symptomatic.[100]

Craniopharyngioma: A benign, often cystic tumor arising from embryonic pituitary stalk cells which were trapped during fetal development in the parasellar area. Frequently calcified (i.e., visible on plain skull film), craniopharyngiomas become symptomatic by compressing the pituitary gland and optic chiasm.[101]

Pituitary Tumor: Any pituitary cell can proliferate into a hormone secreting tumor. Depending on its cell type, the tumor may cause acromegaly (growth hormone),[102] Cushing's disease (ACTH), galactorrhea (prolactin),[103] or hyperthyroidism (TSH). Pituitary tumors slowly bulge upward out of the pituitary fossa (compressing the optic chiasm) or laterally into the cavernous sinus (ophthalmoplegia).

Nasopharyngeal Carcinoma: Because nasopharyngeal carcinoma usually begins near the fossa of Rosenmuller adjacent to the Eustacian tube, be suspicious of any patient presenting with serous otitis media, a condition suggesting a blocked Eustacian tube. Nasopharyngeal carcinoma frequently traps cranial nerves (III, IV, VI, IX, X).[103]

Mucocele: An accumulation of mucus within an obstructed sinus, usually the ethmoid or frontal sinus, rarely the sphenoid sinus. A mucocele slowly expands the sinus, causing exophthalmos and ophthalmoplegia. A mucopyocele is an infected mucocele.[104]

Glomus Tumor (Chemodectoma): Glomus tumors arise from chemoreceptor cells scattered throughout the head and neck: in the ear (glomus tympanicum), along the jugular vein (glomus jugulare), and along the vagus nerve (glomus vagale).[105]

Morton's Neuroma: A tender inflammatory nodule on a small nerve in the foot, usually between the third and fourth toes. The neuroma forms in response to recurrent trauma and compression.[106]

Eaton-Lambert Syndrome: Certain cancers, especially lung cancer, provoke an immune attack which prevents the release of acetylcholine packets at the neuromuscular junction. Unlike myasthenia gravis, the weakness of Eaton-Lambert is usually worse below the neck.[107]

Remote Effets: Besides the Eaton-Lambert syndrome and opsoclonus, remote carcinomas may also cause (by unknown mechanisms) cortical, cerebellar, posterior column, peripheral nerve, and proximal muscle dysfunction.[108]

Atrial Myxoma: A benign gelatinous tumor within the left or right atrium of the heart. The tumor may obstruct the tricuspid or mitral valve, or friable bits of the tumor may embolize to the brain.[111]

Polycythemia Vera: Blood begins to sludge above a hematocrit of 55% (and maybe even less if the blood flow is sluggish). Polycythemia vera may cause cerebral ischemia or, rarely, intracerebral hemorrhage.[112]

Lymphoma: A malignant overgrowth of lymphocytes in lymph nodes and blood. The lymphocytes frequently infiltrate around cerebral blood vessels and the hypothalamus.[113]

Waldenstrom's Macroglobulinemia: Like multiple myeloma, Waldenstrom's is a malignant overcloning of one particular plasma cell. While crowding out other normal bone marrow cells, these malignant plasma cells mass-produce a single large IgM macroglobulin which, by its mere size and interaction with other blood components, causes hyperviscosity (especially when it's cold) and a bleeding diathesis.[114] Multiple myeloma plasma cells mass-produce smaller IgG globulins.

Hand-Schuller-Christian: A malignant overgrowth of macrophages which infiltrate the hypothalamus and bones.

Meningioma: A tumor, only rarely malignant, attached to the meninges but actually arising from connective tissue cells within the arachnoid villi—which explains why most meningiomas are found near major draining sinuses over the hemispheres or along the sphenoid ridge. Meningiomas usually form globular masses, but some 'en plaque' meningiomas creep along the bone as a thick sheet of tumor.[115]

TRAUMA

Depressed Skull Fracture: Instead of simply cracking, the fractured skull bone is displaced inward against the brain, occasionally obstructing a major venous sinus or even injuring a focal area of cortex. The depressed bone may also tear the dura providing bacteria with a passageway into the subarachnoid space.[116]

Carotid Cavernous Fistula: Any hole in the intracavernous carotid artery will allow high pressure arterial blood to shunt into the low pressure cavernous sinus. The rise in cavernous sinus pressure bulges the eye forward, and may adversely affect its vision. As the shunt enlarges, cranial nerves III, IV, and VI may also be affected. Listen for a loud bruit over the eye.[117]

Aortic Dissection: A hematoma dissecting within the aortic wall may occlude the takeoff of the common carotid artery or the takeoff aortic branches to the spinal cord.

Carotid Dissection: Causes neurologic symptoms by obstructing the carotid lumen, or by providing a site for thrombi to form.[118]

CSF Leak: Clear fluid draining from the nose (rhinorrhea) or ear (otorrhea) should be collected to measure the fluid's glucose concentration. A high glucose concentration implies CSF. Usual causes are past head trauma severe enough to tear the dura, but even an empty sella (downward extension of CSF into the sella turcica) may develop rhinorrhea.[119] Because of the risk that bacteria may gain entry into the subarachnoid space, CSF leaks should always be repaired.[120] Recurrent meningitis is often a clue to an occult CSF leak.

Leptomeningeal Cyst: A dural tear beneath a skull fracture may allow CSF pulsations to slowly erode bone on either side of the fracture, and then expand the fracture. Surgical repair of the dural tear is necessary to prevent further bony erosion.[121]

MECHANICAL

Hydrocephalus: Not everyone with hydrocephalus and dementia improves after shunting, and deciding which patients to shunt is controversial. It's generally agreed that symptomatic patients (dementia, gait apraxia, and urinary incontinence) with intermittent elevation of CSF pressures should be shunted.[122] If CSF pressure monitoring fails to reveal elevations of intracranial pressure, it's doubtful that shunting will improve the patient's symptoms.

Pseudotumor Cerebri: Also called benign increased intracranial pressure. A generally self-limited illness of young, obese women in which the brain swells with interstitial water. Since neurons and glial cells don't become waterlogged (only the interstitial space does), the patient is free of confusion, stupor, or seizures. If the elevated intracranial pressure becomes chronic, the optic nerves may suffer permanent damage.[123]

Pseudotumor is associated with almost any endocrine disturbance, oral hormones, vitamin A intoxication, and a large list of other conditions. The pathophysiology is unknown.[24]

Premature Suture Closure: Fusion of the cranial sutures before the brain has finished growing forces the skull to expand in a direction parallel to the fused suture. Surgical re-separation of the child's prematurely closed suture prevents future ostracization by peers.[125]

Giant Aneurysm: Some aneurysms (usually in the internal carotid/middle cerebral distribution) may, by expanding to the size of a golf ball, compress neighboring structures.[126] Aneurysms develop at arterial bifurcations which have inherently weak arterial walls.[127]

Tic Douloureux: A horribly painful condition consisting of lightning jabs of excruciating pain along the upper or lower jaw, frequently precipitated by a trigger point along the face or gums. Thought to be due to a branch of the basilar artery rubbing against the Vth nerve exiting the brainstem.

Atlanto-Axial Dislocation: Just as Atlas supports the world, the first cervical vertebra supports the skull and rotates it on the axis (the second cervical vertebra). These two vertebra are held together, unlike any other two vertebrae, with the help of a vertical finger of bone, the dens, projecting up from the axis. Certain illnesses loosen the ligaments binding the atlas and axis together, illnesses like rheumatoid arthritis, mucopolysaccharidoses (chapter 35), Down's syndrome, and achondroplasia (the most common type of dwarf).[128]

Diastematomyelia: A splitting of the spinal cord by a sand bar of bone protruding into the cord. Frequently congenital, diastematomyelia produces progressive paraparesis by preventing the spinal cord from migrating up the spinal canal during normal childhood growth.[129]

Spinal Stenosis (Neurogenic Claudication): Exercise-induced low back pain associated with weakness and numbness of the legs, all caused by a congenitally narrow spinal column, further narrowed in later life by ligamentous overgrowth and spondylosis within the spinal canal. The abnormally small canal prevents adequate venous drainage of the lower spinal cord and cauda equina, especially during exercise when the cord needs that extra blood. The back pain, leg numbness, and leg weakness are frequently worse in the erect posture and relieved by bending forward; i.e., the patient may be able to ride a bicycle for miles but only walk two blocks.[130]

Saturday Night Palsy ('Honeymoon Palsy'): Wrist drop from compression of the radial nerve wrapping around the posterior humerus in the spiral groove. Saturday night palsy classical occurs in alcoholics who fall asleep slouched on a park bench with their arm draped over the back of the bench, or to a groom the morning after his wife has slept with her head sweetly cradled in his arm.

Tardy Ulnar Palsy: Compression of the ulnar nerve presumably by scar tissue that forms following repeated elbow trauma. (The trauma can be as mild as leaning on your elbows at bars.) Diabetics are particularly susceptible to tardy ulnar palsy, because minor elbow trauma is much more damaging to nerves already weakened by the chemical changes accompanying diabetes.[132]

Cubital Tunnel Syndrome: Compression of the ulnar nerve in the forearm by the proximal flexor carpi ulnaris muscle.

Anterior Interosseous Palsy: Compression of the anterior interosseous branch of the median nerve supplying: pronator quadratus, flexor pollicus longus, and the radial half of flexor digitorum profundus. Produces a pure motor syndrome of weakness of pronation (weakness, not paralysis, because pronator teres is still okay) and inability to flex the distal phalanges of the index finger, long finger, and thumb (i.e., he can't crack a gun and pull the trigger).[133]

Carpal Tunnel Syndrome: Patients are classically awakened at night by hand and wrist pain which they relieve by shaking their wrist.[134] The carpal tunnel syndrome affects people who use their

wrists excessively (e.g., carpenters), or patients with thickened or inflamed connective tissue: rheumatoid arthritis, hypothyroidism, mucopolysaccharidosis (chapter 35), acromegaly, and pregnancy.

Tarsal Tunnel Syndrome: Compression of the posterior tibial nerve passing underneath the medial malleolus. Produces pain and hypesthesia over the sole.[133]

Atherosclerosis: An ischemic cerebral infarction (a stroke) may occur for three different reasons: 1) local thrombosis in an intracerebral artery, 2) embolic occlusion of an intracranial artery from either an intracardiac source (valve vegetation, mural thrombus, left atrial myxoma) or from a thrombus at the common carotid bifurcation where many years of turbulent blood flow predispose to atherosclerosis (rarely, the lung may harbor the embolic source), or 3) complete occlusion of the internal carotid artery without adequate collateral blood supply from the opposite internal carotid.

Many people with adequate collateral flow handle internal carotid artery occlusion without turning a whisker. Collateral blood reaches the ischemic hemisphere from 1) the opposite carotid through the anterior cerebral and anterior communicating arteries, 2) the basilar artery through the posterior communicating arteries, and 3) anastomotic connections through the ipsilateral external carotid artery, like the ophthalmic artery. The ophthalmic artery normally flows outward from the internal carotid to anastomose with distal twigs of the external carotid artery on the face. If the internal carotid becomes obstructed, blood flowing through the ophthalmic artery may reverse itself so that blood reaches the brain by flowing up the external carotid artery, through the ophthalmic, and into the supracavernous portion of the internal carotid artery.

Vertebral Compression: The vertebral artery ascending in the neck travels alongside the spinal column within tiny rings of bone extending from each vertebral body. Vertebral osteophytes may pinch one of the vertebral arteries when the patient turns his head or looks upward. If one of the patient's vertebral arteries is congenitally small, compression of the other vertebral can produce basilar artery symptoms.[126]

Carotid Sinus Syncope: One of the ways the body lowers its own blood pressure is by the carotid sinus, a pressure-sensitive structure located in the neck near the common carotid bifurcation. Whenever it senses hypertension, the carotid sinus signals the medulla to respond with additional vagal output to slow the heart. If the carotid sinus is too sensitive, trivial compression of the carotid sinus may trick it into thinking the blood pressure has risen suddenly. Subsequent bradycardia and peripheral vasodilation may drop a normal blood pressure enough to cause syncope.[127] In the barber chair, carotid sinus syncope (from the apron wrapped around the customer's neck) is loosely known as the 'Samson complex,' after Delilah's famous haircut.

ORGAN DYSFUNCTION

Orthostatic Hypotension: Since blood vessels are normally told to constrict by peripheral nerves, any peripheral neuropathy (that affects the autonomic nerves) may predispose to orthostatic hypotension. Diabetes, Guillain Barre, and alcoholism are three common culprits. Since circulating steroids and epinephrine are also necessary for robust and continuous vasoconstriction, don't forget to consider Addison's disease. And of course blood vessels have to have something to work with, so be sure there's enough blood in the vascular tree. Central nervous system illnesses that interrupt sympathetic fibers anywhere from their hypothalamic origin, descent through the brainstem, and termination in the spinal cord may also contribute to orthostasis.[128]

Vasovagal Hypotension: Some people react to sudden visual or emotional stress with a sudden burst of vagal stimulation to the heart and blood vessels. As with a hypersensitive carotid sinus, these patients respond with dramatic bradycardia and vasodilation. What *you* see is pallor (the body's attempt to redirect flow to the brain) and syncope.

Hypertension: Chronic hypertension hastens cerebral atherosclerosis. Acute, transient hypertension doesn't normally cause problems because cerebral arteries constrict (autoregulate) to sudden hypertension in order to keep the cerebral blood flow constant.[91]

Fever: Fever alone can disrupt normal cortical function, and even kill neurons if the temperature gets above 104–105°. Treat with aspirin, cooling blankets, tepid baths, and especially plenty of fluids to allow the vascular system the luxury of diverting blood to the skin surface to rid the body of excessive heat.

Subclinical Status Epilepticus: Altered brain function (coma, fugue state, confusion) due to, or associated with, ongoing electrical status epilepticus without concomitant jerking ("electrical-mechanical dissociation").[140]

Meniere's Disease: Recurrent vertigo and tinnitus with fluctuating hearing loss due to idiopathic accumulation of fluid in the labyrinths. The hearing loss results from high pressure in the labyrinths being transmitted into the cochlea via the reuniens duct.[141]

Inappropriate ADH (Antidiuretic Hormone): An inappropriate release of ADH from the posterior pituitary; can be precipitated by almost any cerebral insult. If the serum sodium falls below 120 mEq/L, the relative excess of serum water in the denominator (sodium/serum water) causes the brain to equalize the difference in sodium concentration between the blood and brain. Excessive intracerebral water results in seizures and coma.[142]

Panhypopituitarism: Panhypopituitarism should mean failure of the anterior, intermediate, and posterior lobes of the pituitary, but failure of the anterior pituitary alone is usually sufficient for the diagnosis. Anterior pituitary failure is commonly caused by unexplained infarction during the postpartum period (after childbirth), called Sheehan's syndrome.

Hyperthyroidism: In addition to increased sympathetic activity (hypervigilance, nervousness, stare, tremor, widened palpebral fissure, lid lag, and failure of convergence), excessive thyroid hormone has a deleterious effect on pharyngeal and proximal limb muscles. Hyperthyroidism is also associated with periodic paralysis and myasthenia gravis. Older patients with hyperthyroidism may look apathetic instead of nervous and jerky.[144] Rarely, hyperthyroidism can present with pyramidal tract signs.[145]

Hypothyroidism: In addition to slowed mentation (if severe: stupor and coma), hypothyroidism can selectively affect the Neuromuscular system with: psychosis, coma, cerebellar ataxia, peripheral neuropathy, and hung-up reflexes.[146]

Hypercalcemia: It generally takes a calcium level over 12–13 mg% to produce stupor and coma.[147]

Hypocalcemia: Tends to make nerves irritable, producing tetany, and muscle cramps. Often accompanied by hypomagnesemia.[148] Can cause seizures.[149]

Hypophosphatemia: A still somewhat ill-defined entity of diffuse weakness, vaguely mimicking Guillain Barre. Pathophysiology may stem from inadequate supplies of phosphate for ATP production.[150]

Hypomagnesemia: Like hypocalcemia, hypomagnesemia seems to make the nervous system irritable with tetany, seizures, and myoclonus. Magnesium may be necessary for calcium to function normally.[151]

Hyperglycemia: Hyperglycemia from any etiology can precipitate focal seizures and coma.[152] Diabetes causes coma in other ways: ketoacidosis with dehydration, overtreatment with insulin (hypoglycemia), and cerebral edema during therapy of ketoacidosis.[153] Cerebral edema comes about by giving too much hypotonic fluid, or by creating a hyperosmolar serum (hypotonic to brain) with too much insulin (lowering the glucose too far too fast).

Diabetes also causes both a sensorimotor and an autonomic polyneuropathy.[154] More importantly, diabetes accelerates atherosclerosis resulting in ischemic strokes, ischemic cranial and peripheral mononeuropathies,[155] ischemic radiculopathies,[156] and diabetic amyotrophy (atrophy of the pelvic girdle and thigh muscles).[157]

Hypoglycemia: The major immediate effect is stupor and coma. Survival after hypoglycemia may leave the patient demented with pyramidal, extrapyramidal, or cerebellar signs.[158]

Hypercortisol: Cushing's syndrome. Neurologic effects of excess steroids can be pseudotumor cerebri, psychosis, and proximal myopathy.[159]

Hypocortisol: Addison's disease. Neurologic effects are a mild myopathy, muscle cramps, and rarely hyperkalemic paralysis.[160]

Pheochromocytoma: An adrenal gland tumor which intermittently secretes adrenalin-like compounds into the bloodstream causing intermittent bouts of hypertension, orthostatic hypotension, tachycardia, skin flushing, sweating, and headaches.[161] "Pheo" (dusky) is the color this tumor turns when stained with chromium salts.

Hypoxia: Causes the same signs and residuae as hypoglycemia.[162] Recurrent pulmonary emboli may cause spells of hypoxic stupor or coma.

Hypercapnia: Acutely, causes coma; chronically, papilledema because of reflex cerebrovascular dilation which raises the intracranial pressure.

Hyperventilation Syndrome: An hysterical sensation of suffocation which the patient combats by overbreathing. As carbon dioxide is blown off, the serum pH rises and the serum calcium concentration drops, producing light-headedness and tingling about the mouth. If severe enough, hypocalcemia may precipitate tetany and even cardiac arrhythmias.[163]

Neurogenic Pulmonary Edema: Alveolar edema usually results from congestive heart failure which, by raising pulmonary venous pressure, forces fluid through delicate pulmonary capillaries. But in neurogenic pulmonary edema, high pressure comes from the pulmonary *arterial* side, the result of sudden pulmonary artery constriction by massive sympathetic stimulation.[164] The cause of this sudden massive sympathetic outflow is an intracerebral insult that acutely injures the hypothalamus, the fountainhead of the sympathetic nervous system.

Tachy/Brady Syndrome: Recurrent bouts of tachycardia and bradycardia, severe enough to cause hypotension. Usually due to chronic ischemia of the *S-A* node.

Aortic Stenosis: During heavy exercise, a tightly stenotic aortic valve prevents the heart from delivering the additionally required blood, causing easy fatigue, shortness of breath, angina, and syncope.

Valve Emboli: From subacute bacterial endocarditis, systemic lupus erythematosus vegetations, or marantic endocarditis (valve vegetations during chronic cancer).[166]

Idiopathic Hypertrophic Subaortic Stenosis (IHSS): A thickened ventricular wall just beneath the aortic valve may obstruct the valve during vigorous contractions, or the thickened wall may interrupt electrical impulses traveling through the ventricular Purkinje system.[168]

Liver Failure: Typically causes stupor, coma, and asterixis. Seizures are rare. The specific neurologic toxin not metabolized by the failing liver is unknown.[169]

Uremia: The uremic toxin, still unidentified, produces stupor, coma, confusion, seizures (unlike liver failure), and polyneuropathy.[170]

Hypernatremia: High serum sodium attracts water out of the brain causing coma.

Hyponatremia: If the blood is more dilute than the brain, water will switch from blood to brain, raising the intracranial pressure (coma). In addition, swollen neurons may seize.[171] Too rapid a correction of hyponatremia may precipitate central pontine myelinolysis: sudden demyelination in the basis pontis leading to quadriplegia.[172]

Hyperkalemia: Weakness of muscular contraction due to lowered membrane excitability (presumably due to a lowered voltage gradient across the muscle membrane).[173]

Hypokalemia: Also weakens muscular contraction by an uncertain mechanism.[174]

Polycystic Kidneys: Genetically maldeveloped kidneys grossly enlarged with innumerable cysts. Associated with intracranial aneurysms.[175]

Pregnancy:[176] Major neurologic complications of pregnancy and the post-partum period include subarachnoid hemorrhage (from aneurysmal rupture),[177] arterial and venous strokes,[178] more fre-

queer seizures,[179] status epilepticus, eclampsia (the combination of hypertension, proteinuria, and coma or seizures), chorea,[180] carpal tunnel syndrome, and exacerbation of myasthenia gravis.

Pregnant women taking Dilantin are particularly susceptible to status epilepticus because the serum Dilantin level falls during pregnancy;[181] pregnant patients do not absorb Dilantin well,[182] while fluid retention and the fetus dilute Dilantin by expanding the volume of distribution.[183]

Migraine: Vascular headaches apparently entail two physiologic changes. The first one is unexplained spasm of intracerebral arteries (due to a primary cerebral event?[184]), and the second is painful dilation of extracerebral arteries in the scalp, at least in some patients (some patients have pain without vasodilation).[185] If the initial spasm phase is severe enough, transient ischemia or even permanent focal infarctions may ensue, like homonymous hemianopia or hemiparesis.[186] If the basilar artery is affected, stupor, diplopia, and ataxia may occur.[187]

TIA/Light Stroke: Both of these raise the likelihood of a subsequent, potentially catastrophic stroke. Since TIA's and mild strokes are frequently caused by emboli from carotid bifurcation ulcers and stenosis,[188] surgical restoration (endarterectomy) of the carotid bifurcation is often indicated. Aspirin, Persantin, and Coumadin, all of which inhibit coagulation, also have a role in preventing subsequent strokes.

Retinal Emboli: Transient monocular blindness, called amaurosis fugax, may indicate a potentially dangerous (because the next emboli may go the brain) source of embolic material from somewhere upstream; almost always from the carotid bifurcation or the heart.[189] The risk of stroke is probably higher if you can see the embolus in the retinal arteriole.[190]

Subarachnoid Hemorrhage: Surgical repair of the bleeding site (usually an arteriovenous malformation or aneurysm, occasionally a tumor) is indicated if the patient is not too seriously injured by the subarachnoid hemorrhage.

Cerebellar Hemorrhage: Frequently needs surgical drainage, unless the cerebellar hemorrhage is small enough that it doesn't obstruct the fourth ventricle.

Pituitary Apoplexy: Sudden headache, partial or complete visual loss, diplopia, and hypotension. Pituitary tumors may suddenly expand by hemorrhaging into themselves causing either acute compression of the optic chiasm (blindness) if the tumor expands upward, or acute compression of the oculomotor and abducens nerves in the cavernous sinus if the tumor expands laterally. The destroyed pituitary gland, unable to secrete ACTH, precipitates sudden hypotension and hypoglycemia (Addisonian crisis). Pituitary apoplexy requires immediate IV cortisol and urgent surgical decompression of the optic chiasm.[191]

Hypertensive Encephalopathy: Normally, when the blood pressure rises, intracerebral arterioles constrict to keep the cerebral blood flow constant and to protect tight junctions from high arterial pressure. (Tight junctions are welds between capillary endothelial cells that prevent serum from slipping into the brain.[192]) Massive hypertension (usually over 240/130) overwhelms even the most intense vasoconstriction, causing edema between capillary endothelial cells into the brain[73] (not everyone agrees, however, that edema plays a significant role in hypertensive encephalopathy[193]). The now overdistended arterioles allow high pressure and high volume to hammer away at the brain's delicate vascular tree, causing intracranial pressure (stupor, coma, papilledema) and damaging cerebral blood vessels (cerebral infarctions, seizures).

Two problems making the diagnosis of hypertensive encephalopathy: the papilledema you see may only be *local* disc swelling, not increased intracranial pressure.[194] And more importantly, hypertensive encephalopathy is relatively uncommon, rather than a cause of increased intracranial pressure, marked hypertension is more often a response to increased intracranial pressure from a subarachnoid or intracerebral hemorrhage. Hypertensive encephalopathy is a diagnosis made *after* ruling out intracranial bleeding or other intracranial catastrophe.

Superior Sagittal Sinus Thrombosis: Superior sagittal sinus thrombosis may develop from elevated intracranial pressure, local obstruction by tumor, or a hypercoagulable state like dehydration, cancer, sickle cell anemia, or postpartum state.[195] Acute obstruction of the brain's major venous outflow tract, the superior sagittal sinus, produces devastating venous infarctions of both hemi-

spheres and a potentially fatal increase in intracranial pressure. Slow obstruction of the superior sagittal sinus allows the brain to develop enough venous collaterals to prevent cortical infarction, but not enough to prevent venous engorgement of the brain with raised intracranial pressure.

Subclavian Steal: Brainstem signs precipitated by diversion (theft) of blood away from the brainstem into an exercising arm. This redirected blood flow occurs after stenosis develops in one (usually left) subclavian artery proximal to the take-off of the vertebral artery. Left arm exercise diverts blood from the right vertebral *down* the left vertebral into the left subclavian, robbing the basilar of its blood supply to the brainstem.[197]

Aortic Coarctation: A congenital, focal area of narrowing along the descending (usually thoracic) aorta. Associated with intracranial aneurysms, presumably from chronic hypertension above the coarctation.

Anemia: Like hypoxia or hypoglycemia, inadequate oxygen delivery from insufficient hemoglobin causes bihemispheric signs of confusion, agitation, stupor, and rarely coma.

Thrombocytosis: Platelet counts above about 800,000/mm^3 predispose to thrombosis.[198]

Thrombocytopenia: Predisposes to intracranial bleeding. Causes range from inadequate platelet production to a shortened platelet life span.

Hyperproteinemia: Also causes blood to sludge predisposing to thrombotic strokes.

Prolonged PT: Though often iatrogenic from Coumadin therapy (a drug which blocks vitamin K, the vitamin necessary for synthesis of the coagulation proteins), the usual cause of a prolonged prothrombin time is liver disease. Vitamin K therapy may prevent internal bleeding.

Prolonged PTT: Almost always due to excessive heparin, but occasionally due to lupus or a genetic coagulation disorder. Also predisposes to bleeding.

Ankylosing Spondylitis: Progressive inflammatory scarring of vertebrae which, over years and decades, results in a rigid, immobile spine. May also compress the cauda equina.[200]

Fibrous Dysplasia: Overgrowth of abnormal bone. Skull involvement around the optic canals may encroach upon the optic nerves, requiring surgical decompression.[201]

GENETIC ILLNESSES

MANY GENETIC ILLNESSES ARE INDEED UNTREATABLE, but genetic counseling may spare future generations the genetic illness you recognize. Most genetic illnesses affecting the neuromuscular system fall into one of the following categories:

(1) Amino Acidopathies
(2) Mucopolysaccharidoses
(3) Sphingolipidoses
(4) Phakomatoses
(5) Glycogen Storage Myopathies
(6) Lipid Myopathies

Vitamin-Responsive Amino Acidopathies[1]

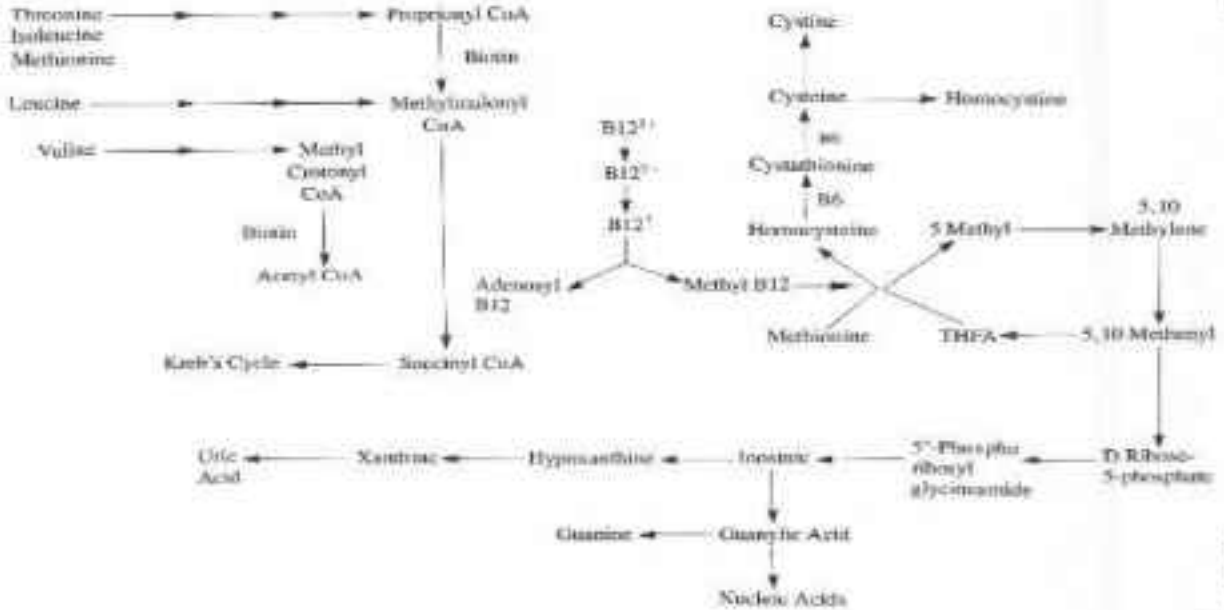
Some inborn errors of metabolism are at least theoretically treatable with vitamins. The flow sheet will help you organize them. You should understand from this flow sheet how two different enzymatic defects in two separate metabolic pathways can, by accumulating the same metabolite, present with a similar phenotype*. For example, homocystinuria can be caused by three different enzymatic defects (steps 1, 2, and 3) responsive to folate, vitamin B12, and pyridoxine (B6), respectively.[2]

A block in steps 4, 5, or 6 accumulates highly toxic organic acids, which, besides inhibiting the breakdown of the vital amino acid, glycine, also get reassembled into long-chain ketones. So as soon as the infants receive protein in their diet, they become hyperglycinemic, ketotic, and acidotic.

Except for the few infants who respond to biotin or vitamin B12, infants with ketotic hyperglycinemia* (step 7) who are fed protein soon stop feeding, vomit, seize, lapse into coma, and invariably die in chemical havoc.

Phenotype: Clinical features—what a patient looks like. Genotype is his genetic makeup.

Ketotic Hyperglycinemia: There is also a nonketotic form of hyperglycinemia due to a block in glycine breakdown.[3]


Threonine
Isoleucine
Methionine
Propionyl CoA
Biotin
Leucine
Methylcrotonyl CoA
Valine
Methyl Crotonyl CoA
Biotin
Acetyl CoA
Krebs Cycle
Succinyl CoA
B12
Adenosyl B12
Methyl B12
Cystine
Cysteine
Homocysteine
B6
Cystathionine
B6
Homocysteine
5 Methyl
5, 10 Methylene
Methionine
THFA
5, 10 Methenyl
Uric Acid
Xanthine
Hypoxanthine
Inosine
5'-Phospho ribosyl glycinamide
D Ribose-5-phosphate
Guanine
Guanylic Acid
Nucleic Acids

Mucopolysaccharidoses[4]

Mucopolysaccharides are long, complex chains of carbohydrates which make up the background substance, connective tissue, and lubricating fluids throughout the body. Consequently, enzymatic defects affecting the metabolism of mucopolysaccharides produce multisystem diseases. Fortunately, the six mucopolysaccharidoses tend to resemble each other clinically, as highlighted in this chart.

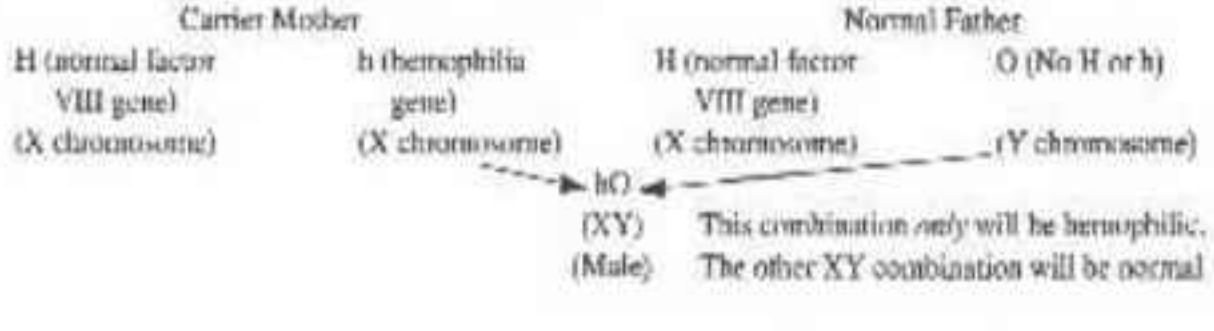
		Hurler	Scheie	Hunter	Sanfilippo	Morquio	Maroteaux Lamy
Skin	Coarse Facial Features	++	+	++	+	+/−	+
Neuro	Mental Retardation	++	−	+	++	−	−
	Myelopathy			+/−		++	−
	Carpal Tunnel Syndrome		−	+			−
	Optic Disc Swelling			+			
Eye	Corneal Clouding	+	−	−	−	+/−	−
Ear	Deafness	−	+/−	+		+	+/−
Card	Valvular Disease	−	−	−	+/−	+/−	+
GI	Hepatosplenomegaly	−	−	+	+/−		
Vasc	Coronary Artery Dis	−	−	−	−		
Bone	Dwarf	+	−	−	−	++	+
	Short Neck	+		−		+	
	Gibbus*	+	−	−		++	
	Joint Contractures/ Claw Hand	++	+	++	−	−	++
	Chest Deformity	+				++	+
Genetics		AR	AR	SL**	AR	AR (autosomal recessive)	

Summary:

	Mild					*Marked*	
Facial Changes:	Scheie	Sanfilippo		Morquio	Maroteaux Lamy	Hunter	Hurler
Bodily Changes:	Scheie	Sanfilippo		Hunter	Maroteaux Lamy	Hurler	Morquio
Mental Retardation:	Scheie	Maroteaux Lamy		Morquio	Hunter	Sanfilippo	Hurler

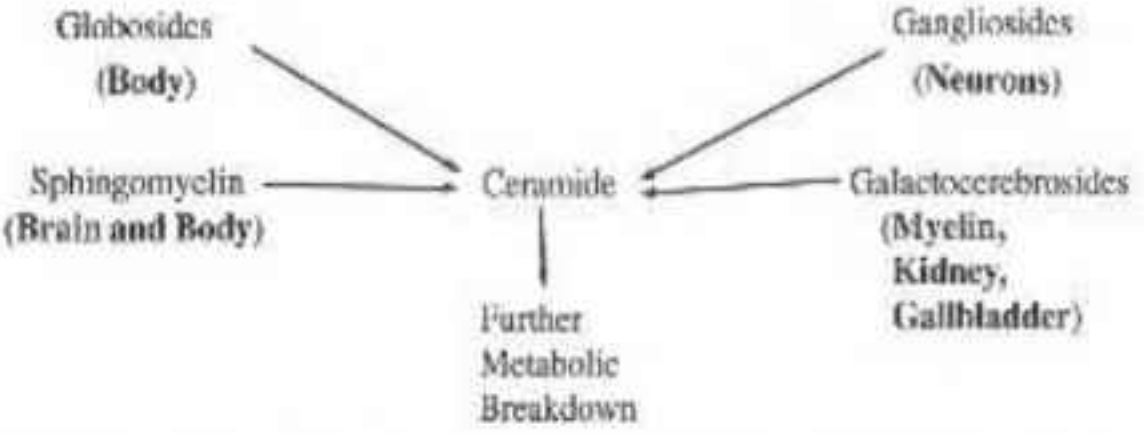
Gibbus: A severe angulation of the spine (hunchback).

**SL (Sex linked): Sexual expression is determined by the X and Y chromosomes. If you receive an X chromosome from your mother and a Y from your father, you're male. If you receive an X chromosome from each parent, you're female. Unlike the long X chromosome, Y is rather short containing little else but male sexual expression. So if a defective gene is present on the X chromosome, in a male there may not be a normal gene on the Y chromosome to override it. Females, however, do have an extra X chromosome and only "carry" the abnormal gene. This situation, called X linked or sex linked, is what happens in such male diseases as hemophilia (abnormal coagulation factor VIII), Duchenne's muscular dystrophy, and Hunter's syndrome (a mucopolysaccharidosis). On the bright side, an affected male with these diseases cannot transmit the illness to his sons, because the abnormal gene is on the X, not the Y, chromosome. Also, only half the male offspring of a female carrier will be affected:

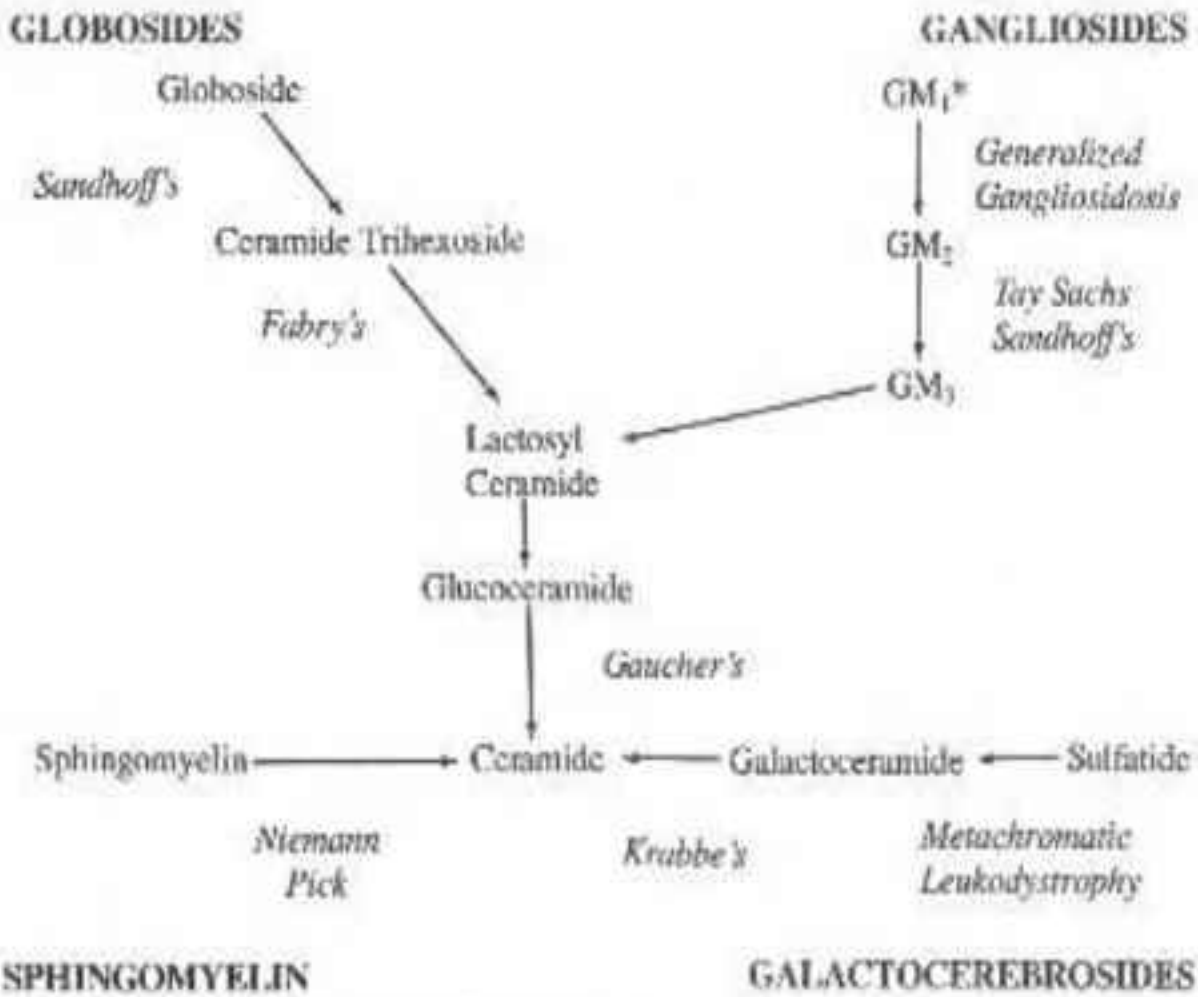


Sphingolipidoses[5]

The sphingolipidoses consist of ten or more separate illnesses, each of which represents a different enzymatic block in the disassembly of long-chain lipids called sphingolipids. There are four general classes of sphingolipids and each class is found in a specific area of the body. The clinical picture for each sphingolipidosis depends more on the *site* of sphingolipid accumulation than it does on which sphingolipid accumulates.



Globosides are found in every cell membrane outside the brain. Gangliosides occur in all *neuronal* membranes (hence the name 'ganglio'), but not in myelin. Galactocerebrosides occur in central *and* peripheral myelin and in the kidney and gallbladder. Finally, sphingomyelin is present in virtually every cell membrane of the body including the brain. Just knowing those few facts allows you to predict (and remember!) the pathological signs for each group of sphingolipidoses.



(Chart modified from Baker and Baker: *Clinical Neurology*)

GM_1: The term sphingolipid stems from the parent molecule, sphingosine—a long chain fatty acid with two important side groups: amine (NH_2) and hydroxyl (OH).

Sphingosine: $CH_3 - (CH_2)_{12} - CH = CH - \underset{OH}{CH} - \underset{NH_2}{CH} - CH_2 - OH$

The first step in the synthesis of any sphingolipid is to attach another long chain fatty acid (FA) onto the amine group to make a new molecule called ceramide.

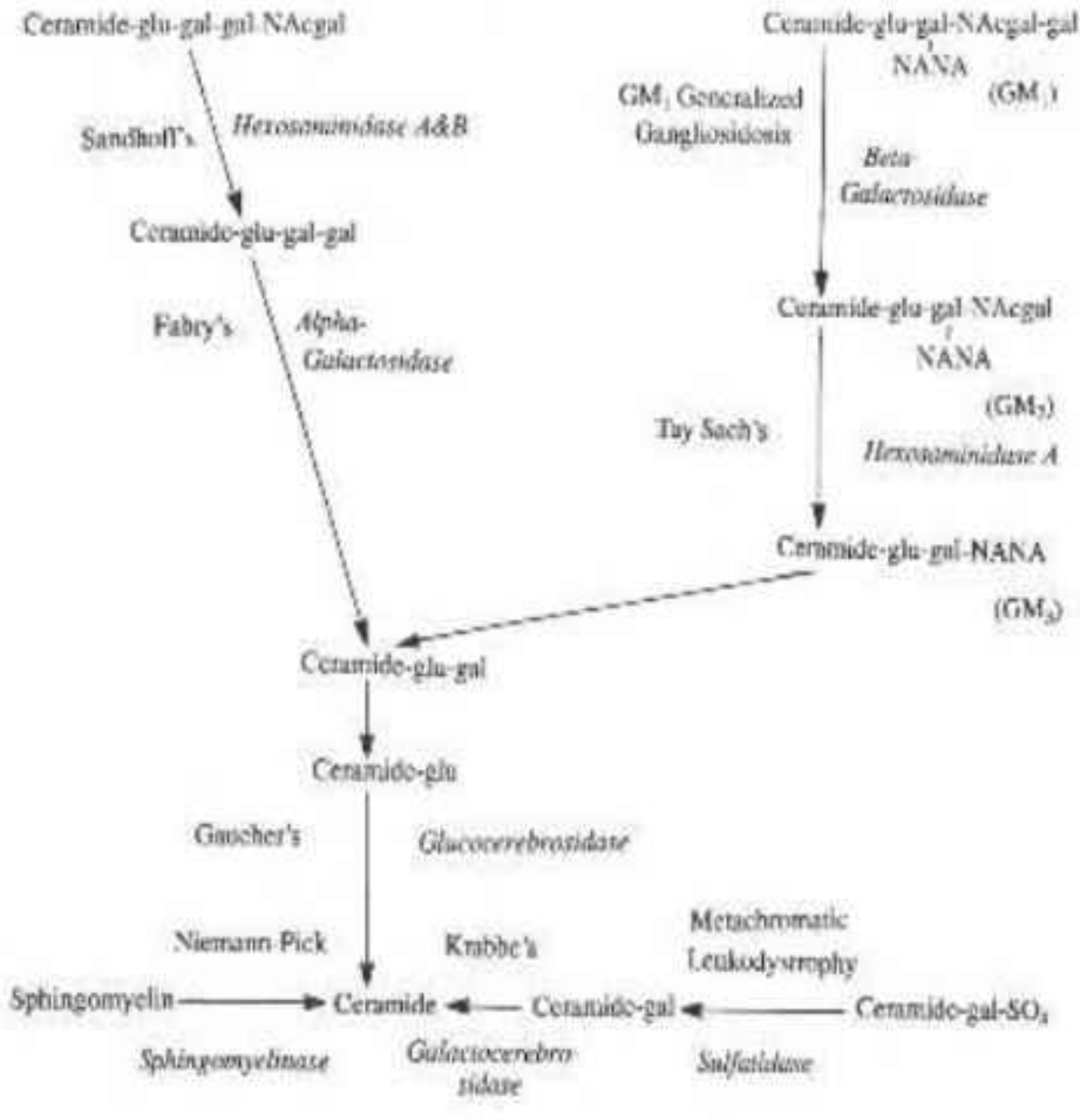
Ceramide: $CH_3 - (CH_2)_{12} - CH = CH - \underset{OH}{CH} - \underset{NH}{\underset{|}{CH}} - CH_2 - OH$
$\qquad\qquad\qquad

It takes only one step from the Cer-glu-gal trunk to make gangliosides. The molecule necessary to do this is N-acetylneuraminic acid (NANA), also known as sialic acid. It's the presence of sialic acid that allows you to call a sphingolipid a ganglioside. So, adding one NANA gives Cer-glu-gal-NANA. The next most complex ganglioside is formed by adding N-acetyl-galactosamine: Cer-glu-gal-NAcgal. Next is the addition of another galactose: Cer-glu-gal-NAcgal-gal.
NANA NANA

We now have three gangliosides which are named in a very specific way. The largest of the gangliosides has four hexoses. A ganglioside with four hexoses is given the title of 1. If there are only three hexoses, it's called 2, and if there are two hexoses, it's called 3. So,
Cer-glu-gal-NAcgal-gal (which we did not synthesize) is called GD_1. The G refers to its being
NANA a ganglioside and the D refers to the number of NANA's, in this
NANA case, two or 'di'.

Cer-glu-gal-NAcgal-gal is called GM1; M means mono (one NANA).
NANA
Cer-glu-gal-NAcgal is GM2, and Cer-glu-gal is GM3. Simple, huh?
NANA NANA

Here are the sphingolipidoses charted by their chemical structure and degradative enzyme.



For example, Generalized Gangliosidosis, Tay Sachs, and Sandhoff's* accumulate neuronal gangliosides to produce a 'gray matter' illness—intellectual deterioration, seizures, cortical blindness, and myoclonic startle responses to sudden sharp sounds. All neurons, even those outside the central nervous system, accumulate gangliosides. Hence, in these three diseases the normally red macula (red from the ciliary circulation) appears cherry red as it stands encircled by a doughnut of ganglion cells stuffed with whitish gangliosides. As an additional twist, Generalized Gangliosidosis accumulates systemic mucopolysaccharides, because the defective enzyme, beta-galactosidase, is also used to cleave systemic mucopolysaccharides. Consequently, these infants have gray matter neurologic signs and a mucopolysaccharide appearance (coarse facial features and hepatosplenomegaly).

Galactocerebrosides accumulate in Schwann cells and oligodendrocytes, hence the two 'white matter' diseases, Krabbe's* and Metachromatic Leukodystrophy*. Both of these illnesses manifest early white matter signs of spasticity and hyperreflexia, ataxia (cerebellar outflow tracts), optic disc pallor, and—because of galactocerebroside accumulation in peripheral nerve myelin—absent ankle jerks. Sulfatides are also found, strangely enough, in the kidneys and gallbladder; children with metachromatic leukodystrophy spill sulfatides into the urine and have an abnormal cholecystogram.*

Sphingomyelin accumulation in Niemann Pick disease affects almost every cell of the body. Not only are there signs of serious brain (*gray and* white matter) dysfunction, but also hepatomegaly and splenomegaly as reticuloendothelial cells in these organs try to digest sphingomyelin accumulating throughout the body. Different clinical forms of this illness exist, some more devastating than others*.

In Fabry's Disease, ceramide trihexoside builds up outside of cerebral neurons and myelin but not outside the brain. Ceramide trihexosides accumulate in the endothelium and smooth muscle* of arterial walls, including those in the brain. As you'd expect, patients with Fabry's disease suffer strokes relatively early in life. They also suffer burning dysesthesias in the arms and legs from peripheral nerve ischemia (and sphingolipid accumulation).[7] Similarly, kidney ischemia, plus local hoarding of glo-

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Sandhoff's: Because hexoseminidase A and B are both deficient in Sandhoff's disease, globosides *and* GM_2 accumulate. As a result, the infants have Tay Sachs features and hepatosplenomegaly.

Krabbe's: Actually, galactocerebrosides aren't terribly elevated in Krabbe's disease, because they are thought to be quickly metabolized to another, highly toxic compound called psychosine:[6]



Metachromatic Leukodystrophy: A leukodystrophy is a progressive deterioration (dystrophy) of white matter. Sulfatides in urine stain an odd, brown color (metachromasia).

Cholecystogram: *Chole* means bile in Greek. A cholecystogram is an xray picture of contrast material concentrated in the gallbladder after intravenous injection.

Others: One purely speculative explanation for these different clinical forms is that the brain may have a different genetic enzyme than the one used by the body to degrade sphingomyelin. Each of the enzymes may then be affected separately, producing a purely cerebral illness, a purely systemic illness, or if both enzymes are affected, both a cerebral and systemic illness.

Smooth Muscle: 'Involuntary' muscle, capable of maintaining the same degree of tension (regardless of its length) for prolonged periods of time. Found in the iris, bronchial tree, gut, bladder, and blood vessels.

boside within the kidney, produces hypertension* and renal failure. And finally, tiny arterioles and venules in the skin and sclera dilate into prominent telangiectasias over the trunk, called angiokeratoma corporis diffusum.

The most common sphingolipidosis is Gaucher's disease which stores glucocerebroside. There are several different forms of Gaucher's disease: a purely systemic and a combined systemic and cerebral form*.

Phakomatoses

The phakomatoses* are a collection of multisystem illnesses which primarily affect the skin, eyes, and brain. The skin lesions—involving dermal pigment, connective tissue, and small blood vessels—are relatively harmless. More serious is involvement of the eyes, brain, and, in some phakomatoses, the internal organs by relatively benign hamartomas or frankly malignant cancers. The phakomatoses include: tuberous sclerosis, Sturge-Weber, Von Recklinghausen's disease (neurofibromatosis), ataxia-telangiectasia, and Von Hippel-Lindau. Clinically the phakomatoses have little resemblance to each other. The characteristic clinical constellation for each is as follows:

Tuberous Sclerosis:[9] Seizures, mental retardation*, adenoma sebaceum over the nose and cheeks*, mountain ash leaf spots*, periungual fibromas*, lumbosacral shagreen patch*, retinal hamartomas*, malignant brain tumors*. Autosomal dominant.

Hypertension: In the 1930's, Dr. Goldblatt produced hypertension by partially clamping one renal artery. Subsequent work demonstrated that the ischemic kidney releases renin (an enzyme) which, through several steps, unleashes another protein, angiotensin. Angiotensin, in turn, produces hypertension by direct arterial constriction and also by stimulating the adrenal gland to produce aldosterone, the hormone that raises the blood pressure by telling the kidney to retain salt.

Systemic and Cerebral Form: Like Niemann-Pick, the different forms of Gaucher's disease may be due to two different enzymes: one in the brain and one in the periphery. Cerebral gangliosides and systemic globosides are both degraded through glucoceramide. If the enzyme which degrades *cerebral* glucoceramide were missing, cerebral gangliosides would accumulate as a cerebral form of Gaucher's disease.[8] Alternatively, inadequate degradation of systemic glucoceramide would back-up systemic globosides into a systemic form of Gaucher's disease. And, of course, if both enzymes were missing, the patient would develop a decimating cerebral (gray matter) and systemic (hepatosplenomegaly) form of the disease.

Phakomatoses: Phako means spot, referring to the skin lesions.

Mental Retardation: This autosomal dominant illness does not have to affect intelligence, so check any infant that seizes for the characteristic mountain ash leaf spot of tuberous sclerosis.

Nose and Cheeks: Adenoma sebaceum is a collection of small papules over the nose and cheeks resembling bad acne.

Mountain Ash Leaf Spots: A mountain ash leaf shaped patch of hypopigmented skin oriented along a sensory dermatome. An ultraviolet light may help accentuate these white macules.

Periungual Fibroma: Small firm nodules around the fingernails and toenails.

Shagreen Patch: A plaque of dark, somewhat rough skin (shagreen means shark skin) over the lumbosacral area.

Retinal Hamartoma: Visible as small whitish growths on the retina.

Malignant Brain Tumors: These tumors typically evolve from hamartomas along the walls of the lateral and third ventricles. Hamartomas bulging into the ventricles look like candle drippings, and in cortical gyri like potato tubers, hence tuberous sclerosis.

Sturge-Weber:[10] Port-wine stain in the trigeminal distribution, glaucoma, seizures, perhaps mental retardation, intracranial 'tram line' calcifications* on skull xray.
Von Recklinghausen's:[11] Cafe-au-lait* spots, axillary freckling*, peripheral nerve tumors*, acoustic neuromas, malignant optic nerve tumors and malignant brain tumors*, pheochromocytomas*, bony defects in the skull*. Autosomal dominant.



Ataxia-Telangiectasia:[12] Childhood onset of cerebellar ataxia, telangiectasias in the antecubital fossae, ears, and conjunctivae, mild mental slowing, affectionate nature, and susceptibility to respiratory infections during infancy and to malignancies during later childhood. Autosomal recessive.
Von Hippel-Lindau:[13] Retinal and spinal cord angiomas*, cerebellar hemangioblastoma, pheochromocytoma, and renal carcinoma. Autosomal dominant.

'Tram Line' Calcifications: Microscopic bits of calcium deposit within the cortex. Parallel planes of calcium within two abutting gyri give the planes of calcium—viewed from the side—a double layered appearance (like a tram line).

Cafe-Au-Lait: The light tan color of coffee with cream. Since many normals have this birth mark, more than six cafe-au-lait spots are needed to make the diagnosis of neurofibromatosis.

Axillary Freckling: Small cafe-au-lait spots in the axillae are virtually pathognomonic of Von Recklinghausen's disease.

Peripheral Nerve Tumors: Two types of peripheral nerve tumors occur: pure Schwannomas which can be removed, and neurofibromas which can't. A schwannoma grows as an easily removable solid mass of pure Schwann cells, but in neurofibromas, the Schwann cells grow in and among the peripheral nerve axons. Schwannomas in neurofibromatosis frequently occur on the acoustic nerve (often bilaterally) and on spinal nerve roots.

Malignant Brain Tumors: Though any CNS site may be affected, the optic nerve and hypothalamus are the most common sites.

Pheochromocytoma: The adrenal gland was originally a neural crest cell.

Skull Defects: When the sphenoid bone, separating the middle fossa from the orbit, is missing, the eye, now unprotected from the pulsating temporal lobe behind it, bulges forward and pulsates (called pulsating exophthalmos).

Angioma: A small (cherry size or smaller), benign tumor composed of capillaries and small venules.

Glycogen Storage Diseases

Two enzymatic illnesses obstruct the smooth delivery of glucose from muscle glycogen to mitochondria: McArdle's disease and phosphofructokinase deficiency. Patients with McArdle's disease are missing muscle glycogen phosphorylase*, the enzyme which cleaves glucose off muscle glycogen for transit through the glycolytic pathway. These patients suffer painful contractures during exercise, but are asymptomatic at rest when the bloodstream can still deliver adequate amounts of free glucose.

In phosphofructokinase deficiency, neither muscle glycogen nor serum glucose is of any use because neither one can bypass the blocked enzyme, phosphofructokinase, sitting halfway down the glycolytic pathway.[14] Instead, patients with phosphofructokinase deficiency must rely on lipids to supply mitochondria with acetyl CoA during both rest and exercise*.

Pompe's disease, a fatal glycogen storage disease of infancy, weakens virtually all muscles including the heart. Occasional milder forms present later in childhood or adulthood. The deficient enzyme is acid maltase whose exact role in cellular metabolism has so far eluded researchers.

Lipid Myopathies

Disruption of palmityl CoA delivery into mitochondria may occur for two reasons: either carnitine isn't available to escort palmityl CoA into mitochondria, or the palmityl CoA transport enzyme, carnitine-palmityl transferase, is defective.[17] In either of these two situations, a prolonged fast, which depletes liver and muscle of their glycogen stores, would be very dangerous since the muscles would be left stranded without an alternative source of energy, namely, lipid.

Despite their similar biochemistry, carnitine deficiency and carnitine-palmityl transferase deficiency are clinically quite different. Carnitine deficiency produces slowly progressive proximal weakness, while carnitine-palmityl transferase deficiency causes bouts of widespread weakness and myoglobinuria.

Muscle Glycogen Phosphorylase: An analogous enzyme deficiency, called Von Gierke's disease, occurs in the liver. The enzyme, liver phosphorylase, cannot respond to the beckoning of either glucagon or epinephrine. As a result, these infants and children cannot respond to hypoglycemic stress by the usual process of mobilizing glucose from hepatic stores of glycogen. Eventually, the children learn to depend on lipid for acetyl CoA. The liver, meanwhile, oblivious to its overstocked glycogen, continues to synthesize additional glycogen. At some point abdominal enlargement draws attention to the distended liver—all dressed up with glycogen and nowhere to go. Weakness is minimal in Von Gierke's disease because *muscle* glycogen phosphorylase is unaffected.

Cori's disease, like Von Gierke's disease, also limits the ability of liver glycogen to mobilize free glucose. Because of the structure of glycogen, Cori's disease is not as severe as Von Gierke's. Normally, glycogen is synthesized into the shape of a branching tree. To free the glucose, twigs are clipped off by glycogen phosphorylase until a branch point is reached, whereupon another enzyme—debrancher enzyme—snips that linkage, and phosphorylase picks up again to the next branch point. A deficiency of that debrancher enzyme causes Cori's disease.[12]

Rest and Exercise: You can demonstrate that a patient's muscles depend solely on lipid for acetyl CoA by shutting off the oxygen to a muscle. This is done by having the patient exercise his arm with a blood pressure cuff inflated above systolic blood pressure. Without oxygen, the cytochromes can no longer relieve the Kreb's cycle of accumulating DPNH, and the Kreb's cycle grinds to a halt. Which means that pyruvate can no longer enter the mitochondria, and instead, accumulates as lactate—in normals. If the patient has an enzymatic block anywhere along the glycolytic pathway between muscle glycogen and pyruvate, his serum lactate will not rise during ischemic exercise.[16]

EMERGENCY ROOM

YOUR ABILITY TO RECOGNIZE TREATABLE NEUROLOGIC PROBLEMS is most fully tested in the emergency room. Acute neurologic insults often require rapid therapy, therapy based on heads up thinking and sound judgment. With little time to mull things over, the emergency room can quickly turn into a frightening place to handle acute neurologic illnesses, especially without a bona fide neurologist or neurosurgeon to hold your hand.

Common neurologic problems in the emergency room cluster around six areas: lowered level of consciousness, confusion, seizures, weakness, pain, and dizziness. Before focusing on each of these areas, keep in mind the following general rules which may spare you time, fear, and embarrassment:

(1) Make herculean efforts to locate family, friends, or ambulance drivers: how did they find the patient? did the patient complain about a headache? what was his level of consciousness? could he talk, walk, see, and use his hands? and what medicines does he take? Be sure to write down the telephone number of the patient's physician and any witnesses you talk to in case the ward physicians want to call them later for more historical details.

(2) Respiratory depression will sneak up on you unless you're specifically watching for it. The patient may simply be too confused or stuporous to complain of any difficulty breathing. For this reason, avoid sedatives if at all possible, and intubate* before you wish you had.

(3) Do not dilate the pupil to see the discs and fundi better. Iatrogenically dilated pupils obliterate *the* sign of herniation.

(4) Use some common sense about coordinating the CAT scan and lumbar puncture. Many physicians are too stringently cautioned never to do a lumbar puncture before a CAT scan for fear of precipitating herniation*. Meanwhile, some patients are dying of meningitis while waiting for their CAT scan. If you suspect meningitis, do the lumbar puncture then and there*. The only signs which should stay your hand are those suggesting 1) actual transtentorial herniation (stupor,

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Intubate: To pass an endotracheal tube through the nose or mouth into the trachea to insure an adequate airway, to control the depth and rate of respiration, and to prevent aspiration in case the patient vomits.

Precipitating Herniation: High intracranial pressure by itself is not enough to precipitate herniation after an LP. After all, we tap patients with pseudotumor cerebri all the time and their CSF pressures may be as high as 500–600mm. Lumbar punctures are dangerous when there is a block to CSF flow through the subarachnoid spaces. Without free communication between the supratentorial and spinal subarachnoid spaces, removal of CSF through a lumbar puncture needle can contribute to herniation by creating an irresistable pressure and volume gradient.

Then and There: Meningitis is about the only diagnosis that demands an immediate lumbar puncture. Even a subarachnoid hemorrhage can await the CAT scan. In fact, if the CAT scan can make the diagnosis of a subarachnoid hemorrhage, it may be best to forget the LP altogether. Some subarachnoid hemorrhage patients have done poorly following a lumbar puncture.

hemiparesis or decerebrate posturing, pupil dilation, hyperventilation, hypertension, and changing pulse rate), 2) potentially *impending* transtentorial herniation (stupor and papilledema, or stupor and hemiparesis (or decerebration), or papilledema and hemiparesis), or 3) elevated posterior fossa pressure (occipital headache, vomiting, stupor, ataxia, ophthalmoparesis, dysarthria, poor gag, and irregular respirations).

If you're afraid to tap a patient with apparent meningitis (fever and stiff neck), a reasonable compromise is to quickly obtain blood, urine, and sputum cultures, begin antibiotics, get the CAT scan, and *then* tap the patient. The gram stain should still be positive even though the cultures may not grow out.

(5) In the early minutes, it may be easier to examine a comatose patient if you stand at the head of the stretcher where you're out of the way of other doctors and nurses inserting tubes and attaching wires. Respirations, homonymous hemianopia, eye movements, eyelid closure, jaw closure, facial weakness, swallowing movements, and asymmetrical use of the extremities can all be easily observed from the head of the stretcher.

(6) Try to rule out the most explosive but treatable diseases first (the upcoming chapters will emphasize those explosive diseases).

(7) While looking for the cause of unexplained fever, don't forget to keep the patient's temperature below 102° if possible. Hyperthermia alone can exacerbate cortical dysfunction and, above 104°, may even cause permanent neuronal injury.

LOWERED LEVEL OF CONSCIOUSNESS

THE FIRST QUESTION YOU SHOULD ALWAYS ASK YOURSELF about any patient in the emergency room is, 'How much time do I have before the patient is dead?' Lowered level of consciousness is one of those situations which may not give you or the patient much time. You need to know how much neurologic room there is between the patient and his brainstem so that you can rule out those illnesses which need immediate, definitive therapy. You must step in before your patient herniates, because once he does, his chances of recovery drop dramatically.[1]

Initial Assessment

The first step in assessing a stuporous or comatose patient is to look at the chest wall to make sure the patient is breathing adequately. Intubate if there is hypoventilation*, upper airway obstruction, or an absent gag reflex*. Be careful about intubating unconscious patients. If the neck is broken, hyperextending the neck during intubation may transect the spinal cord. Either get a cervical spine film first, or ask an anesthesiologist to intubate through the nose, which avoids hyperextending the neck*.

After drawing blood for electrolytes, BUN, glucose, liver functions, CBC, calcium, phosphate, CPK and drug screen, give 50 cc of 50% glucose IV* and 100 mg of thiamine to prevent the glucose from precipitating Wernicke's encephalopathy*. Have someone obtain a blood gas and urinalysis.

While this is being done, assess the highest level of consciousness and specifically look at the size of the pupils. If the pupils are small and reactive*—suggesting

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Hypoventilation: You may need to draw a blood gas to convince yourself that the patient is indeed hypoxic (pO_2 less than 75mm) or retaining pCO_2 (greater than 40 mm)

Absent Gag Reflex: Should the patient vomit, a poor gag reflex won't close the epiglottis to prevent aspiration of gastric contents into the trachea and lungs. The subsequent pneumonia may be particularly nasty because of the gastric acid.

Hyperextending the Neck: Hyperextending the neck to intubate any elderly patient is potentially hazardous because their cervical spondylosis may compress the spinal cord.[2]

50cc 50% Glucose IV: Don't leap to a diagnosis of hypoglycemia if the patient improves after IV glucose. The osmotic load may have drawn enough water out of the brain to reduce the elevated intracranial pressure from a subdural hematoma or brain tumor.

Wernicke's Encephalopathy: Your bolus of glucose is rapidly metabolized down the glycolytic pathway to pyruvate. Since pyruvate requires thiamine to enter the Kreb's cycle, a bolus of glucose can precipitate Wernicke's encephalopathy by mopping up what little thiamine an alcoholic (or any malnourished patient) has.[3] Be very liberal with the use of thiamine, especially in a suspected alcoholic. Korsakoff's psychosis is preventable and may not be that uncommon.[4]

Small and Reactive: Get a good close-up look at small pupils. Even a 1 mm pupil will constrict to light if you use an intense enough light.

narcotic* overdose—give .4 mg Narcan* IV twice over a few minutes, and repeat if necessary.

If one or both pupils are fixed and dilated, the patient has presumably herniated, especially if you see a contralateral hemiparesis with decerebration, hyperventilation, a rising blood pressure, and a changing pulse rate. Call immediately for neurosurgical help and then quickly inspect the face and scalp for a bruise*, a hematoma, a palpable skull fracture, or a foreign body (broken-off ice picks are not unheard of). Check the nose and ears for CSF or blood; look for blood behind the tympanic membrane (hemotympanicum), and feel the cervical spinous processes for a broken neck. If there is any chance the neck is broken, don't do doll's eyes, don't flex the neck (looking for meningismus*), and don't hyperextend the neck (to intubate) until a cervical spinal film says it's okay to do so. Unless the neurosurgeon says no, intubate (through the nose if necessary), hyperventilate* (the fastest way to shrink the brain[6]), administer dexamethasone*, and obtain a CAT scan.

The same urgency applies for unilateral or bilateral decerebrate posturing without pupillary dilation, though you do have a little more time to work with if a pupil hasn't dilated yet.

The other reason to call the neurosurgeon early is discuss whether to give mannitol. The temptation in comatose patients with suspected increased intracranial pressure is to reach for the mannitol. When given intravenously, mannitol shrinks the brain by leeching water from *normal* areas of brain.[5] Mannitol must be used judiciously: too much too often may worsen the very condition you're trying to treat because each time mannitol is given, some of it leaks into brain through the leaky blood-brain barrier surrounding the lesion. Intraparenchymal mannitol then draws water *into* the brain, a vicious cycle called rebound.[5] In general, mannitol is given on the way to the operating room to buy several hours of time, so it's best to wait until you've spoken with the neurosurgeon before administering the mannitol.

Narcotic: Synonymous with the term opioid; any drug which mimics opium or its derivative, morphine. Examples include propoxyphene (Darvon), codeine, pentazocine (Talwin), oxycodone (Percodan), hydromorphone (Dilaudid), meperidine (Demerol), Methadone, and heroin.

Narcan: Naloxone (the chemical name) counteracts narcotics by blocking morphine receptors.

Bruise: After a fracture along the base of the skull, it takes hours for the blood to dissect to the skull surface: classically, around the eyes ("raccoon eyes") and behind the ear over the mastoid bone (Battle's sign).

Meningismus: Meningismus is a stiff neck due to meningeal irritation from inflammation (meningitis) or mechanical stretching (posterior fossa mass). Bacterial and fungal meningitis can be mimicked by a subarachnoid hemorrhage, the blood causing a "chemical" meningitis. Stretching of the meninges usually occurs when a cerebellar tumor or other mass herniates the cerebellar tonsils through the foramen magnum. A stiff neck in a patient with a posterior fossa mass may be an explosively dangerous sign. Look carefully for other signs of pontine or medullary compression.

Hyperventilate: Hyperventilation doesn't lower intracranial pressure after trauma as well as it does with brain tumors and abscesses, because hyperventilation depends on vessels that have retained their ability to autoregulate.[5] Loss of autoregulation is one of the primary reasons trauma patients suffer increased intracranial pressure: the intracerebral vessels remain wide open allowing too much blood (and pressure) into the head.

Dexamethasone: Corticosteroids (such as dexamethasone) tighten the tight junctions binding adjacent capillary endothelial cells. New blood vessels encircling tumors and abscesses have leaky tight junctions which steroids help to seal.[7]

Without the concomitant signs of herniation—falling level of consciousness, hemiparesis, decerebration, rising blood pressure, and changing pulse rate—the dilated pupil is not quite as ominous. You can take the time to confirm that the fixed, dilated pupil does indeed represent a complete IIIrd nerve palsy. Inject up to 100–150 cc of ice water into the contralateral ear*; if there is a IIIrd nerve palsy, the eye with the fixed pupil won't adduct across midline.

A IIIrd nerve palsy in a comatose patient doesn't automatically mean herniation, nor even a midbrain lesion. For example, a subarachnoid hemorrhage from a posterior communicating artery aneurysm will also precipitate coma and a IIIrd nerve palsy, the coma being due to blood in the CSF and to the elevated intracranial pressure.

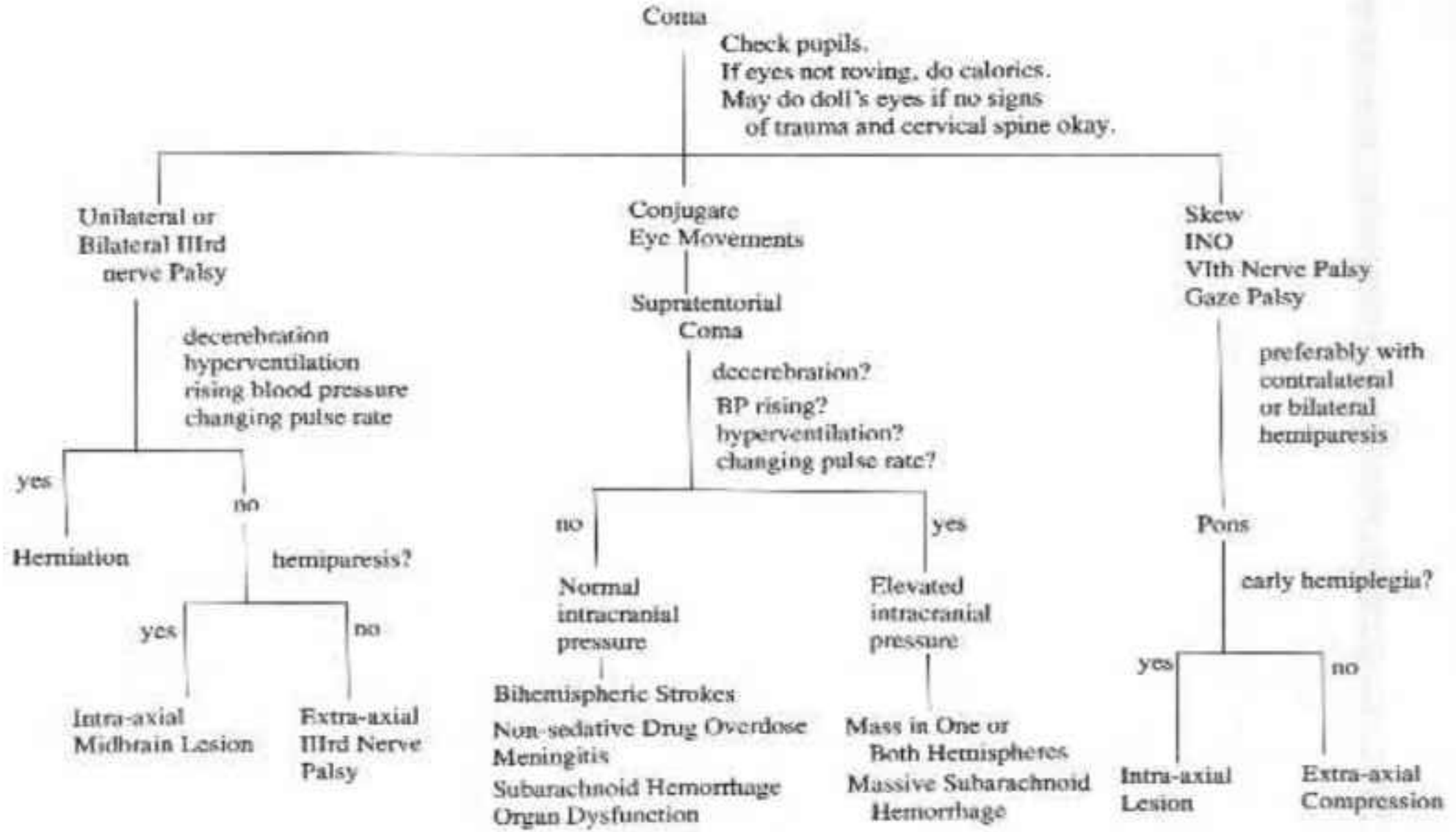
If the patient has a fever and stiff neck, decide now if he is on the verge of herniation. Unless there are signs of early herniation, you have to do the lumbar puncture without a lot of hand wringing or head scratching. You need to know if this patient has meningitis now, not after his cortex is shot. A reasonable alternative is to treat presumptively and postpone the lumbar puncture until you feel it's safe.

Hypertension is often mistaken as the cause of coma when actually hypertension is a consequence of the coma, namely a sign of elevated intracranial pressure with impending herniation. The patient may need that blood pressure to perfuse his brain, so don't lower the blood pressure until you've ruled out increased intracranial pressure. Subarachnoid and intracerebral hemorrhages are often mistaken for hypertensive encephalopathy.[10]

The most practical early sign of papilledema is hyperemia of the optic discs which are normally a creamy yellow with a light salmon hint. If you see that yellow disc go rolling by against the red retina, there's probably no papilledema. But if, as the disc rolls by, you have difficulty distinguishing it from the red retina, be very suspicious of papilledema. The presence of hemorrhages near the disc, even without papilledema, strongly suggests a recent sudden increase in intracranial pressure.[11] Don't be lulled by the absence of papilledema; it usually takes a day or two for papilledema to develop once the intracranial pressure becomes elevated.[12]

The neurologic exam from here on requires careful anatomic thinking to sort out all the possible insults to the reticular activating system. Mindlessly harvesting lots of signs will leave you and the patient out in the field. Remember from chapter 22 that insults to the reticular activating system may attack from above (supratentorially), from behind (cerebellum, 4th ventricle), and from in front (basilar artery and clivus). One approach is as follows:

Contralateral Ear: Obviously you don't need to do cold calories if the eyes are roving. Likewise, cold calorics are unnecessary if you can elicit doll's eyes; cold calorics are simply a more intense stimulus to the labyrinths than head rotation.


Coma
Check pupils.
If eyes not roving, do calories.
May do doll's eyes if no signs of trauma and cervical spine okay.
Unilateral or Bilateral IIIrd nerve Palsy
decerebration
hyperventilation
rising blood pressure
changing pulse rate
yes
no
Herniation
hemiparesis?
yes
no
Intra-axial Midbrain Lesion
Extra-axial IIIrd Nerve Palsy
Conjugate Eye Movements
Supratentorial Coma
decerebration?
BP rising?
hyperventilation?
changing pulse rate?
no
yes
Normal intracranial pressure
Bihemispheric Strokes
Non-sedative Drug Overdose
Meningitis
Subarachnoid Hemorrhage
Organ Dysfunction
Elevated intracranial pressure
Mass in One or Both Hemispheres
Massive Subarachnoid Hemorrhage
Skew
INO
VIth Nerve Palsy
Gaze Palsy
preferably with contralateral or bilateral hemiparesis
Pons
early hemiplegia?
yes
no
Intra-axial Lesion
Extra-axial Compression

Upper Brainstem

Once you know that the patient is breathing and maintaining a blood pressure, that he doesn't respond to Glucothiocan (glucose, thiamine, and Narcan), and isn't frankly herniating (fixed dilated pupil, decerebration, hyperventilation, rising blood pressure, and changing pulse rate), your next question is: 'Is the upper brainstem structurally intact?' As pointed out by Robert Scott, you can liken the midbrain and upper pontine reticular activating system to an electrical generator producing electricity for a light-bulb in each hemisphere.[1] To knock out someone's lights, you can either damage both lightbulbs or the brainstem generator. Since the reticular activating system is entangled in and around the IIIrd nerves and cerebral peduncles in the midbrain and both medial longitudinal fasciculi in the upper pons, you can indirectly infer structural damage to the reticular activating system by finding midbrain or upper pontine eye signs and a contralateral (or bilateral) hemiparesis. Upper brainstem eye signs are, of course, a IIIrd nerve palsy*, internuclear ophthalmoplegia, and skew deviation.

An example of an upper pontine lesion would be a stuporous, hemiplegic patient in whom one or both eyes, despite equal reactive pupils, won't adduct across the midline by doll's eyes or cold calorics. The equal, reactive pupils tell you the midbrain is structurally intact, so the adduction palsy cannot be a IIIrd nerve lesion, but instead a lesion of the medial longitudinal fasciculus. The coma, then, is due to structural damage of the reticular activating system in the upper pons.

Pons

Signs of the lower half of the pons include:

VIth nerve palsy and contralateral hemiparesis
Unilateral gaze palsy and contralateral hemiparesis
Bilateral gaze palsy (usually with quadriplegia)
Lower motor neuron facial palsy and contralateral hemiparesis
The one-and-a-half syndrome (preferably with a contralateral hemiparesis).

A lower pontine lesion by itself cannot cause coma, because the reticular activating system only extends as far as the mid-pons. Coma with lower pontine signs is not uncommonly due to a cerebellar or 4th ventricular mass compressing the lower pons and with it, the 4th ventricle. The coma results from the elevated intracranial pressure of non-communicating hydrocephalus. Another explanation for the coma is simultaneous compression of the reticular activating system in the upper pons.

An early hemiplegia with pontine signs usually means an intra-axial pontine lesion; without a hemiparesis the same pontine signs suggest extra-axial compression from a mass behind the brainstem. Look for early papilledema and vomiting to suggest 4th ventricular obstruction, listen for dysarthria, and if you can, walk the patient to see if he's ataxic. Tone in the arms and legs should be increased if pontine compression occurs above the vestibular nucleus, decreased below.

In looking for ophthalmoplegia, don't conclude anything if the eyes are resting 'wall-eyed'—it can be normal in any unconscious person, even you if you're sleeping. Rock the head from side to side. If the eyes doll properly, the coma is not due to structural damage of the brainstem, or to sedative overdose which suppresses doll's eyes. If the eyes don't doll, do ice water calorics; you have to know *now* if the eyes move conjugately.

IIIrd Nerve Palsy: Intra-axial midbrain lesions often don't damage all the parasympathetic fibers en route to the IIIrd nerve, so the pupil may not be widely dilated in midbrain lesions.

A gaze palsy or total horizontal ophthalmoplegia (bilateral gaze palsies) on ice water calorics usually means trouble. Look carefully for other pontine signs like skew deviation, internuclear ophthalmoplegia (the one-and-a-half syndrome), absent jaw closure, absent corneals, facial palsy*, and irregular respirations. Train your attention on the medulla: are the gag reflex and spontaneous swallowing absent? Is the tone flaccid and the respiratory effort poor? Are the blood pressure and pulse falling? What about a stiff neck (tonsillar herniation through the foramen magnum)?

A unilateral or bilateral VIth nerve palsy should also lead you to the lower pons. Take the same steps as you did for a unilateral or bilateral gaze palsy, but keep in mind that unilateral or bilateral VIth nerve palsies in a comatose patient may also be due to symmetrical increased intracranial pressure.[14]

Supratentorial Coma With Increased Intracranial Pressure

Roving or ice-water-induced conjugate eye movements are reassuring because it means the brainstem is structurally intact between the oculomotor nucleus in the midbrain and the abducens nucleus in the lower pons. The cause of the coma must, therefore, be something that affects both hemispheres*.

The critical question at this point is whether the patient is on the verge of herniating from elevated supratentorial pressure. Unilateral or bilateral stiffening of the limbs—with or without an obvious hemiparesis—indicates early decerebration and impending herniation. Hyperventilation*, rising blood pressure, and a changing heart rate should also immediately alert you to impending herniation. Papilledema, or more likely, retinal hemorrhages (splinter, flame, or subhyaloid) strongly suggest increased intracranial pressure.

The easiest way to detect a hemiparesis is simply to watch the patient use his limbs spontaneously. If he doesn't move, make him thrash and grope by pinching first one, and then the other sternocleidomastoid. If asymmetrical limb use still isn't obvious, lift his arms up and yell encouragement to keep them up.

Once you detect a hemiparesis, the lesion you can't afford to miss is an epidural hematoma which can kill while you're writing up the history and physical*. Seek out a history of relatively mild head trauma with only a brief loss of consciousness*

Facial Palsy: Perhaps the most ominous sign in medicine (besides an absent pulse or absent respirations) is a comatose patient with partially open eyelids exposing a crescent of sclera. The patient is so deeply comatose that he can't even generate enough strength to fully close his eyes, a sign—to give you some idea of its seriousness—readily seen on any cadaver.

Both Hemispheres: Though blood-borne chemicals probably cause coma by directly depressing the reticular activating system,[15] it's easier to think of blood-borne lesions as depressing the cortex in both hemispheres (per the analogy of a brainstem generator and two hemispheric light bulbs).

Hyperventilation: Keep in mind that hyperventilation without decerebration is usually *not* a sign of rising intracranial pressure, but rather a sign of a metabolic acidosis (like diabetic ketoacidosis), hypoxia (pneumonia, pulmonary emboli, heart failure, or neurogenic pulmonary edema), or CSF acidosis (from meningitis).

History and Physical: Rarely, epidurals may present subacutely.[16]

Brief Loss of Consciousness: Epidurals probably result more commonly from severe head trauma than minor head trauma. But minor head trauma *needs* to be emphasized so that you don't overlook the possibility of a rapidly expanding intracerebral mass just because the child only fell off her bicycle.

Epidural *venous* hematomas may also occur, but they compress the brain more slowly than epidural arterial hematomas.

followed minutes to hours later by headache, nausea, vomiting, and stupor with a hemiparesis. The reason mild head trauma can be so lethal is that the thin temporal bone can fracture from a relatively mild, but direct blow. Embedded in the temporal bone is the middle meningeal artery which is easily torn by the temporal bone fracture. Arterial blood begins to accumulate in the epidural space at a pressure of 120 mm mercury. Normally, pressure within the head (lumbar puncture opening pressure) is less than 200 mm water, or 15–16 mm mercury. A blood clot under 120 mm mercury pressure would be the equivalent of an opening lumbar puncture pressure of 1500 mm water! For this reason if you suspect an epidural hematoma, do not leave the patient's side until the neurosurgeon arrives. If you cannot get an emergency CAT scan, accompany the patient to radiology for two emergency lateral skull xrays, the film against one and then the other temple. If there's a temporal bone fracture, the film with the sharper edges along the fracture line will tell you which side the fracture is on. At the first sign of a falling level of consciousness, intubate (if you have not already done so), hyperventilate, keep the head of the bed up,[17] and administer mannitol when the neurosurgeon tells you to. (Intravenous steroids won't do much good in this situation, because steroids take hours to effectively tighten leaky tight junctions, but give the steroids anyway.)

Subdural hematomas, being venous, are less virulent than epidural hematomas. Besides oozing out under a pressure of only 2–5mm of mercury, a subdural hematoma can, at least for a while, "decompress" itself by spreading out over the surface of the brain in the subdural space*. In this respect, subdural hematomas resemble subarachnoid hemorrhages which, by exerting diffuse pressure, are generally less dangerous than equally high pressure epidural hematomas exerting virtually direct pressure on the midbrain through the temporal lobe.

The veins that bleed in subdural hematomas are those traversing the subdural space draining blood from the brain to the epdural venous sinuses*.[19] In elderly shriveled brains, relatively minor head trauma can tear these tautly stretched veins, but in a young full-sized brain firmly wedged up against the dura, it takes terrific forces to tear the bridging veins. In fact, in young people the head trauma necessary to tear the bridging veins is so severe that the underlying brain is usually seriously damaged, which is the major reason for the coma, not the subdural blood clot*. Urgent surgical removal of the subdural hematoma is indicated, but because of the underlying brain damage, don't harbor high hopes for a dramatic soap opera recovery.[20]

In the Subdural Space: In a patient with a hemiparesis, the presence of a homonymous hemianopia usually distinguishes a stroke from a subdural hematoma. Subdurals do not, in general, cause a homonymous hemianopia because the optic radiations lie deep in the temporal, parietal, and occipital lobes, relatively far away from the subdural space. Infarctions, on the other hand, often do damage the optic radiations in the deep white matter.

Epidural Venous Sinuses: Shenkin argues that subdural hematomas may also be caused by tears in small cortical arteries.[18]

Subdural Blood Clot: By history you can often distinguish a subdural from an epidural: a clear interval between the trauma and loss of consciousness does not occur with subdurals because of the severe trauma necessary to tear the bridging veins (at least, in young people). But the converse—no clear interval means subdural—is certainly not true. Severe head trauma—enough to cause coma from the start—may fracture the skull and tear an epidural artery.

Supratentorial Coma Without Increased Intracranial Pressure

If the patient is breathing and maintaining his own blood pressure (medulla); Glucothiacan does not awaken him; neither pupil is fixed to light (midbrain); the eyes move fully with doll's eyes or ice water calorics, and the corneal reflexes, jaw closure, and facial grimacing are all okay (pons); and if there's no decerebration, hyperventilation, rising blood pressure, or changing pulse rate (to suggest impending herniation), you have a little more time to work with because there's still some neurologic room between the patient and his brainstem. Your job now is to guard against herniation until you're certain the intracranial pressure is not elevated.

From the initial neurologic exam you know how close the patient was to herniation. Now return to the patient and recheck his level of consciousness. This second neuro check will tell you if and how fast the lesion is approaching the brainstem. If the level of consciousness is lower, contact a neurologist or neurosurgeon, intubate if necessary, and keep rechecking the level of consciousness. A CAT scan, hyperventilation, dexamethasone*, and even mannitol are in your holster, so don't feel overwhelmed by the patient or his illness.

In the meantime, you need to think through all the etiologies that cause coma by a mechanism other than elevating the intracranial pressure*. You've already checked for fever and a stiff neck to rule out meningitis or subarachnoid hemorrhage. Treatable causes of *hypo*thermic coma include Wernicke's encephalopathy,[22] hypothyroidism, cold exposure, and rarely, barbiturate poisoning or hypoglycemia. Don't forget to give steroids when treating hypothyroid coma. Chronic, severe hypothyroidism also makes patients relatively Addisonian. Thyroid replacement without steroids may throw a patient into acute Addisonian crisis, i.e., hypotension and hypoglycemia.[23]

Distinguishing among all the other possible diagnoses by physical examination alone won't be easy. You may get some clues to internal organ failure by finding hyperventilation (diabetic ketoacidosis, renal failure, liver failure, congestive heart failure, and hypoxia), multifocal myoclonus (liver failure, renal failure, anoxia), focal twitching (subclinical status epilepticus from hyperosmolar states), asterixis (liver failure, renal failure, anoxia), hypothermia, puffy face, bradycardia, and distant heart sounds (myxedema), and jaundice (liver failure).

Seizures only mean that the cortex is the presenting site of dysfunction; renal failure, hypoxia, hypoglycemia, hyperglycemia, and meningitis all cause seizures. Even a hemiparesis may fool you into diagnosing a structural hemispheric lesion when, in reality, the hemiparesis is nothing more than an old, dormant pyramidal tract lesion revived by organ dysfunction (especially hypoglycemia).

Certain tricky situations to watch out for are occasional decerebration in liver failure, and dilated fixed pupils from glutethimide (Doriden), atropine, or perhaps amitriptyline overdose. Suspect atropine or amitriptyline if you see other anticholinergic effects: a warm, dry, flushed face and tachycardia. Ophthalmoplegias on cold

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Dexamethasone: Because dexamethasone takes hours to begin working, some neurosurgeons recommend giving dexamethasone when you first see comatose patients.[21] The side effects are minimal and the potential benefits of giving dexamethasone early may be life-saving, especially if the patient also happens to be Addisonian (hypoadrenal).

Elevating the Intracranial Pressure: Subarachnoid hemorrhages elevate the intracranial pressure, but the patient won't wake up if you lower his intracranial pressure with a lumbar puncture. The coma is due to direct irritation of the cortex (or reticular activating system) by the blood.

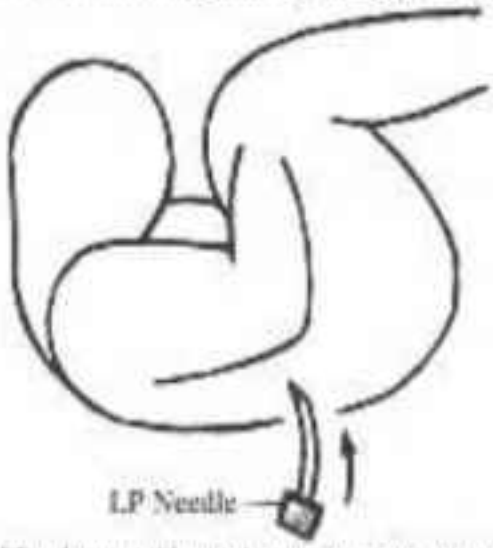
caloric testing have been reported in tricyclic overdose and liver failure.[24] High fever and a stiff neck may not be meningitis, but instead, the neuroleptic malignant syndrome. Watch out for myoglobinuria.

Another mistake is to overlook that the patient isn't unconscious, just paralyzed. You can be fooled by botulism, the descending form of Guillain Barre, and rarely the dreaded 'locked-in' syndrome—complete paralysis of the body except for vertical eye movements and reactive pupils, all without loss of consciousness! The lesion, usually a stroke, is located in the ventral pons, sparing the reticular activating system but intercepting the descending pyramidal tracts destined for the pontine gaze centers and all points south.[25]

Lumbar Puncture

To perform the spinal tap*, curl up the patient on his side. After cleansing the back with iodine, use a 25 gauge needle to raise a bleb of local anesthetic between two lumbar spinous processes. Through that bleb insert a 22 gauge needle and inject local anesthetic continuously as you advance the needle all the way to the hub (the less pain, the easier the LP). Follow this path with the lumbar puncture needle, removing the stylet every few millimeters to check for undetected entry (no 'pop') into the subarachnoid space. Measure the opening pressure with the manometer*.

If you have difficulty getting into the L3-4 or L4-5 interspace, you may find it helpful to bend the LP needle and direct its pathway rostrally. Also, don't hesitate to try the L2-3 or L1-2 interspace, or else the relatively large L5-S1 interspace. If you still have trouble puncturing the subarachnoid space, sit the patient up and try again, but lay the patient back down again before measuring the opening pressure*.



Bending the needle helps it hook under the spinous process.

Spinal Tap: Learning to do procedures is of fundamental importance, in many ways as important as learning the vocabulary and physiology of medicine. It's often said that procedures—lumbar puncture, bone marrow aspiration, thoracentesis (drainage of a pleural effusion), blood gases, wound debridment, etc.—can be learned during your internship, and that medical students should concentrate on concepts. Wrong, you need procedures, and lots of them. You need to believe in yourself, that you can actually *do* what doctors do. Learn how to do procedures early so you can see yourself treating patients and realize why you need to learn the vocabulary and pathophysiology of diseases.

With the Manometer: The opening pressure is the CSF pressure before any CSF has been removed for tests. A manometer is a tube divided into millimeter increments to measure the height of CSF pressure.

Before Measuring the Opening Pressure: The opening pressure in the sitting position should rise to about the level of the foramen magnum, but it is more accurate, reproducible, and meaningful to lay the patient back down before recording the opening pressure.

If the spinal fluid takes too long to ascend in the manometer, rotate the manometer horizontally and when the fluid reaches 200 mm, return the manometer to the vertical position. The meniscus will then fall to the opening pressure.

If the opening pressure is greater than 250 mm, don't panic. Fully extend the patient's legs and remove the pillow to allow the meniscus to fall to the true (lowest) opening pressure. If the meniscus remains above 250 mm, collect enough fluid for stains and culture, another milliliter for cell count and glucose, and then measure the closing pressure. A dramatic pressure drop between the opening and closing measurements suggests (but only suggests) that one temporal lobe or the cerebellar tonsils may have just herniated, preventing the elevated intracranial pressure from being transmitted to your manometer.

Fortunately, patients with elevated intracranial pressure commonly take six to eight hours to herniate following a lumbar puncture, enough time to organize defensive measures. First, don't keep the elevated spinal fluid pressure a secret—neurosurgeons get paid to handle elevated intracranial pressure. In the meantime make a sheet of signs for the nurse to monitor; don't rely on 'neuro checks,' a list of motions that nurses (at least, non-neuro nurses) go through without really appreciating their significance. Tell the nurse looking after your patient exactly what to watch for*.

If the spinal fluid entering the manometer is pink, you must distinguish between true hemorrhagic spinal fluid and a traumatic* spinal tap. One way is to count the number of red cells in the first and last tube of CSF. The red cell count in true hemorrhagic CSF won't vary between the first and last tube, while the first tube of a traumatic tap will have many more red cells than the last tube as the bleeding stops. The other way to tell if the red cells were iatrogenically introduced is to centrifuge the CSF and look for xanthochromia of the supernatant*. The presence of xanthochromia

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What to Watch For: Typical neuro checks focus on things like pupillary constriction to light, but a fixed pupil is awfully late to discover herniation. Complaints of a worsening headache, progressing stupor and hemiparesis, rising blood pressure, and changing pulse rate should warn you of impending herniation with enough time to do something about it.

When ordering neuro checks, tell the nurse exactly what you want, and make it simple:

	12 MN	2 AM	4 AM	6 AM	8 AM
Patient can say the date					
Denies a headache					
No arm drift					
Blood Pressure/Pulse					

Traumatic: All sorts of veins lie within the spinal epidural space. Nicking one on the way in may introduce blood into the CSF which you can misinterpret as a true subarachnoid hemorrhage.

Xanthochromia of the Supernatant: Xantho = yellow, chromo = color. When red cells lyse (break open) in the CSF (because of the sudden absence of serum proteins?), the released hemoglobin is disassembled into yellow metabolites that may persist in the CSF for up to 10–14 days.[26] For this reason, it's essential to know if hemorrhagic spinal fluid was due to a traumatic tap, because subsequent xanthochromic spinal taps may simply reflect metabolized blood from the first, traumatic tap.

Of course not every subarachnoid hemorrhage represents a bleeding aneurysm. Any blood that hemorrhages directly into the subarachnoid space (not just dissects out to the subarachnoid space from an intracerebral hematoma) qualifies as a subarachnoid hemorrhage, including cerebral contusion (bruise on the surface of the brain), bleeding arteriovenous malformation, and bleeding from a normal vessel because of a bleeding diathesis.

Jaundice in the blood may attach itself to CSF proteins and also make the CSF xanthochromic.

means there was enough time for the RBC's to burst, release the hemoglobin, and for the hemoglobin to be metabolized to bilirubin—i.e., that the blood was there for at least 4-6 hours before you did the lumbar puncture. Crenated* red cells are of no use in dating the time of hemorrhage, and therefore of no use in distinguishing a traumatic lumbar puncture from a true subarachnoid hemorrhage.

Remember that the spinal needle taps the subarachnoid space. A *subdural* hematoma will not disturb the normally clear subarachnoid fluid unless the patient also suffered a cerebral contusion that, independent of the subdural hematoma, leaked red cells (and subsequent xanthochromia) into the subarachnoid spinal fluid. Conversely, the absence of RBC's does not rule out a catastrophic intracerebral hemorrhage. As long as the hemorrhage doesn't communicate with the ventricles or subarachnoid space, you may see no red cells at all.

Spinal fluid white cells should number less than three or four lymphocytes per cubic millimeter with no polys. If the tap is traumatic, you're allowed the peripheral blood ratio of one white cell per one thousand red cells (plus the 3–4 WBC's allowed normally). For example, a traumatic tap that allows 14,000 RBC's/mm^3 into the CSF will also admit 14 WBC's. So anything above 17 WBC's/mm^3 (14 plus the 3 allowable WBC's) cannot be accounted for by the traumatic tap. You must then decide what the white cells are responding to: blood, infection, demyelination, infarction, whatever. Once the CSF cell count reaches about 150 cells/mm^3, you ought to be able to shake a tube a CSF and see that it is not perfectly clear.[26]

You're allowed 1 milligram of protein (above the normal upper limit of 45mg%) for each thousand red cells, which is simply the ratio of protein to red cells in the peripheral blood. So, for example, a protein of 70mg% and 1000 RBC's/mm^3 would be too high to attribute to a traumatic tap (maximum allowable protein would be 46mg%). The spinal fluid protein may rise for hundreds of reasons: peripheral neuropathies (especially demyelinative ones), benign and malignant brain or spinal cord tumors, cerebral arteritis, strokes, hypothyroidism, etc.

A CSF protein of 100-150mg% turns the CSF slightly xanthochromic. If the protein is that high, be cautious about diagnosing a past subarachnoid hemorrhage based on xanthochromia without red cells. Above 500mg%, begin looking for a block to CSF flow somewhere along the spinal canal. Without free access to arachnoid villi above the foramen magnum, the CSF protein rapidly accumulates in the lumbar sac.

Immunoglobulins should total less than 13% of the total spinal fluid protein*. Three CNS illnesses typically raise the immunoglobulin fraction: multiple sclerosis, syphi

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Crenated: Shriveled in such a way that the red blood cells resembles a sea urchin. The mechanism of crenation is unclear since you'd expect red blood cells to expand into a sphere as spinal fluid is drawn into the protein-filled red cells.

Total Spinal Fluid Protein: Because serum may contain more than 13% IgG, a leaky blood brain barrier may allow serum into the spinal fluid and spuriously raise the CSF IgG. To avoid mistaking serum IgG for CSF IgG, the CSF IgG is compared to the CSF albumin level. This fraction is then compared to the serum IgG/albumin ratio in what's called a 'CSF index':

(CSF IgG/CSF albumin)/(serum IgG/serum albumin) = CSF Index

An elevated index means the CSF IgG originated within the central nervous system.[27]

Electrophoresis of the CSF immunoglobulin fraction may reveal certain characteristic bands of protein called oligoclonal bands. The presence of oligoclonal bands is highly suggestive of multiple sclerosis.[28]

lis, and subacute sclerosing panencephalitis*, but many other chronic infections and immunologic diseases may also raise the CSF immunoglobulin.[33] Most hospitals measure the IgG level instead of total immunoglobulin, but since almost all CSF immunoglobulin is IgG—very little is IgM or IgA—IgG and total immunoglobulin are roughly the same.

A CSF glucose less than two-thirds of the serum glucose is considered pathologically low. However, the CSF glucose at the time of the LP is actually the serum glucose level a full hour before (it takes that long to equilibrate).[31] So be cautious about interpreting the CSF glucose if you have reason to suspect the serum glucose at the time of the LP was much different than an hour prior to the LP.

Any meningitis—bacterial, fungal, parasitic, carcinomatous,[32] or chemical (blood)[34]—can lower the CSF glucose by inhibiting glucose transport across the meninges into the subarachnoid space. Viral meningitis, with the exception of mumps meningitis, generally leaves the CSF glucose alone. Viral *encephalitis**, especially herpes encephalitis*, not uncommonly lowers the CSF glucose.[34] Carcinomatous meningitis also lowers spinal fluid glucose and raises the protein but unlike infections, does so without markedly raising the CSF white cell count. The clinical picture is usually one of multiple cranial nerve or nerve root dysfunction as the nerves get 'clipped off' passing through the infiltrated meninges. A cytologic* search for malignant cells in the CSF usually clinches the diagnosis.[35]

What's difficult about analyzing inflammatory CSF is that TB meningitis, fungal meningitis, herpes encephalitis, and partially treated bacterial meningitis can all look the same: polys and lymphs, elevated protein, and low sugar.[36] Which combination of antibiotics to begin is almost impossible to judge based on the CSF alone; the clinical picture usually dominates the choice of drugs.

The Queckenstedt maneuver was commonly used before the advent of myelography to detect spinal fluid block*. The test is performed during the LP by measuring the rise in lumbar pressure after compressing the jugular veins in the neck. Normally, pressure build-up in the jugular veins is transmitted intracranially and then down the spinal canal. If there's no spinal canal obstruction, the lumbar pressure rises immedi-

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Subacute Sclerosing Panencephalitis (SSPE): In the early days of neurology all pathologic insults were thought to be scarring (sclerosis) which prompted names like multiple sclerosis, diffuse sclerosis, disseminated sclerosis, amyotrophic lateral sclerosis, tuberous sclerosis, and subacute sclerosing panencephalitis. *Panencephalitis* means that both the white and gray matter are affected.

The etiology of SSPE was proved about fifteen years ago to be due to measles virus which somehow becomes chronically active in a child's (or teenager's) brain, producing slow, progressive neurologic deterioration.[38]

Encephalitis: Encephalitis means that there are cortical signs like confusion, aphasia, and seizures. Meningitis alone implies no cortical signs. The two together are called meningoencephalitis.

Herpes Encephalitis: A devastating, hemorrhagic, necrotizing encephalitis with a predilection for the temporal lobes.

Cytologic: A microscopic analysis of cells for telltale signs of cancer. The best example is the cervical Pap smear seeking cancerous changes in cells scraped off the cervix.

Block: Obstruction to the flow of dye up the spinal canal.

ately with jugular compression. A sluggish Queckenstedt response suggests a mass or adhesions* (arachnoiditis) in the spinal canal.

Some patients develop a headache after a lumbar puncture, presumably related to continued leakage of CSF into the lumbar epidural space through the dural needle hole.[37] The leakage and the headache are worsened by sitting or standing which raises the pressure gradient across the hole. Sometimes acetazolamide (Diamox) 250 mg TID-QID*, a drug which slows the production of spinal fluid,[38] may reduce the pressure gradient enough for the dural hole to repair itself. Naturally, the smaller the lumbar puncture needle, the smaller the dural hole and, therefore, the less likely a post LP headache. And to give the dural hole a head start on sealing itself, patients should lie flat for four to six hours following an LP, preferably prone to keep the dural hole above the level of the spinal fluid*.

CAT Scan

Computerized axial tomography is an xray test that produces pictures of the brain's internal anatomy. Each picture depicts a slice of brain anywhere from one to ten millimeters thick, often permitting astonishingly accurate localization of structural lesions. Despite the virtually infinite variety of CAT scan findings in comatose patients, there are enough structural landmarks on a CAT scan to guide you in the middle of the night.

Hydrocephalus: This is probably the most easily seen abnormality. Concentrate on the size of the 3rd and 4th ventricles to rule out non-communicating hydrocephalus. Communicating hydrocephalus enlarges all four ventricles, while in non-communicating hydrocephalus, the 4th ventricle will remain small (aqueductal obstruction) or be obliterated*. If all four ventricles are enlarged, distinguish hydrocephalus 'ex vacuo' (brain atrophy) from communicating hydrocephalus by looking for enlargement of the Sylvian fissure and the cortical sulci.

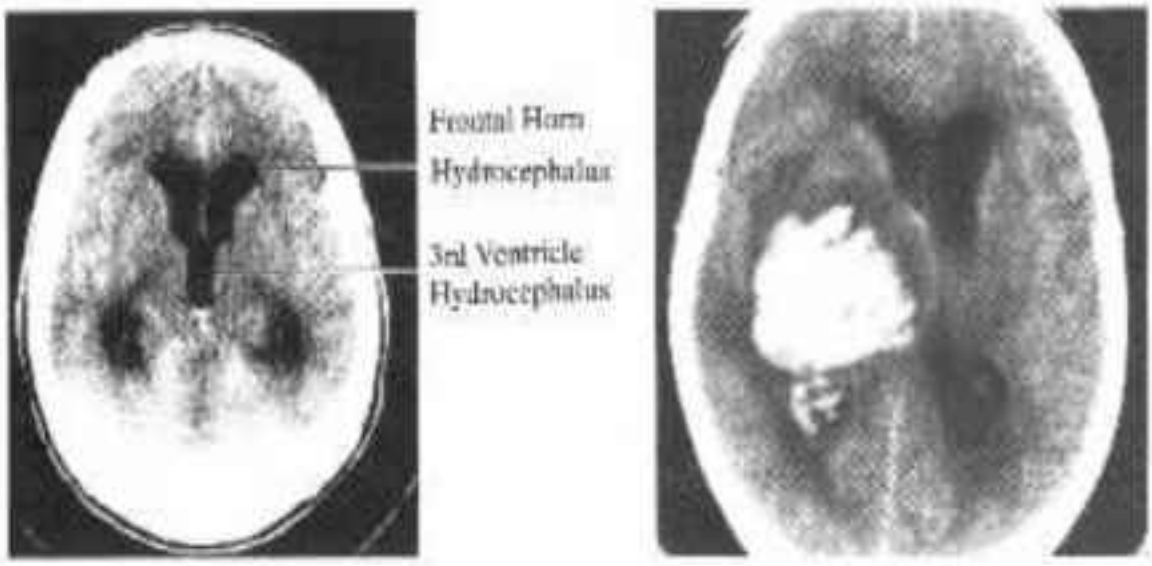
Adhesions: An abnormal strand of scar tissue which binds two structures together. Adhesions cause problems by 1) obstructing an organ (especially the gut), 2) compressing an organ's vascular supply, or 3) by prolonging surgery (in two ways: by disrupting the normal architecture, and by making it necessary for the surgeon to take additional time to cut through the adhesions to reach the operative problem).

TID-QID: Thrice In the Day; Quarter (four) times In the Day. QD means once a day and BID means twice a day.

Spinal Fluid: Despite the tradition of keeping patients flat in bed after a lumbar puncture, whether patients get up or remain flat probably has no bearing on the incidence of post lumbar puncture headache.[39] What does make a difference is the size of the LP needle; the larger the needle, the more likely the headache.

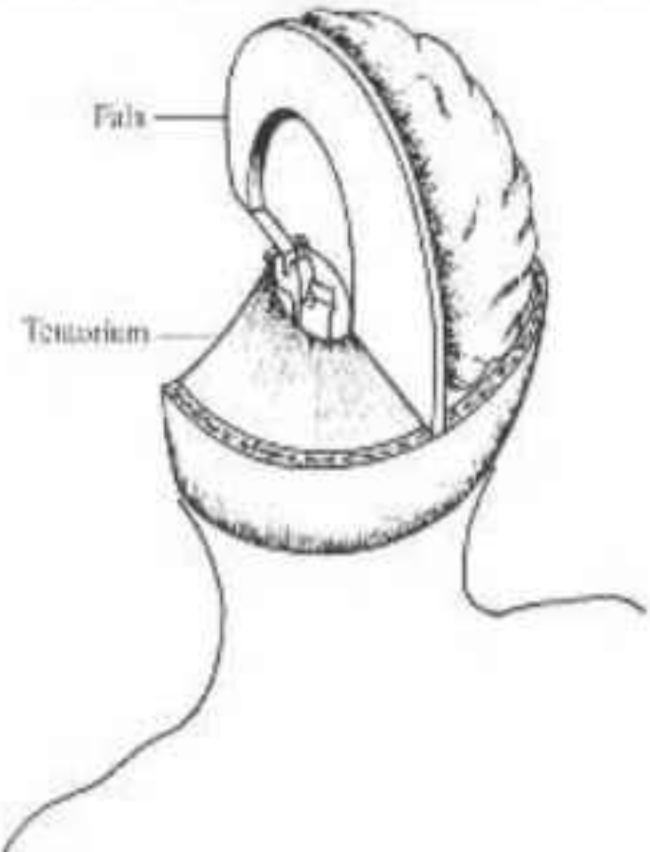
Obliterated: Non-communicating hydrocephalus could conceivably enlarge the 4th ventricle if an infiltrating tumor or adhesions obstruct the foramina of Magendie and Luschka without compressing the 4th ventricle.

Mass Effect: First confirm that the midline structures—the septum pellucidum, 3rd ventricle, pineal, and 4th ventricle—are indeed midline. Look carefully at the extracerebral space over each hemisphere to be sure that bilateral masses are not preventing a midline shift*. Is one choroid plexus in the atrium of the lateral ventricle shifted forward by a parieto-occipital mass?



Posterior fossa mass effect is evident by obliteration or shift of the 4th ventricle, loss of the perimesencephalic cisterns, and hydrocephalus. In young people hydrocephalus may not manifest as massively dilated lateral ventricles, but rather as obliterated cortical sulci and dilated temporal horns (the temporal horns are not usually visible).[40]

Midline Shift: The frontal lobes shift across the midline more than the parieto-occipital lobes do because only in the posterior head region does the rigid falx dip deeply between the two hemispheres.





Normal Perimesencephalic Cistern



Obliterated 4th Ventricle



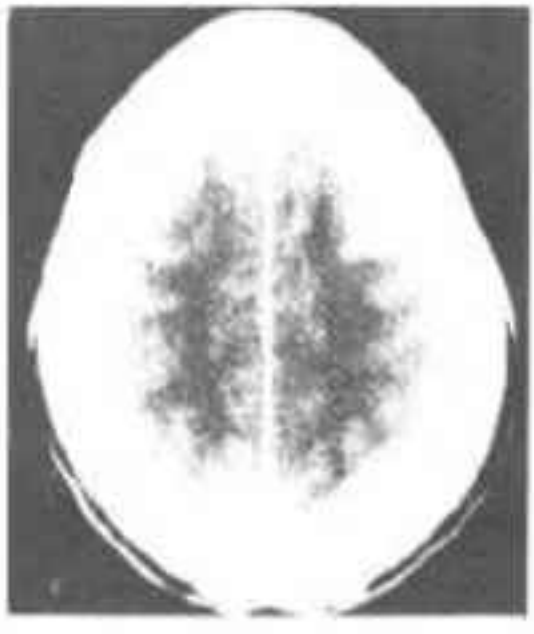
Dilated Lateral and 3rd Ventricles



Shifted 4th Ventricle



Dilated Temporal Horns



Loss of Cortical Sulci

It's difficult to spot lesions around the pituitary fossa and cavernous sinus because masses there do not usually cause major structural shifts, and the region itself is already filled with prominent bony structures that camouflage adjacent lesions. Coronal slices are a great help in assessing the suprasellar space and neighboring cavernous sinus.[41]

Subarachnoid Hemorrhage: Blood accumulates in certain characteristic places: in the occipital horns and along the interhemispheric fissure. Look in the occipital horns for a subtle fluid level*, and after IV contrast, check along the falx for enhancement dipping into the sulci.[42]

Infection: Look carefully at each temporal lobe for a low density mass to suggest herpes simplex encephalitis; is one lateral ventricle flattened along its lateral border? Subdural empyemas often collect alongside the falx* in the parieto-occipital region (because the patient lies supine for his CAT scan).[43] Look for a low density sliver along one side of the falx, and then recheck the sinuses (especially the frontal sinuses) for any cloudiness to suggest a source of infection.[45]



Collection of Pus Alongside the Falx

Sensitivity of the CAT scan notwithstanding, the single most important factor that allows accurate and relevant CAT scan interpretation is your knowledge of the patient's history and neurologic findings. Knowing where to look on the CAT scan and how to weave the CAT scan findings into the clinical picture frequently allows you to abandon traditional arithmetic—one plus one may indeed equal three. That is, a subtle abnormality on neurologic exam (which you might otherwise wrinkle your nose at) plus a subtle abnormality in the corresponding area of the CAT scan, an abnormality you might normally pass off as artifact, suddenly summate into major significance.

Fluid Level: Blood, being heavier than CSF, layers out like a tablespoon of water in a glassful of cooking oil.

Alongside the Falx: Subdural empyemas (or subdural hematomas) alongside the falx, by injuring the medial aspects of the motor strip, produce a hemiparesis resembling that of anterior cerebral artery ischemia: worse in the leg.[43]

CONFUSION

IT'S COMMON TO MISTAKE WERNICKE'S APHASIA FOR CONFUSION. Try to establish if the patient understands the spoken word by his response to simple commands, and when he speaks, listen for spelling or grammatical mistakes. In any confused or stuporous patient the single most important neurologic question is, "Do you have a headache?" An affirmative nod suggests something in the head that doesn't belong there. Confusion accompanied by a headache (without fever or stiff neck) demands a CAT scan regardless of any other neurologic signs.

Confusion, headache, and unexplained fever, with or without a seizure, is meningitis, herpes simplex encephalitis, or rarely subdural empyema until proven otherwise. If you find any suggestion of meningismus, carefully inspect the patient's scalp for a puncture wound, and look at the posterior neck and back for a midline dimple suggesting a congenital sinus tract through which bacteria may have gained entry into the CSF.

A key CSF finding for herpes encephalitis (besides the white cells) is red cells,[1] but even without them, confusion, headache, fever, and especially seizures should keep herpes encephalitis on the front burner.[2] Until better tests for herpes encephalitis arrive, you have to commit yourself to early, presumptive therapy, because delaying therapy seriously jeopardizes recovery.[3] If a confused, febrile patient has bland spinal fluid, look for another source of infection, the confusion simply being a sign of sepsis*.

Don't overlook hypoglycemia, myocardial infarction, hypoxia, or even non-convulsive status epilepticus* as other Distant Domino etiologies of confusion. In children, increased intracranial pressure from lead intoxication or Reye's syndrome can cause acute delirium. Finally, assume that all psychotic patients—especially patients who've just recently begun to act psychotic—are suffering from an organic etiology until you know for sure that organic etiologies have been ruled out*.

Sepsis: Or you may need to relap the patient in 8-24 hours, having missed the developing CNS infection.

Non-Convulsive Status Epilepticus: The two best examples are complex partial partial status (continous temporal lobe seizures)[4] and absence status (petit mal status)[5]

Been Ruled Out: In chronically psychotic paticats without focal neurologic findings, the likelihood that a CAT scan will demonstrate significant pathology is slim.[6]

SEIZURES

PATIENTS ARE FREQUENTLY BROUGHT to the emergency room following a 'spell,' with or without loss of consciousness. Though seizures are certainly one cause of spells, there are many things besides seizures that come and go in the nervous system:

	Neuromuscular	Vascular	Hematologic	Coverings & Connective Tissue
Drugs:	Almost any drug			
Infection:	Viral encephalitis			Viral meningitis
Genetic/ Degenerative:				
Immunologic:	Multiple sclerosis Postinfectious demyelination Postvaccination demyelination Guillain Barre Myasthenia gravis	Temporal arteritis		
Tumor:	Malignant brain tumor*		Polycythemia vera	Meningioma
Trauma:				
Mechanical:	Chronic subdural† 3rd ventricular colloid cyst Arnold Chiari*	Hypersensitive carotid sinus		
Organ Dysfunction:				
Systemic:	Hypotension orthostatic vasovagal Acute hypertension			
Skin:				
Neuro:	Seizure Narcolepsy Cataplexy			
Eyes:				
Ears:	Vestibular disturbance			

Brain Tumor: Both benign and malignant brain tumors may rarely present as transient ischemic attacks, presumably by transiently impairing the vascular supply of nearby brain tissue.[1]

Arnold Chiari: The cause of cough syncope, though unknown, is probably related to the fact that any rise in intracranial pressure must be dissipated throughout the subarachnoid spaces, or else potentially dangerous pressure gradients can develop. In Arnold Chiari, the cerebellar tonsils wedged into the foramen magnum prevent free and easy access into the subarachnoid spaces surrounding the brain and spinal cord. Sudden increases in intracranial pressure accompanying exercise or coughing may therefore cause sudden loss of consciousness.[2]

Endocrine:	Hypoglycemia
	Hypercalcemia
Respiratory:	Hypoxia
	Cough syncope[2]
Cardiac:[3]	Arrhythmia
	Sinus bradycardia
	Congestive heart failure
	Myocardial infarction
	Aortic stenosis
	Atrial myxoma
	Idiopathic hypertrophic subaortic stenosis
GI:	Hepatic failure
RE:	
Urologic:	Renal failure
	Periodic paralysis
	Micturition syncope*
Genital:	
Vascular:	Basilar artery migraine[7]
	Basilar artery TIA
	Carotid artery TIA
	Recurrent pulmonary emboli[8]
Hematologic:	Hyperviscosity
Bone:	
Coverings:	

By history, spells are probably not seizures if:

(a)* The spells are not stereotyped. The patient should not faint on one occasion, convulsively shake on another, and smack his lips on another.

(b)* There is a gradual onset of the spell, enough time for him to sit down, take his medicine, or see the floor coming up at him. (Ask if anyone thought he was pale, i.e., hypotensive.)

(c)* The spells are abortable or delayable by some tactic.

Micturition Syncope: While urinating, some men develop excessive vagal tone that slows the heart and reduces peripheral vascular resistance, both of which drop the blood pressure.[1] Solution: sit down to urinate.

(a): Since most patients have only a single cerebral focus, the vast majority of focal seizures should follow the same pattern. Occasionally a patient with focal seizures and secondary generalization will skip the focal part and experience a generalized seizure from the onset. Only rarely will a patient have two or more types of focal seizures. Automatisms, however, can vary considerably from seizure to seizure.[9] The converse—that stereotyped spells represent true seizures—is not always reliable.[10]

(b): Some people can tell they are going to have a seizure that day by a feeling of unwell. But once a seizure begins, the discharging brain and the patient are too preoccupied with each other to allow a relaxed stroll to the medicine chest or couch.

(c): Some rare patients can stop a focal seizure by intense concentration or by grabbing the jerking hand, actually preventing secondary generalization. This is a bona fide phenomenon, though the inhibitory physiology is not well understood.

(d)* The spells consist of pure syncope (without tonic-clonic convulsive activity).
(e)* The spells only occur in the standing position, or on standing up from a lying position.
(f)* The patient was conscious during the spell, or can recall events that happened during the spell at a time when the abnormal motor activity involved *both* sides of the body.
(g)* There was purposeful, well-organized, or premeditated behavior during the spell.
(h)* There was no postictal confusion, lethargy, or headache.
(i)* The patient's spells continue unabated despite adequate anticonvulsant medication.
(j)* The EEG is normal during a spell, or immediately afterwards.

There are enough exceptions to these tips to make each one only a guideline, not a firm rule. The simultaneous occurrence of two or more of these, however, markedly raises the improbability of a seizure disorder. Statistical reasoning like this is frequently used in medicine. If X% is the likelihood of event A occurring, and Y% the likelihood of event B (which is completely independent of event A), then the likelihood of both A and B occurring simultaneously in the same patient is their product: $(X) \times (Y)$%.

(d): Pure syncope is almost always due to hypotension, bradycardia, hypoglycemia, or hypoxia.[11] Only rarely will a temporal lobe seizure manifest as pure syncope without automatisms or focal jerking.[12] A purely tonic seizure (stiffness without jerking) doesn't have to be a seizure; rarely, brainstem ischemia produces tonic spasms of the arms and trunk, called 'cerebellar fits.'[13]

(e): Prolonged standing allows blood to pool in the legs instead of returning to the heart. Prolonged lying lulls veins into excessive laxity. When the patient stands up, the veins don't constrict fast enough to prevent pooling in the legs and abdomen, so the patient faints from orthostatic hypotension.

(f): Convulsive jerking on both sides of the body means both hemispheres are seizing and cannot, therefore, maintain consciousness too.[14] Ask the patient what people said about him during the seizure to confirm that he was conscious.

(g): It may take EEG monitoring during the disturbed activity to distinguish truly epileptic from functional behavior. Some patients are legitimately combative during psychomotor seizures, especially if attempts are made to restrain them. Other patients may be confused and combative postictally.

(h): Focal seizures and petit mal seizures may leave a person mentally clear immediately after a seizure, but grand mal convulsions and temporal lobe seizures should always be followed by a postictal state.[15]

(i): Anticonvulsants work. If they make no inroads into a patient's spells despite adequate blood levels, you're probably not treating a seizure disorder.

(j): Any seizure—temporal lobe, grand mal, petit mal—that impairs consciousness should be apparent on the EEG.[16] Grand mal convulsions exhaust the brain (by exhausting neurotransmitters?), so postictally the EEG should be slow and remain slow for 12–24 hours. Between seizures, however, the EEG is frequently normal.

(X) x (Y): This is what makes experienced physicians so uncannily accurate in their diagnoses—they know the likelihood of each individual event and, after statistically combining them, wisely choose the most likely diagnosis.

So, if you estimate that 5% of seizures are unaffected by medication, and that 2% of patients can 'will' a seizure to stop once it's in progress, then the likelihood of both these events occurring in the same patient is 5% x 2% or 1 in 1000, a rather slim statistical likelihood though still conceivable. Add another, unlikely independent event, like a normal EEG right after a spell (which may occur, liberally, 5% of the time), and you're now facing the remote possibility (5% x 2% x 5% = 1/20,000) that these spells represent seizures.

When statistical reasoning makes you skeptical about seizures, it's no crime to withhold treatment. The diagnosis of epilepsy is not the same as a diagnosis of pneumonia; it has many social, emotional, marital, legal, economic, and insurance implications. If you want to try anticonvulsants, consider them a diagnostic test not a treatment. And even if a patient's syncopal spells do respond to anticonvulsants, it doesn't necessarily mean the spells are seizures. All you can really say is that the patient has 'anticonvulsant responsive syncope,' a diagnosis that includes hysterical fainting, syncope from cardiac arrhythmias,[17] and even basilar artery migraine*.

Often, it may help to clarify spells of unconsciousness by teaching the patient's spouse how to take the patient's pulse. Then the next time the patient feels a spell coming on, or during the syncopal period itself, the spouse can measure the patient's heart rate and rhythm. Instruct her also to lay the patient down* and check for skin pallor and sweating. And mention that if the patient convulses during the spell, the only necessary acute treatment is to 1) cradle the head to cushion it from hard surfaces, 2) pull the jaw forward to open the airway, and then 3) turn him on his side after the spell to prevent aspiration should he vomit. There is no need to stick anything in the mouth hoping to prevent patients from swallowing or chewing their tongue. Pulling the jaw forward prevents 'swallowing the tongue' (closure of the epiglottis), and the rich vasculature of the tongue insures rapid healing if it's bitten. Besides, a spoon forced into the mouth may chip a tooth.

Acute Seizure Treatment

An acutely seizing patient amidst the glamour of the emergency room is an alarming sight, but remain cool. You need to take your hands out of your pockets, but don't pull any yahoo-cowboy antics. First ask yourself how much time you've got before the patient is dead. If the patient is focally seizing but conscious, the threat of metabolic complications (acidosis, hyperkalemia, hypoglycemia) is mild, so go slow. Be sure the potential complications of your treatment (apnea* and hypotension) won't be more dangerous than an uncomplicated focal seizure. Check the serum osmolarity; a high serum osmolarity is a common cause of focal motor status (epilepsia partialis continua).[18]

Basilar Artery Migraine: Focal basilar artery spasm may cause syncope from ischemia to the midbrain-upper pontine reticular activating system.

Lay the Patient Down: If the blood pressure is falling, laying him down and raising his feet will increase venous return to the heart and raise the blood pressure. If, however, the patient is losing his blood pressure because of acute congestive heart failure, laying him flat to increase his venous return may further weaken the already overloaded heart.

Apnea: No breathing.

A convulsing, unconscious patient does indeed need your uninterrupted attention. After checking his respiratory efforts, pulse, and blood pressure, draw blood for chemistries (electrolytes, BUN, creatinine, glucose, liver function tests, CPK) and anticonvulsant blood levels. Next, administer 50 cc of 50% glucose IV with 100 mg of thiamine, apply an oxygen* face mask, and begin intravenous Dilantin.[21]

Hang a bottle of normal saline* (without glucose*) and begin a 250 mg ampule* of Dilantin IV by soluset* at no more than 50 mg/min, and preferably 25 mg/min (250 mg over 10–15 minutes).[23] Repeat the 250 mg of Dilantin three more times (total of 1 gram) to 'load*' the patient. Keep a close eye on his blood pressure and check his pulse (or heart monitor*) for arrhythmias.[24] Slow or stop the Dilantin if his blood pressure begins to fall or the arrhythmia looks potentially serious (PVC's, A-V block, brief runs of ventricular tachycardia).

Oxygen: The oxygen is not for the brain because a convulsing brain produces lactic acid, extracellular potassium, and other vasodilating metabolites. The resulting five-fold increase in cerebral blood flow more than makes up for the systemic hypoxia produced by impaired respirations. (A debate remains, however, whether the continuously discharging brain is capable of using the extra oxygen, and whether an increase in oxygen delivery can prevent damage to continuously hypermetabolic neurons and glia.[3])

Regardless, the additional oxygen you administer is a welcome relief to hypoxic internal organs, especially the heart which is already facing the prospect of life-threatening arrhythmias from other dangerous developments: hypotension, hyperthermia, tachycardia, congestive heart failure, hypoglycemia, hyperkalemia, and the adverse side effects of drugs administered to control the seizure.[25]

Normal Saline: The salt (saline) concentration in the IV solution is the same ("normal") as the body: 0.9mg%. Intravenous salt keeps fluid in the vascular tree, fluid which would otherwise be osmotically drawn into the body's cells by their higher salt and protein concentration. Hypotonic fluids (0.5 or 0.25 normal saline) exacerbate cerebral edema by allowing water to enter the already swollen brain. The danger of normal saline, of course, is overloading the vascular tree and throwing the patient into acute congestive heart failure.

Without Glucose: Dissolved glucose releases a hydrogen ion that makes the IV solution slightly acidic. Dilantin is very alkaline and when mixed with the acidic glucose solution, precipitates. Though Dilantin crystals may redissolve in the bloodstream, it's always better to administer a solution rather than a suspension of crystals.

Ampule: A small vial with a snap-off neck containing a sterile solution (or dry crystals) of a drug, electrolyte, glucose, whatever.

Soluset: A 100cc reservoir hung below the IV bottle to allow more accurate administration of fluids. Some doctors inject Dilantin directly into the IV line ("IV push") to avoid any possible precipitation of Dilantin in the soluset and to shorten the time of Dilantin loading. It's okay to administer Dilantin this way, but you'll probably end up giving it faster than 50 mg/min (and causing hypotension); besides, your attention is needed elsewhere to solve other immediate problems.

Load: Dilantin attaches itself to Dilantin receptors throughout every organ of the body including serum albumin. To get enough Dilantin into the brain, you first have to load up these noncerebral receptors with about 1000–1500 mg of Dilantin (15–20 mg of Dilantin per kg of body weight).

If the patient is already taking Dilantin, be a little more conservative with your Dilantin therapy. Acute, severe Dilantin intoxication may cause permanent cerebellar injury.[22] If you're not sure whether the patient has been taking Dilantin and he has stopped seizing, slow down the IV until the lab reports the blood Dilantin level (one of the emergency blood tests you drew when the patient first arrived).

Monitor: Wires attached to the patient's chest monitor the heart for bradycardia, tachycardia, and arrhythmias.

If the seizure continues for more than three or four minutes, or if the patient has several seizures in the emergency room without awakening between them, intubate.[25] Intubate early because, besides seizing, the following problems are gathering force: dehydration, hypoxia (from apnea, aspiration, or neurogenic pulmonary edema), hypertension or hypotension, hyperthermia, acidosis (which exaggerates the toxic effects of Dilantin and Valium on the heart), arrhythmias, congestive heart failure, hypoglycemia, hyperkalemia, and myoglobinuria*.[28]

While Dilantin is infusing, you can usually control any ongoing seizures with a short-acting anticonvulsant like Valium or pentobarbital. For Valium, give only 2–3 mg per minute for several minutes. Do not give higher doses of Valium until you can be reasonably confident that the patient's blood pressure is not falling.[29] Besides, you may only need small doses of Valium to control the seizures.

Valium is not always the drug of choice for status epilepticus for the following reason. If Valium works, fine, but if Valium and Dilantin fail to control status epilepticus and you decide to add phenobarbital, the combination of Valium and phenobarbital is very likely to cause hypotension. If you do want to use Valium, give 2–3 mg boluses every minute with the Dilantin (preferably through another venipuncture site) until you control the ongoing seizures. Do not use larger doses of Valium until it is clear that 2–3 mg is inadequate. Valium is dynamite and even without phenobarbital can produce hypotension and apnea just when you think you are in control of the seizures.[31]

Valium should never be the mainstay of treatment for status because Valium is too short-acting to have any lasting effect on seizures[31] Getting Dilantin on board is far more therapeutic in the long run than trying to stamp out individual seizures with Valium. If the patient fully awakens between seizures, you may even try to avoid Valium altogether because the risk of an occasional seizure during Dilantin loading is probably less than attempts to suppress them acutely with overly enthusiastic doses of Valium.

Myoglobinuria: After 15–30 minutes, continuously seizing muscles begin leaking myoglobin, the muscle protein which binds oxygen.[26] Intravascular myoglobin precipitates in the kidney tubules, obstructing them, and so causing renal failure. To prevent this, check the urine for myoglobin and treat any myoglobinuria with vigorous IV fluids to flush the kidneys.

At times it may be difficult to decide if the elevated serum CPK signifies a myocardial infarction or continuously seizing muscles.[27]

If seizures persist despite 1 gram of Dilantin, give another 250–500 mg IV. If they still persist, begin IV phenobarbital* (you've intubated him, right?). It's not clear how much phenobarbital is necessary for loading, but begin with 250–300 mg and then give a 130 mg ampule after each seizure. If a gram of phenobarbital won't stop the seizures (plus the 1500 mg of Dilantin given previously), you and the patient are in trouble. Ship him to intensive care where other drugs can be tried like lorazepam (2 mg IV),[32] pentobarbital[33] (130mg IV Q* seizure, or 130mg Q1–3H*), paraldehyde* (begin a 5% solution at 10 cc/hr and titrate* to seizure control),[34] Valium drip (10 mg/hr),[35] or lidocaine 1–2 mg/min IV.[36]

Somewhere amidst all this throat-clutching excitement you need to find out why the patient began to seize. For example, if he's febrile, tap him (unless there are signs of increased intracranial pressure or posterior fossa mass effect); don't be too willing to attribute the patient's fever to uncontrolled muscular contractions during the convulsions.[37] You probably don't need an emergency CAT scan if he is a known seizure patient (particularly a non-compliant* one) or a known alcoholic on a recent binge*, there are no signs of head trauma, the patient is waking up, and the exam is normal (other than the postictal stupor).[39]

Phenobarbital: In 1864, von Baeyer synthesized the first barbiturate from urea and named it after someone named Barbara (Barbara + urea).

Q: Means 'every.' 'PRN seizure' would mean as needed for each seizure, to be given at the discretion of the nurse.

Q1–3H: Every one to three hours.

Paraldehyde: Some physicians don't like paraldehyde because it dissolves plastic, but changing the IV tubing every eight hours seems to prevent this complication. You also have to wrap the bottle and IV tubing in aluminium foil because light breaks down paraldehyde into toxic metabolites.

Titrate: Begin with a low dose and slowly increase until the desired effect is obtained.

Non-compliant: Doesn't take his medicines.

Recent Binge: Alcohol withdrawal seizures begin 6–48 hours after the patient stops drinking. The seizures are relatively brief, never focal, and usually terminate within 6–8 hours. The patient should awaken between his seizures and have no focal signs (at least no new ones).[38]

WEAKNESS

WEAKNESS COMES IN FOUR MAJOR PATTERNS: cranial nerve weakness; diffuse weakness; hemiparesis; and paraparesis.

Cranial Nerve Weakness Without Sensory Loss

Cranial nerve weakness causes ophthalmoplegia, ptosis, unreactive pupils, difficulty chewing, facial weakness (including eye closure), dysarthria, dysphagia, difficulty keeping the head erect (neck muscles), and weakness of the tongue. The first step, anatomy, is relatively uncomplicated. Without long tract signs or brainstem eye signs (skew deviation, internuclear ophthalmoplegia, gaze palsy, coarse nystagmus, upbeat or downbeat nystagmus), the lesion causing one or more motor cranial neuropathies is almost certainly outside the brainstem. And pure motor signs predominantly above the neck strongly suggest neuromuscular junction.

Etiologically, if the patient's pupils are fixed to light, and you also find other motor (but no sensory) cranial nerve signs, botulism is the first, second, and third choice*.[1] Send someone to retrieve any suspicious food, and be sure to check for a wound that may have become contaminated with Clostridia botulinum. Watch for early respiratory paralysis, and if you're sure of the diagnosis (by exposure history, clinical presentation, injection of mice*, or demonstration of a neuromuscular block on repetitive nerve stimulation*), give polyvalent vaccine*.

If the pupils do react, and the motor cranial nerve signs have been fluctuating (better after a night's rest), suspect myasthenia gravis. Go ahead and do a Tensilon test if the patient has unequivocal weakness*, like ptosis, ophthalmoplegia, or dysarthria.

Third Choice: The fourth choice would be the Fisher variant of Guillain Barre. Botulism is more dangerous because it is more likely to progress to respiratory failure. Also, by thinking of botulism early, you may prevent someone else from eating the contaminated food.

Injection of Mice: Mice are particularly sensitive to botulinus toxin.

Repetitive Nerve Stimulation: By recording from electrodes taped over the belly of a muscle, you can display on an oscilloscope the muscle's response to peripheral nerve stimulation. If you demonstrate no (or markedly reduced) response to peripheral nerve stimulation, then the electrical block must be somewhere between the point of stimulation and the muscle. Directly stimulating the muscle will tell you if the muscle itself is paralyzed. Repetitive nerve stimulation will demonstrate neuromuscular blockade—see chapter 44.

Polyvalent Vaccine: Polyvalent vaccine is serum containing a high concentration of antibodies directed against the three types of human botulinus toxin (A, B, and E). Unfortunately, the antibodies only attach themselves to free botulinus toxin, not the toxin already bound to neuromuscular junctions.[2] Nevertheless, the vaccine probably prevents any free toxin from attaching to newly synthesized neuromuscular junctions.

Unequivocal Weakness: Unless the weakness is clear to begin with, it's easy to overcall a 'positive' Tensilon test. For example, depressed patients looking for an organic explanation of their fatigue may improve with Tensilon. Don't be in a rush to make the diagnosis of myasthenia in patients who complain of weakness below the shoulders. Use electromyography (chapter 44) and serum antibody titers against the neuromuscular junction for more objective evidence of myasthenia.[3]

The Tensilon test is performed in two steps: first administer 2mg of Tensilon IV and wait. Sometimes only 2mg is necessary to get improvement and 10mg may be too much. This happens when the patient has too few post-synaptic receptors left. An initial bolus of 10mg may flood such a neuromuscular junction with so much acetylcholine that the post-synaptic membrane can't recover a full electrical potential before more acetylcholine discharges it again. The result is acute paralysis, potentially jeopardizing the respiratory muscles.

The other reason to give 2mg at first is to check for the most serious side effect of Tensilon—bradycardia, or worse, asystole* (other side effects include abdominal cramping, nausea, and excessive salivation). To avoid these side effects, it's advisable to mix a .4mg ampule of atropine with the 10mg of Tensilon, and to administer the two simultaneously as a single solution, still the 2mg first and then—if there's no improvement—the remaining 8mg.

If the patient is a known myasthenic on Mestinon, and complains of shortness of breath, get blood gases and a vital capacity*. If you have any concern, have anesthesia intubate without doing a 'Tensilon test*. 'Tensilon may push a weak patient into acute respiratory failure.[4] Once in the ICU, you can either withdraw the Mestinon and retitrate to the proper dosage, or else try steroids while treating the likely infection (pneumonia, bronchitis) that precipitated the patient's acute respiratory weakness.

Wernicke's is another readily treatable cause of external ophthalmoplegia (i.e., the pupils are unaffected).[5] The eye signs are always bilateral (not necessarily symmetrical), and can be as subtle as bilateral ptosis or nystagmus alone. Long tract signs are usually absent, so unless the eye signs are characteristic brainstem ones, it's easy to overlook a brainstem site. Moreover, it's easy to miss ptosis or nystagmus in a confused, ataxic alcoholic, so give thiamine liberally to all suspected alcoholics.

Don't forget that ophthalmoplegia amidst the constellation of stupor, headache, vomiting, ataxia, and dysarthria—without hemiplegia—could well be a cerebellar hemorrhage. Get a CAT scan and bring this patient to the attention of the neurosurgeons early.

Asystole: No heart beats. Acetylcholine released by the vagus nerve suppresses the SA node and also prevents the AV node from kicking in to take over from the paralyzed SA node.

There are two types of acetylcholine receptors—ones stimulated by muscarine and others by nicotine. Muscarinic receptors are found in the exocrine glands and also on smooth muscle in the iris, lungs, heart, GI tract, bladder, uterus, etc. Muscarinic stimulation produces bradycardia, salivation, lacrimation, urination, defecation, and intestinal cramping.

Nicotinic receptors are the neuromuscular receptors on skeletal muscle. Tensilon stimulates *both* muscarinic and nicotinic receptors. Atropine blocks only muscarinic receptors, and curare blocks only the nicotinic ones.

Vital Capacity: The number of cc's of air a patient can blow out after taking a deep breath. You and I generate 3.5 to 4.5 liters. Concern rises as the vital capacity nears 1 liter. Intubation and respiratory support are usually required below about 600 cc.

Tensilon Test: The Tensilon test is also administered prior to the next Mestinon dose to adjust the dose of Mestinon. If Tensilon improves a patient's weakness (or his vital capacity), Mestinon is increased. If the patient's strength remains unaffected or worsens with Tensilon, then Mestinon is reduced.

Widespread Symmetrical Weakness[6]

The most common sites for diffuse weakness are peripheral—in the nerve or muscle. Two of the most dangerous diseases causing acutely developing, diffuse weakness are hypokalemia (less than 3.0 meq/L) and early Guillain Barre*. If the reflexes are absent, or hypoactive out of proportion to the weakness (suggesting a polyneuropathy), make a presumptive diagnosis of Guillain Barre. Check the vital capacity and strongly consider admitting the patient to the ICU for close observation during the next 24–48 hours to gauge the pace of progressing weakness.

A fortunately uncommon site for acute, diffuse weakness is bilateral corticospinal tracts—quadriplegia. This is when the Babinski sign is a real help in distinguishing central from peripheral weakness. During the first week, the muscles will not have had enough time to atrophy, and in *acute* corticospinal lesions, the tone is flaccid and the reflexes absent, a condition called spinal shock.

In trauma patients, you can easily miss the quadriplegia if the patient is comatose. Feel the spinous processes, sandbag the head, and *before* doing a CAT can of the head, get an emergency set of cervical spine films, being sure to pull the shoulders down far enough to obtain a good x-ray view of the C7 vertebral body. If the patient is awake with weak or paralyzed limbs, be sure that the apparently complete spinal cord transection isn't, in reality, the anterior spinal artery syndrome or the central cord syndrome.



Note the Large Gap Between the Dens and Anterior Arch of C1

Guillain Barre: Guillain Barre probably begins proximally in the nerve roots with inflammatory demyelination (polyradiculitis) that blocks electrical transmission. The demyelination quickly spreads centripetally into the peripheral nerves (either that or, as apparently happens in some patients, the peripheral demyelination begins simultaneously with the proximal root demyelination).[7] Typically, the resulting weakness (and loss of reflexes) begins distally at the feet and, over hours to days, spreads into the legs, arms, respiratory muscles, and face, usually sparing the eyes and eyelids.[8] Unlike most other polyneuropathies, the weakness in Guillain Barre may be as bad (or worse) in proximal muscles as in distal ones.

Transient Hemiparesis

Transient episodes of hemiparesis almost always represent transient ischemia. Because the patient's next spell may be a permanent hemiparesis, you need to define his vascular anatomy as soon as possible. If the common carotid bifurcation is more than about 60% stenotic (with or without endothelial ulceration*), the bifurcation needs surgical repair, because a symptomatic patient like this faces the significant risk of a subsequent stroke*.[12]

A flurry of TIA's, especially if the patient doesn't return to baseline between attacks, requires urgent attention; the patient is likely on the verge of occluding the internal carotid artery or flipping a large clot distally into the intracerebral circulation.[13] Similarly, TIA's precipitated by hypotension suggest that a focal area of brain is critically dependent on an adequate blood pressure, i.e., that the collateral flow to that area is poor. The anatomy of the cerebral circulation should probably be defined with angiography* to locate the critically stenosed artery.[15]

Persistent Hemiparesis

An acute persistent hemiparesis is usually due to an atherosclerotic stroke; once in a while it'll represent postictal Todd's paralysis*, subdural hematoma, brain tumor, meningitis, hypoglycemia, or even a focal seizure.[14] Stroke therapy varies consider-

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Endothelial Ulceration: Ulceration of the arterial endothelium exposes the underlying collagen to the bloodstream. Platelets and clot adhere to this exposed collagen, forming rich sources of emboli. Tight stenosis of one internal carotid artery, with or without ulceration, may also become symptomatic if collateral flow from the opposite carotid is inadequate.

Subsequent Stroke: Ulceration without stenosis may not need an endarterectomy (surgical removal of the ulcer) to prevent a second stroke. Aspirin, which thins the blood by preventing platelets from aggregating at the ulcerative site, might impair platelet adhesion long enough for the endothelium to re-cover the ulcer.[8] In fact, a combined regimen of aspirin and antihypertensives might stand up surprisingly well to endarterectomy in a prospective study (patients would be randomly assigned to surgical or medical therapy). Should the internal carotid artery stenose on aspirin and antihypertensive therapy, surgery could still be done before complete occlusion occurs. (Whether to step in before complete occlusion occurs is still being debated because most people tolerate internal carotid occlusion surprisingly well.[9]) The decision to operate before complete occlusion occurs should also take into account that thrombotic occlusion at the carotid bifurcation will usually propagate up to the next major arterial branch, the ophthalmic artery, well beyond the reach of surgical repair.[11]

Angiography: Injection of dye into a blood vessel to demonstrate the anatomy of the vessels downstream. Angiography was developed by the Portuguese genius, Edgar Moniz, who also: pioneered prefrontal lobotomies; served as ambassador, Minister of Foreign Affairs, and President of the Portuguese delegation to the Paris Peace Conference in 1918; wrote an operetta; taught mathematics; and authored a history of playing cards and a biography of Pope John XXI. In 1951, he declined the offer to serve as President of Portugal.[16]

Todd's Paralysis: Self limited (hours to days), focal weakness (usually hemiparesis, occasionally aphasia or homonymous hemianopia) following a seizure.[7] Todd's paralysis represents a previous, static lesion made symptomatically worse for a while by the seizure (for unclear reasons).[7]

ably around the country because there is, as yet, no one accepted approach. The major thrust of stroke therapy, however, is to prevent a mild hemiparesis from progressing during the first week into a complete hemiplegia*.

Three illnesses, polycythemia, thrombocytosis, and temporal arteritis—each capable of sudden worsening and each readily treatable*—should be ruled out as soon as possible with a stat* CBC, platelet count, and sed rate. The CAT scan will rule out other illnesses which mimic an ischemic stroke, like an intracerebral hemorrhage*,[22] subdural or epidural hematoma, arteriovenous malformation, or brain tumor. An LP will rule out other treatable causes of stroke: subarachnoid hemorrhage, syphilis, and cryptococcal meningitis.

If all these tests are normal (and they usually are), what do you do with an ischemic infarction that leaves much of the hemisphere (or posterior fossa) still intact? You want to prevent the patient from worsening, but there is no way to predict which patients will progress. Most physicians wait until the patient does begin to progress before instituting treatment, but unfortunately, patients do not gradually progress—they jump from mild hemiparesis to complete hemiplegia before effective therapy can be started*.

Complete Hemiplegia: A *complete* stroke means the weakness is a total hemiplegia, while a *completed* stroke means the hemiparesis has become stable regardless of the amount of weakness. An incomplete stroke means the patient is conscious with only a mild to moderate hemiparesis (or other neurologic deficit).

Why patients with mild to moderate hemiparesis progress to complete hemiplegia is still unknown. What does seem clear is that only neurons in the center of an infarction are dead; surrounding the bull's eye is a ring of dazed and reeling neurons ready to fight again if given enough time (? hours) and nutrients to recover.[19] Your job is protect, and hopefully improve, the collateral circulation to those neurons.

Readily Treatable: Removing a unit of polycythemic blood and replacing it with normal saline will lower the hematocrit and improve the patient's cerebral blood flow and oxygen delivery.[20] Chemotherapy will probably be necessary to slow the production of platelets in the bone marrow.[21] Steroids should halt temporal arteritis.

Stat: Immediate.

Intracerebral hemorrhage: Intracerebral hemorrhages often recover more function than ischemic strokes, because hemorrhages dissect along tissue planes *between* major structures. Infarctions, instead of pushing structures aside, destroy them.[22]

Be Started: What you *don't* want to do in acute strokes is to rapidly lower an elevated blood pressure, because blood vessels around a recent stroke lose their ability to autoregulate—to dilate when the blood pressure falls, thereby keeping the cerebral blood flow constant. If you drop the blood pressure too fast, blood flow to the injured area around the stroke will also drop, extending the stroke into injured but potentially recoverable areas around the infarction.[24] On the other hand, lowering the blood pressure in someone with mild congestive heart failure may improve the cardiac output, and with it, the cerebral circulation.

One approach to this dilemma, an approach adopted by the University of Alabama and others[25], is to anticoagulate small ischemic strokes (with heparin) while gradually lowering the blood pressure. (Heparin is a naturally occuring anticoagulant synthesized in the liver and lungs.)

Other approaches include calcium channel blockers,[26] naloxone,[27] volume expanders (to improve the collateral circulation),[28] prostacyclins,[23], and perhaps plasminogen activators.

If the patient doesn't progress, or improves, during the first week, he still faces a small but significant risk of another, more serious stroke within the next five years.[30] The doctor's role in altering the natural history of this disease is to treat the patient's hypertension (the most important risk factor for strokes), and to find a source of emboli or a narrowed artery that might have caused the mild stroke. The most common embolic source is an ulcerative plaque at the carotid bifurcation where enough plaque can accumulate to narrow the internal carotid artery.

Carotid angiography will demonstrate carotid ulceration and stenosis, but *when* to perform the angiogram (and endarterectomy) after a stroke is still debatable*.[31] The presence of a carotid bruit, signifying probable stenosis of the carotid artery, generally moves the date of angiography forward, so listen carefully for a carotid bruit (and orbital bruit[32]) in every stroke patient. The bruit does not have to be over the carotid ipsilateral to the infarcted hemisphere. Sometimes the ipsilateral carotid may be so tightly stenosed that the contralateral carotid must assume responsibility for blood flow to both hemispheres. The excess blood flow up the contralateral carotid produces a bruit in that carotid artery. So, really, a bruit in either carotid moves the date of angiography forward.

To be sure the bruit is coming from the carotid bifurcation and not the heart, listen specifically for a high pitched bruit which gets louder as you move the stethoscope north. Transmitted bruits from the heart become louder as you inch the stethoscope toward the base of the neck, and can often be traced right to the aortic area (aortic stenosis). Transmitted bruits should also be audible in both carotids. And check that the bruit is not coming from the external carotid; see if you can diminish the intensity of the bruit by compressing the superficial temporal and facial arteries, reducing flow through the external carotid artery.[33]

Paraparesis

Acute and subacute spinal cord or cauda equina lesions are among the most catastrophic in medicine. The one condition causing acute or subacute paraparesis which you absolutely cannot, must not miss is the spinal epidural abscess. Be sure to check for fever and for focal spine tenderness to fist thumping. Look for a sensory level which will tell you, the neurosurgeon, and the radiologist where to concentrate your attention on the upcoming emergency myelogram. Get plain spine films while waiting for the neurosurgeon, but do not do an LP in the emergency room; it can ruin the upcoming myelogram if spinal fluid leaks into the subdural or epidural space. When the radiologist repeats the lumbar puncture, instead of injecting dye into the subarachnoid space, he may mistakenly inject into a puddle of CSF within the subdural or epidural space.

At the myelogram, inject 2cc of dye and check for a block. If there is no block, inject another 10cc and complete the myelogram. If there is a block, watch out for sudden worsening after the myelogram. By removing CSF from below, you've created a pressure and volume gradient which may dislodge the mass and convert a paraparesis into a paraplegia.

Still Debatable: One way to reduce the risk of stroke from arteriography is to limit the number of arteries injected. Inject the symptomatic artery first and if the artery is normal, go home.

PAIN

Pain In General

IN ASSESSING PAIN THE FIRST STEP, as always, is to localize the organ system that hurts. Find out exactly what the patient was doing when the pain began, where the pain was maximal, where it radiated, how long it took to crescendo, how long it lasted, its quality, any exacerbating or ameliorating factors, the pain's pattern of recurrence, and its response to medications. On exam, search thoroughly for the source of the pain. Don't be afraid to palpate deeply, or thump hard with the heel of your fist, or bend a few joints—patients won't break. To keep your interest up, assume the pain is potentially life-threatening—cancer, osteomyelitis, aortic dissection, angina, or occult gallstones.

If you find no localizing signs on exam, you face a difficult clinical problem: being a symptom, not a sign, pain is nearly impossible to verify. When a patient says he hurts, who's to say he doesn't? As long as governments and insurance companies continue to compensate patients (and their doctors) for symptoms without signs, the problem will always be with us. The best you can do is seek signs to corroborate the patient's complaints. But even then, a negative exam does not automatically mean the patient is being paid to hurt. The absence of proof is not a proof of absence. So how far should your laboratory investigation go? There are no good guidelines, but in general, the more recent the pain and the more the patient seems genuinely bothered by it, the more you should pursue it, at least to rule out the dangerous diagnoses like cancer and infection.

Only after a negative exam and negative laboratory investigation, when you're satisfied that you can't find the source of the pain, is it safe to focus on psychological causes. Why does the patient need his chronic pain—to resolve conflicts over dependency or anger? to manipulate loved ones? to take some time off work? You can try probing these areas, but unfortunately, many (and probably most) patients simply won't accept psychological explanations for their chronic pain, especially if they need the pain.[1] Patients who need their pain simply don't want anyone poking holes in their psychic defenses.

Many doctors work their way out of this impasse by attributing the patient's chronic pain and associated symptoms to an organic diagnosis, like migraine, mitral valve prolapse, pinched nerve, arthritis, etc. An organic diagnosis gives psychologically resistant patients a face-saving way out of their chronic pain—if they want one. If they don't, the best you can do is help the patient develop ways of adapting to his pain while you probe for fertile areas of emotional conflict.[2] Many doctors disagree with this approach, arguing that it's unhealthy to "legitimize" a functional disease by giving it an organic label (instead of making the patient solve his emotional conflict).

Successful pain therapy is often patterned after a chiropractic approach: 1) I believe you—that you're having pain and that it's as severe as you say it is ("*Finally* someone believes me"). 2) I understand the cause of your pain. And 3) I'm going to give you

something that will stop the pain by getting at the *cause* of the pain*. Your own enthusiasm and confidence will hopefully infect the patient with an optimistic attitude. Once the patient has realistic hopes that your therapy will help, your medications have a much better chance of success, particularly if he falls into that third of the population of placebo* responders who respond to any medication, just as long as it's medicine.[3]

In patients with clear, temporary, organic reasons for pain (post-surgical, post-traumatic, terminal cancer), don't hold back analgesics. You're a doctor and doctors relieve pain, period—whatever it takes.[4] Don't worry about addiction. They may have some withdrawal symptoms when you stop the medicine (so taper the medicine or add methadone[5]), but addiction: unlikely.[6]

Be a lot more judicious using narcotics with *chronic* pain. Love, money, and depression usually complicate chronic pain at some point. Narcotics will only further complicate the picture. You may not stamp out all the patient's discomfort, but take solace: pain never hurt nobody. As long as you keep an open mind that you may have overlooked a potentially dangerous source of the pain, work with the patient on non-narcotic solutions. If these attempts fail and push comes to shove, narcotics used judiciously may be a helpful supplement to non-narcotic therapy.

E.F. Hutton Headaches

Headaches may herald, often by days or weeks, life-threatening pathology. Elderly people with recent headaches are particularly bothersome. It's not uncommon to get a story that Grandma, in retrospect, did begin to complain about headaches a week or two prior to her stroke*. In any old person with recent headaches, always seek symptoms suggestive of TIA's: episodes of monocular blindness, difficulty speaking, hand incoordination, hemiparesis, gait disturbances, or diplopia. At the very least, any old person with bad headaches needs his superficial temporal arteries palpated and a sedimentation rate to rule out temporal arteritis*.

Eyebrow raising headaches awaken the patient during the night or are worst on awakening in the morning, suggesting increased intracranial pressure.[9] Sleep apnea is an overlooked cause of morning headaches. An occipital (not just posterior cervical) headache is also frequently ominous: check carefully for fever, meningismus, and posterior fossa signs. Even more ominous is headache and lethargy, even without a hemiparesis, aphasia, or ophthalmoplegia; there are lots of clinically silent areas in the cerebral hemispheres for tumors and subdurals to hide out. Fever and a headache suggest meningitis or acute sinusitis. One of these days you may be fooled by acute glaucoma: severe pain over the eye and forehead with an injected conjunctiva, a sluggishly reactive pupil, and a mildly edematous cornea.[10] And someday you may stumble across a patient suffering recurrent bouts of sudden headache, hypertension, tachycardia, and facial flushing, all from a pheochromocytoma.[11]

Cause of the Pain: It's best not to treat pain with narcotic analgesics alone (milder analgesics, okay). It's more rational and healthier to treat the cause of the pain, be it muscle spasm, inflammation, aberrant signals from a partially injured nerve, depression, etc, and to supplement this therapy with narcotic analgesics only if the pain breaks through.

Placebo: From Latin: I shall please.

Prior to Her Stroke: The exact mechanism of ischemic headaches is debatable,[7] but they may represent painful reflex vasodilation in response to acute cerebral ischemia.

Temporal Arteritis: The sedimentation rate is usually reliable, but occasionally it'll be normal in temporal arteritis.[8]

In the emergency room if you're unsure about the headache and you don't really think a CAT scan is warranted, no one can fault you for doing an LP to rule out a subarachnoid hemorrhage or early meningitis. A simple PA* and lateral skull film may reveal an enlarged pituitary fossa or clouded sinuses (chronic sinusitis).



Normal Sella Turcica



Enlarged Sella Turcica

Migraine

Reassuring aspects of a headache are a history of previous headaches as bad as the present one (especially ones which occur around the menstrual period), visual scintillations*, a normal blood pressure, and no fever, stiff neck, lethargy, confusion, ophthalmoplegia, hemiparesis, or ataxia. Vomiting doesn't help much one way or the other; it may occur with elevated intracranial pressure or migraine.

Chronic headache therapy should begin with simple things first. If she's taking hormones (for birth control or menopausal symptoms), recommend that she stop them. If the patient is hypertensive*, begin him on oral antihypertensives or refer him to hypertension clinic. Only later, when the headaches break through these initial steps, should you begin specific antiheadache therapy.

PA: The xray is taken posterior to anterior (with the patient's forehead against the xray film).

Scintillations: Sparkles or jagged lines, not just black spots ("floaters"). Scintillations are typical (but not pathognomonic) of migraine, especially when the scintillations precede the headache. Instead of scintillations, some patients experience hemiparesis, aphasia, or homonymous hemianopia before the headache. The mechanism for these neurologic signs is presumably ischemia, but it's still not clear if the ischemia is a primary event, or secondary to a primary cortical insult.[12] What *is* clear is that the usually transient neurologic deficit prior to the headache can become permanent.[13] It's still unclear if the pain of migraine results from dilation of the external carotid artery and its branches, or from a pain-inducing chemical that *also* causes vasodilation.[14]

Hypertensive: Though it's said that hypertension does not cause headaches, good headache control is often obtained with antihypertensive medications alone. Besides, controlling his hypertension will probably be the best thing you can do for your patient.

If the patient is neither hypertensive nor taking the pill, I favor treating chronic headaches as migraine (or cluster headaches*) instead of muscle contraction, or tension, headaches. Undoubtedly there *are* patients with tension headaches, but there is no clear-cut way to identify them clinically*.[24] For example, many patients with chronic daily (tension?) headaches give a history of past migraine headaches.[25] Migraine can be precipitated by tension and stress,[26] and—like tension headaches—can also occur on a daily basis.[27] Moreover, it's been repeatedly demonstrated that migraine patients have as much, or more, muscle contraction and tenderness in their scalps as muscle-contraction headache sufferers*.[28] (In fact, it's even been hard to demonstrate that patients with muscle-contraction headaches have any more scalp contraction than normals do![30]) Even the biochemistry of muscle contraction headaches resembles that of migraine.[31]

In other words, migraine is a *clinical* diagnosis, and for my money, the best working definition of migraine is a headache that resolves with migraine medication. Many so-called tension headaches benefit from migraine medication.[32] Besides, the armamentarium for migraine—Cafergot*, propranolol, amitriptyline*, ergonovine, methysergide, phenylzine, papaverine, and cyproheptadine (Periactin),[32] daily aspirin[34] or 4–6 aspirin tablets at the onset of headache, calcium channel blockers,[39] and

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Cluster Headaches: 'Cluster' refers to their temporal profile: after a long period of quiescence, cluster headaches suddenly attack on a daily basis for weeks or months at a time, only to dissipate spontaneously for another few months of painless freedom. Each attack begins with sudden swiftness, often awakening the patient—usually a male—from sound sleep with 30–45 minutes of excruciating periorbital pain. The eye becomes injected and tearful, sometimes with a transient Horner's syndrome. The ipsilateral nostril, meanwhile, develops rhinorrhea and congestion. Even though clusters are not usually accompanied by nausea, vomiting, or scintillations, at times cluster headaches look suspiciously like migraine headaches, and not infrequently respond to migraine medication.[23] So far, however, the pathophysiology of cluster headaches is unknown.[42]

Identify Them Clinically: For that matter, I'm not even sure the distinction between tension and migraine is even the right way to look at headaches. In my experience there are only two kinds of headache patients: those that want to get better and those that don't. It doesn't matter what you do for the latter group, and the former group generally seems to suffer from migraine and/or depression (rarely, chronic sinusitis).

Since any chronic pain can be depressing, it may be difficult to decide which is the chicken and which is the egg.[17] Taking a double barreled aim at both the pain and the depression with a drug like amitriptyline may break the cycle.[18] And if the patient fails that therapy, you've still got a dozen other migraine medications, short-acting sedatives to make them go to sleep,[19] biofeedback, relaxation training, cervical collar, and even cluster headache therapy like lithium,[20] indomethacin,[21] prednisone, 100% oxygen,[22] and sphenopalatine ganglion block.[23]

Muscle-Contraction Headache Sufferers: Muscle contraction headaches are probably most characterized by *neck* (not occipital) pain and spasm.[28]

Cafergot: For ergot medications to be effective, patients must take them at the very onset of the headache, not after the headache peaks. Presumably, dilated arteries allow fluid to leak into the arterial wall, making the wall thick and turgid. Ergots constrict best when the arterial walls are still thin and pliable.

Amitriptyline: For chronic therapy a drug like amitriptyline is particularly useful because it's a good analgesic by itself,[37] inhibits substance P in the spinal cord (by raising the serotonin level),[38] improves the effectiveness of narcotics[39] (allowing you to use lower doses of narcotics), lightens the depression of chronic pain,[16] and helps patients sleep through the night. Any patient in chronic pain who finally gets a good night's sleep will automatically feel better, and grateful.

thermal biofeedback[40]—is so much better than the treatment for tension headaches (relaxation therapy, muscle biofeedback[41], cervical traction, minor tranquilizers), that in diagnosing tension headaches, you automatically paint yourself into a corner of limited therapy. If your antimigraine therapy fails, you've lost nothing; you can still try biofeedback, minor tranquilizers, or any other reasonable therapy for tension headaches.

One of the hardest questions in chronic headache therapy is whether and when to get a CAT scan, EEG, skull xray, and lumbar puncture. A history of prior sinus infections or recurrent sinus drainage dictate a set of sinus xrays (or CAT scan of the sinuses) and an ENT opinion. The history and physical may tip you off to polycythemia, temporal arteritis, fungal meningitis, pituitary tumor, or intracerebral pathology, but without a suspicious history or positive physical findings, only laboratory tests can rest your mind. 95% of the time no focal neurologic findings means there will be no focal CAT abnormalities to explain the headaches.[42] On the other hand, a skull xray or CAT scan may detect a pituitary tumor long before neurologic signs develop.[43] Depending on the patient's concern, the family's concern, your fear of malpractice suits, concern for the cost of medical care, financial interest in a CAT scanner, and insecurity about your neurologic history and physical, you may obtain these laboratory tests at the beginning or wait until initial attempts at therapy fail.

In the emergency room, if you're convinced the headache is benign and you want to stop the headache in the emergency room, you can try an acute migraine medication like DHE 45* (1 ampule IM Q30 min × 2–3) or a phenothiazine.[45] If that fails, comes time to face the use of narcotic analgesics. Rewarding drug-seeking behavior with narcotics may cure his headache, but *you'll* end up with one every time he returns for another cure from your little pleasure chest of drugs. Use your judgment handling these patients, especially repeaters. An occasional shot of narcotics is probably okay, but the definitive, long-term solution must be a non-narcotic one, or at least as low a dose of narcotics as possible.[46] There's no point in solving one problem—pain—only to create another—drug seeking behavior. Explain this point of view to your patient; it'll help avoid an adversarial relationship.

DHE45: One of several parenteral (IV or IM) preparations of ergot, a chemical which constricts dilated arterioles.[44]

Ergot is made by a fungus which contaminates wheat. Eating such wheat produces "ergotism"—severe arterial constriction, severe enough to cut off all arterial blood flow to the arms. Because their arms turned black and fell off, people in the Middle Ages thought that the affliction was caused by "St. Anthony's Fire." Similar ergotism may occur today if patients take too many ergot-containing pills.

Low Back Pain

Back pain is the same thing. Don't expect an acute cure for a chronic problem. Just be sure the back pain isn't an epidural abscess, metastatic tumor, aortic aneurysm, kidney infection, pancreatitis, local hip disease*, etc.

When thinking about diseases affecting the spinal cord and cauda equina, ask about bilateral leg weakness, bilateral sensory complaints, and bowel or bladder disturbances. Can he tell when his bladder is full? Does he have to run to the toilet (urgency)? Can he start his stream at will, or does he have to wait (hesitancy)? How is the force of his stream? Does he empty his bladder, or does he have to return to the toilet to empty his bladder (double void)? Does he ever dribble or urinate in his underwear? Does toilet paper feel normal? When was the last time he urinated?

Back pain that's worse in the supine position strongly suggests an extramedullary tumor stretching sensitive nerve roots when the patient lies down. Absolutely red flag symptomatology is chronic low back pain that suddenly gets worse or suddenly improves, leaving in its wake perianal sensory loss, sphincter weakness, or lower extremity sensory or motor signs. The intervertebral disc in that patient has just extruded from the disc space into the epidural space or through the dura into the subarachnoid space, acutely injuring the cauda equina. Surgical intervention may be urgently needed.[48]

Local Hip Disease: Even though radicular pain often radiates to the hip, be sure to rule out local causes of pain within the hip. Feel for tenderness in the hip by working your fingertips over the greater trochanter into the hip joint. Rotate the hip joint (Patrick's maneuver), abduct the leg, and pound the greater trochanter, anything to irritate locally inflamed tissues in or around the hip joint.

The same goes for shoulder and arm pain. Fully abduct, flex, extend, and rotate the shoulder joint; feel high up into the axilla for focal tenderness in the glenoid capsule.[47] Palpate the radial nerve coursing around the elbow through the proximal extensor digitorum muscle. Inflammation in this area is one of the causes of 'tennis elbow.'

DIZZINESS

FORCED INTO THE UNENVIABLE POSITION OF BEING UNABLE TO SEE THE LESION, physicians shift uncomfortably when confronted with a patient complaining of dizziness. Like numbness, dizziness means different things to different people. To some, dizziness is vertigo but to others it's confusion, difficulty seeing, ataxia, weakness, or near syncope.[1] Try to rule out the dangerous diagnoses first, in this case, episodes of hypotension or basilar artery ischemia.[2] For basilar artery ischemia, ask if the dizziness was accompanied by blindness (both occipital lobes), diplopia, facial numbness, facial weakness, tinnitus, ataxia, dysarthria, dysphagia, or bilateral upper extremity weakness or incoordination*. Be sure to listen for carotid or supraclavicular bruits—evidence of carotid or vertebral artery stenosis—which might suggest cerebral ischemia.

Another worrisome source of dizziness is hypotension secondary to orthostasis, tachy or brady arrhythmias (ask about chest symptoms), or a hyperactive carotid sinus. Rarely, episodic dizziness may actually be brief seizures.[3]

Beyond these few situations, it's difficult to give dogmatic rules which will bail you out of all circumstances. In general, in deciding between basilar artery ischemia and labyrinthine or VIIIth nerve pathology (central versus peripheral pathology), if there are no cranial nerve or cerebellar signs, then the *worse* the vertigo, the more benign (peripheral) the lesion,[3] especially if the vertigo is precipitated by sudden head movements. Be sure to look in the ears for a mass behind the tympanic membrane. Repeated attacks of vertigo, preferably with tinnitus and hearing loss, suggest Meniere's disease.

Incoordination: In 1972, Fisher reported a disconcerting series of cerebellar infarctions which presented with acute vertigo *without* cerebellar or brainstem signs.[3]

EMERGENCY ROOM CASE HISTORIES

THE FOLLOWING ACTUAL EMERGENCY ROOM CASE HISTORIES represent important treatable illnesses which could become disasters if missed, but which almost always retreat from the onslaught of proper medical therapy. And you don't need to be a neurologist to recognize them.

These case histories will also give us an opportunity to practice the logical steps in physical diagnosis. Diagnosing cases from a completed history and physical differs considerably from starting with the chief complaint. When you begin with the chief complaint, you immediately establish an anatomic differential diagnosis for that symptom. You use the history to narrow the anatomic differential diagnosis and to simultaneously consider specific etiologies for each anatomic site.

When given a whole history and physical, you need only pick out the 'unusual' physical finding, the one that has a small etiologic differential diagnosis. Knowing which signs are 'unusual' takes a little experience. In the following case histories, I'll mention the 'unusual' sign, but I'll also interject the anatomic differential diagnosis so you can see how the etiologic differential diagnosis was obtained.

Recognizing the unusual sign is the easy part; the hard part is knowing all the signs of each disease so that you can compare them to your patient's signs. You also have to know which signs are almost always seen in a particular disease and which signs are only rarely seen. To help determine what you do and do not know about each etiologic diagnosis, think about what further questions or physical findings you would seek if you could return to the patient for ten more minutes.

In the emergency room, when you structure the etiologic differential diagnosis, don't worry about being right. The role of the first doctor seeing the patient is to rule out those diseases which, if missed, would have the most serious, irreversible consequences. So what if the next day someone laughs at you because you considered a rare but explosive disease at 2 am in the emergency room. The last doctor to see the patient is *always* the smartest doctor. Don't worry about being right; worry about being safe. You can be right tomorrow.

CASE #1

A 35 year-old woman complains of a three day history of weakness combing her hair, walking, climbing stairs, opening jars, and turning keys in locks. She has no cranial nerve, sensory, or sphincter symptoms.

On examination her mental status is normal. The cranial nerves are also normal except for modest weakness of neck flexion. Motor exam reveals a cautious, narrow-based gait, no atrophy, no fasciculations, normal tone, and no muscle tenderness. She does have, however, modest bilateral weakness of opponens, grip, biceps, and deltoids in the arms, and modest bilateral weakness of psoas, quadriceps, tibialis ante-

rior, gastroc, hamstrings and gluteus maximus in the legs. She has difficulty hopping on either foot and can barely do a deep knee bend. Rapid alternating movements are performed well and finger-nose-finger is normal. Sensory exam is normal to vibration and proprioception in the feet. Reflexes are 1+ and symmetrical with downgoing toes. Where is the lesion and what tests would you perform?

The first step, as always, is the anatomic diagnosis; which subsystem is malfunctioning? When assessing any motor problem, try to decide among the following choices: is the patient weak, stiff, slow, or incoordinated (or in pain)? Each of these categories has an anatomic differential diagnosis.

In this case, the woman's motor complaints are fully accounted for by her weakness. There's only one CNS subsystem that causes weakness: the pyramidal tract. But since she has no other signs of pyramidal tract dysfunction (spasticity, slowing of rapid alternating movements, hyperreflexia, or Babinski), the abnormal subsystem must therefore lie in the peripheral neuromuscular system—either in the lower motor neuron, root, peripheral nerve, neuromuscular junction, or muscle. Let's consider each of these anatomic sites separately, listing those etiologic diagnoses that cause acute or subacute weakness:

	Lower Motor Neuron	Vascular	Hematologic
Drugs			
Infection	Polio		
Genetic/Degen	ALS		
Immunologic			
Tumor			
Trauma			
Mechanical			
Organ Dysfunction			

Bilateral weakness from lower motor neuron dysfunction occurs in polio and amyotrophic lateral sclerosis*. But, polio is a meningoencephalomyelitis, i.e., fever, headache, photophobia, and stiff neck amidst a rapid, *a*symmetric paralysis—not the picture here. ALS is a slowly evolving illness lasting years producing a mixture of progressive lower and upper motor neuron weakness.

	Peripheral Nerve	Vascular	Hematologic
Drugs	Arsenic		
	Tick Bite		
Infection	Diphtheria		
Genetic/Degen	Porphyria		
Immunologic	Guillain Barre	Arteritis	
Tumor			
Trauma			
Mechanical			
Organ Dysfx			

Amyotrophic Lateral Sclerosis: ALS is an idiopathic, invariably fatal illness (1–15 years depending on pharyngeal and respiratory muscle involvement) of the pyramidal tracts and anterior horn cells. Because vibration travels in part up the lateral columns, ALS usually has some vibratory loss too.[1]

Any polyneuropathy can cause diffuse weakness, but the weakness is usually distal and associated with stocking/glove sensory loss and absent distal reflexes, the major exception being Guillain Barre, which early on can involve proximal muscles and have little if any sensory loss. And in the early stages of Guillain Barre, the relexes may be only slightly diminished instead of absent.

Arsenic polyneuropathy mimics Guillain Barre, but with additional GI disturbances—nausea, vomiting, and abdominal pain. Porphyria, a rather rare polyneuropathy could conceivably fit this woman's picture, but without signs of resting tachycardia or mental disturbance, and without a history of previous bouts of weakness, seizures, emotional problems, or abdominal pain, porphyria is also unlikely.

Diphtheric polyneuritis, also very rare, follows diphtheric pharyngitis or cutaneous diphtheria. Prominent early symptoms are blurred vision (paralysis of accommodation) and dysphonia (paralysis of the palate), followed by other cranial and peripheral nerve symptoms. Tick paralysis should be considered in anyone with acute, symmetrical weakness, particularly children. A widespread arteritis affecting peripheral nerves may be seen in a large number of immunologic diseases, but it's rare for those diseases to *present* with widespread weakness.

	Neuro muscular Junction	Muscle	Vascular	Hematologic
Drugs	Mestinon under/over dosage			
Infection	Botulism	Influenza myositis*		
Genetic/Degen		Periodic paralysis		
Immunologic	Myasthenia gravis	Polymyositis Eaton Lambert	Arteritis	
Tumor				
Trauma				
Mechanical				
Organ Dysfx		Hyperthyroidism Cushing's disease* Addison's disease* Hypophosphatemia Hypokalemia		

Neuromuscular illnesses—botulism and myasthenia gravis—present predominantly above the shoulders: ophthalmoparesis, ptosis, difficulty chewing, facial weakness, dysarthria, dysphonia, dysphagia, and neck weakness. In some patients, especially older ones, weakness below the shoulders can dominate the clinical picture.

Influenza Myositis: A viral infection of muscle causing widespread muscle necrosis and myoglobinuria.

Cushing's Disease: Excessive steroids cause proximal weakness by an unknown mechanism.*

Addison's Disease: No one is clear about the mechanism of weakness; the patients are just fatigued and poopy.

Unlike typical myasthenia gravis, the Eaton Lambert syndrome usually presents below the neck (Eaton Lambert is a remote effect of carcinoma affecting neuromuscular junctions). Eaton Lambert is a consideration here, but for this 33 year-old woman to have unrecognized carcinoma (estimated probability 1:10,000) and if she did, to have the Eaton Lambert syndrome, too (about 1:1000) requires the multiplication of these unlikely possibilities (1/10000 x 1/100 =1/10,000,000), statistically too remote.

Chronic myopathies are usually proximal, but acute myopathies often affect all muscles of the body. Sensation would be spared and the reflexes could be depressed in proportion to the weakness. Of all the diagnostic possibilities, muscle dysfunction fits this woman's clinical picture best.

Influenza myositis is a viral infection causing acute, widespread muscle necrosis and myoglobinuria[2] The stigmata of Cushing's disease should be obvious. Addison's disease is not so obvious, but the weakness is more chronic than this woman's. Hypophosphatemia mimics Guillain Barre, but without a reason for hypophosphatemia (diabetic ketoacidosis, chronic alcoholism, or hyperalimentation*), this diagnosis is untenable. Of course, periodic paralysis should have a history of recurrent attacks.

After considering each etiologic diagnosis and asking any additional questions and reexamining for any pertinent physical findings, you then order the necessary lab tests to confirm each possibility. Of all the diagnoses, the one to rule out first is hypokalemia.

As it turns out, this woman was taking diuretics to lose weight for her job and her serum K^+ was only 1.8 meq/L (normal 3.5-5.0). Correction of the potassium deficiency returned her strength to normal.

CASE #2

A 40 year-old man complains of three days of fatigue and weakness with perhaps subtle tingling of his feet.

On exam he is alert and oriented with clear speech and appropriate mentation. Cranial nerves reveal normal visual fields, 20/20 vision bilaterally, and normal discs and fundi. Extraocular movements are full without nystagmus or ptosis; pupils are equal and reactive. Facial sensation and strength are normal. Gag is intact and the tongue is normal.

Motor exam reveals an unsteady, narrow-based gait with asymmetrical arm swing. There is no atrophy of the arms or legs, and no fasciculations. Tone is normal in the arms and legs. On strength testing, he has modest weakness (grade 4) of the hand intrinsics, grip, and wrist extensors, and moderate weakness (4-) of the biceps, triceps, and deltoids. In the legs he has modest weakness of psoas, quads, hamstrings, and gluteus maximus, but moderate weakness of tibialis anterior, gastrocs, and toe flexors. The patient cannot raise his hands above his head and cannot rise from a chair without pushing off with his arms. Rapid alternating movements in the hands are performed well. Cerebellar testing, within the limits of weakness, reveals no diffi-

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Hyperalimentation: Routine IV solutions cannot possibly meet a patient's caloric needs. If a patient is losing weight and his GI tract can't handle a large caloric load, a highly nutritious IV solution, called hyperalimentation (or total parenteral nutrition), is administered through a central line (an IV line that reaches into the superior or inferior vena cava).

culty with tandem gait, finger-nose-finger, and heel-shin. Reflexes are absent throughout with downgoing toes. Sensory exam reveals modest diminution of vibration at the feet with normal proprioception and pin. What is the most likely diagnosis and what would you do now?

As in case #1, the absence of pyramidal tract signs helps narrow the anatomic choices to sites outside the central nervous system. The absence of atrophy and fasciculations makes sense because it takes weeks for those signs to appear. The anatomic differential diagnosis is the same as in case #1. Is there any sign which helps distinguish myopathic from neuropathic weakness? Yes, the absent reflexes. Loss of the reflexes early on, before there has been much weakness, usually indicates a polyneuropathy (affecting the large heavily myelinated afferent arm of the reflex arc). Statistically, Guillain Barre is the most likely acute polyneuropathy. Once in a great while, arsenic poisoning will happen along, very rarely porphyria or tick bite, and over the rainbow, diphtheric polyneuropathy.

Having made a tentative diagnosis of Guillain Barre, the next question is, what's the pace of his illness? It wouldn't be that unusual for the patient to slip into respiratory failure while you're seeing another consult or waiting for lab work to return. For this reason it's best to admit the patient to the intensive care unit where his vital capacities can be monitored hourly until you feel confident that impending respiratory paralysis is unlikely. Guillain Barre can be a nasty illness and will sting you if you don't respect it.

CASE #3

A 23 year-old male complains of intermittent diplopia for approximately six months and shortness of breath for two days. The diplopia occurs when looking to the right or left, and the images are side by side. These symptoms improve somewhat in the morning. He has had no difficulty with headaches, blindness, facial weakness, dysarthria, dysphagia, or incoordination of his arms or legs.

On examination his mental status is normal. Cranial nerves reveal normal visual fields, 20/20 visual acuity OU*, and flat discs. Extraocular movements reveal bilateral medial rectus weakness. He has no difficulty looking up or down. There is mild ptosis of the right eye, but the pupils are equal and reactive. Facial sensation and movement are normal. Gag and speech are also normal. Motor exam reveals a normal gait, tone, strength, coordination, and cerebellar function. Reflexes are 2− and symmetrical with downgoing toes. What is the differential diagnosis?

First, what is the anatomic differential diagnosis for medial rectus weakness (in this case bilateral medial rectus weakness)? The medial rectus muscle itself, the neuromuscular junction, the branch of the oculomotor nerve to the medial rectus muscle, and the medial longitudinal fasciculus—internuclear ophthalmoplegia. The other two features of internuclear ophthalmoplegia weren't mentioned, but nystagmus of the abducting eye is easy to overlook and convergence is frequently not looked for.

For each anatomic site there's an anatomic differential diagnosis. Not many diseases affect a single muscle in the orbit. A good working rule is that *any* ophthalmoplegia is myasthenia gravis until proven otherwise. And here's a man with a pure motor syndrome above the shoulders which improves somewhat in the morning, a

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*OU: OU means each eye. OS (ocular sinister) is the left eye, and OD (ocular dexter) is the right eye.

nutshell description of myasthenia gravis. Thyroid eye disease (Grave's disease*) is another common cause of myopathic ophthalmoplegia.[4] Of the few diseases that might injure a branch of the oculomotor nerve, Tolosa Hunt would be the most likely. This disease is usually accompanied by orbital discomfort and mild proptosis.

Bilateral internuclear ophthalmoplegia in a young person would almost certainly be multiple sclerosis, a reasonable consideration but not a diagnosis that needs to made in the emergency room.

Which test to order? The most dangerous diagnosis is myasthenia gravis, and the Tensilon test is relatively easy to perform (chapter 26). With clear signs to observe (medial rectus weakness and ptosis), do the Tensilon test right in the emergency room. If the eyes improve, as they did in this patient, you have your diagnosis.

CASE #4

A 30 year-old woman with a past history of 'schizophrenia' complains of two weeks of difficulty walking and seeing.

On examination she thinks this is 1977; she knows that you are a doctor and that she is in a hospital, but not which hospital. She follows all simple commands and her speech is not dysphasic. Her response to questions is somewhat slow and uncertain, but she answers most questions correctly. Cranial nerves reveal normal discs, 20/20 vision bilaterally, and intact visual fields. There is moderate bilateral weakness of the lateral rectus muscles with prominent coarse nystagmus on lateral gaze in either direction. The pupils are equal and reactive and there's no ptosis. Facial sensation is normal and facial movements are sparse, but not weak. Gag is intact. Motor exam reveals a somewhat wide-based, unsteady gait with symmetrical armswing. Tone, strength, and rapid alternating movements are performed normally. Finger-nose-finger and heel-shin are moderately dysmetric. She is unable to tandem walk more than one step. Ankle jerks are absent, but the reflexes elsewhere are 1-2+ and symmetrical with downgoing toes. Sensory exam is remarkable for stocking hypesthesia to pin, vibration, and proprioception. What is the differential diagnosis?

It should be apparent that a single neurologic subsystem or a single blood vessel cannot account for all these signs. First of all, she thinks it's 1977 and is unsure of which hospital she's in—evidence of modest bihemispheric cortical dysfunction. She has bilateral VIth nerve palsies implying bilateral lesions somewhere between the lateral rectus muscles and abducens nerves in the pons. She also has truncal ataxia—cerebellar vermis—and stocking hypesthesia with absent ankle jerks—a peripheral neuropathy.

Which signs should we choose for the anatomic differential diagnosis? The bilateral lateral rectus weakness would generate the smallest etiologic differential diagnosis. So what's the anatomic differential diagnosis of bilateral lateral rectus weakness? The VIth nerves begin in the lower pons, exit the pons ventrally, climb alongside the clivus to the cavernous sinus, and enter the orbit through the superior orbital fissure. We know that the lesion cannot be in the VIth nerve nucleus; a lesion there would cause a gaze palsy.

Grave's Disease: Immunologically mediated infiltration of the eye muscles by inflammatory cells in association with inflammatory thyroid disease.

	Intra-axial VIth Nerves	Extra-axial VIth Nerves	Lateral Rectus Muscles
Drug	Wernicke's encephalopathy		Penicillamine (myasthenia gravis)
Infectious	Cerebellar abscess	Basilar meningitis	
Genetic/ Degenerative		Arnold Chiari	
Immunologic	Lupus arteritis Polyarteritis Multiple sclerosis	Tolosa Hunt	Myasthenia gravis
Tumor	Brainstem tumor 4th ventricular tumor	Pituitary tumor	
Trauma		Trivial trauma with a tumor at base of the brain	
Mechanical	Brainstem compression by cerebellar or fourth ventricular tumor	Symmetrically increased intracranial pressure with herniation (false localizing VIth nerve palsies)	
Organ Dysfx	Brainstem stroke	Cavernous sinus thrombosis	

DRUGS: Wernicke's encephalopathy is the constellation of confusion, cerebellar ataxia, and virtually any ophthalmoparesis (including ptosis) affecting both eyes.[5] All of her signs could fit Wernicke's, but she denies alcohol use. Penicillamine and certain antibiotics can cause myasthenic weakness but not confusion; besides, she's not taking penicillamine or antibiotics.

INFECTION: Without fever, headache, lethargy, or irritability, it's hard to imagine any kind of meningitis. Perhaps a cerebellar abscess could cause this picture by compressing the pons to get the bilateral VIth nerve palsies, and by obstructing the 4th ventricle to produce non-communicating hydrocephalus (confusion). Perhaps. Against this diagnosis is the absence of fever, headache, or signs of increased intracranial pressure (papilledema, lethargy, vomiting). Herniation of a *diffusely* swollen brain may cause false localizing VIth nerve palsies. Perhaps she has a diffuse infectious process like toxoplasmosis or viral encephalitis causing increased intracranial pressure and herniation. All of these infections, unlikely as they are, are in the differential because of their treatability.

GENETIC/DEGENERATIVE: How about Arnold Chiari (cerebellar tonsil herniation and aqueductal stenosis)? The tonsillar herniation might account for her cerebellar ataxia and a recent worsening of aqueductal stenosis might be causing subacute non-communicating hydrocephalus with herniation. Maybe.

IMMUNOLOGIC: Lupus arteritis or polyarteritis, both treatable diseases of young people, commonly affect more than one neurologic subsystem. But to infarct both sides of the pons without involving the pyramidal tracts is too remote a possibility. Multiple sclerosis is another immunologic disease in a young woman, but being a central nervous system white matter disease, multiple sclerosis doesn't usually cause

acute confusion or peripheral neuropathies. Neither Tolosa Hunt nor myasthenia gravis causes confusion or polyneuropathy.

TUMOR: A large pituitary tumor growing laterally into both cavernous sinuses could damage the VIth nerves, but how to explain the confusion, ataxia, and polyneuropathy?

A brainstem glioma affecting both VIth nerves and the middle cerebellar peduncles but not the pyramidal tracts is highly unlikely. Interesting enough, brainstem gliomas can cause a change in personality, but not a polyneuropathy.

What about a cerebellar or 4th ventricular tumor obstructing the 4th ventricle (confusion) and compressing the pons (VIth nerve palsies). Possibly, but without signs of increased intracranial pressure, keep these diagnoses in mind and watch for signs of increasing intracranial pressure while you consider:

TRAUMA: Sometimes a tumor along the base of the brain will allow trivial head trauma to cause ophthalmoplegia. This wouldn't explain the bihemispheric cortical signs (confusion) or the polyneuropathy. Bilateral subdural hematomas could cause confusion, unsteadiness of gait, and diffuse increased intracranial pressure with herniation. But, again, no headache, papilledema, or vomiting.

MECHANICAL: A diffusely swollen brain might mechanically distort the brainstem and cause false localizing VIth nerve palsies. Non-infectious causes of a diffusely swollen brain include Reye's syndrome, pseudotumor cerebri, hyponatremia, and superior sagittal sinus thrombosis. She denies a headache and has no signs of increased intracranial pressure, but these diagnoses are clearly in the running.

ORGAN DYSFUNCTION: Multiple brainstem infarctions, as mentioned for lupus arteritis, would be very unlikely without pyramidal tract signs.

Cavernous sinus thrombosis is a serious illness causing stupor, proptosis, conjunctival injection, and usually complete ophthalmoplegia. Moreover, the thrombosis is usually a thrombophlebitis with fever and prostration.

So here you are in the emergency room with all these thoughts going through your head. What do you do now? What lab tests do you send, and what therapy do you begin? Electrolytes, CBC, BUN, creatinine, glucose have routinely been sent and you can order drug screening on urine and blood. Should you do a lumbar puncture now? Because of the possibility of a cerebellar mass or elevated intracranial pressure, and without signs of infection (fever, stiff neck), it would probably be best to wait until after the CAT scan.

Is there any diagnosis that needs immediate treatment before the CAT scan? Yes, Wernicke's encephalopathy. As unlikely as this diagnosis is in a 30 year old woman, Wernicke's needs immediate treatment, especially since thiamine is so benign. Within hours of thiamine therapy, she began to improve. About four months prior to admission she had moved to the city to implement her new diet, subsequently losing about 40 pounds and all her thiamine stores*. Thiamine (and Haldol) helped her confusion and ophthalmoplegia, but her ataxia never completely abated during the following year.

Thiamine Stores: Thiamine (B1), pyridoxine (B6), niacin, Vitamin C, and folate are all water soluble and subject, therefore, to metabolic attrition through the urine unless there is frequent dietary replacement. The fat soluble vitamins (A, D, and E), being stored in fat, are relatively resistant to dietary depletion. Vitamin B12, though water soluble, is stockpiled by the liver for a full 2–3 year supply.

CASE #5

A 20 year-old male is brought to the emergency room because of a six hour history of double vision and difficulty swallowing.

On examination the patient is alert with dysphonic speech. Cranial nerves reveal a bilateral visual acuity of 20/30, no red washout, no field cut, and flat discs without optic atrophy. There is, however, a marked impairment of gaze in all directions. Pupils are 6mm and unreactive. There is moderate bilateral ptosis. Facial sensation is normal, but there is moderate weakness of eye closure and smiling. Gag is poor, and the tongue is weak. Motor exam reveals that the patient can neither rise from a chair nor take a few steps without major assistance. There is no atrophy or fasciculations, and the tone is normal. He has moderately severe weakness of grip, wrist extension, biceps, triceps, deltoids, tibialis anterior, hamstrings, and psoas muscles bilaterally. Cerebellar testing reveals no intention tremor in the arms or legs. Reflexes are 1+ and symmetrical with downgoing toes. Sensory exam is probably normal. What do you think he has and what would you do now?

First of all, there are no pyramidal tract signs. Since the only subsystem in the central nervous system that affects strength is the pyramidal tract, the lesion must be somewhere in the peripheral neuromuscular system—somewhere between the lower motor neuron cell body and the muscles.

We can further narrow the anatomic differential diagnosis with the one sign that slaps you in the face. If that sign doesn't make you gulp and start, go back and reread the history. The fixed pupils. Thinking anatomically, where can the pupils become fixed to light? We can immediately reject bilateral optic neuropathies because he has no optic disc pallor or swelling, no red washout, no field cut, and a visual acuity consistent with poor accommodation. This leaves the following etiologic differential diagnosis for bilateral fixed pupils.

	Iris Muscle	Parasympathetics	Midbrain
Drugs	Atropine eye drops Botulism		Syphilis Parinaud's syndrome Dorden* overdose
Infection		Adie's tonic pupil	
Genetic/ Degenerative			
Immunologic	Uveitis	Fisher's syndrome	
Tumor			
Trauma			
Mechanical			
Organ Dysfx		Diabetes	

As you work your way through this list, saying to yourself, "if he had this diagnosis, he should have these signs:...", certain diseases can be rapidly eliminated. The abrupt onset, conscious state, absence of pyramidal tract signs, and absence of fever or headache allows us to discard the vast majority of possibilities, leaving only one

Doriden: A sleeping pill.

that produces a pure motor syndrome predominantly (but not exclusively) above the shoulders: botulism*. Treatment is polyvalent vaccine and intubation at the first sign of pCO_2 retention or a falling vital capacity.[6] The botulinus toxin attaches itself to terminal axonal boutons, preventing the release of acetylcholine packets into the neuromuscular cleft. With support, the patient should recover as terminal axons resprout to establish new neuromuscular junctions.

CASE #6

A 64 year-old woman is brought to the emergency room by ambulance from her apartment where she was found unconscious. On exam she has a blood pressure of 140/90, pulse 110, a respiratory rate of 22, no fever, and a moderately stiff neck. She does not open her eyes spontaneously, but will open the left eye to painful pinching of her sternocleidomastoid. She follows no commands, but does grimace symmetrically and grab your hand when you pinch her sternocleidomastoid. Speech is mumbling and incoherent with occasional phrases of normal sounding English. Her discs are flat and there are no hemorrhages in the fundi. On lifting her eyelids, you find that the right pupil is 7mm and fixed, the left 3mm and reactive. On rocking her head to the right, the left eye deviates laterally, but the right eye does not cross the midline. The corneal reflexes are present bilaterally and facial grimacing is symmetrical. She swallows spontaneously and has a gag. Her tone is normal bilaterally, and she seems to use both hands equally well to grab your hand when you pinch her sternocleidomastoids. When you pick up both her arms while yelling encouragement to keep them up, the arms drift symmetrically. Reflexes are brisk bilaterally and both toes go up. She withdraws to pin in either arm.

The oculomotor nerve palsy is pretty clear, and the etiologic differential diagnosis for a IIIrd nerve palsy should be smaller than that for coma or meningismus. Let's start with a simple anatomic question: Is the lesion in or out of the brainstem? To diagnose an intra-axial third nerve lesion, you need a contralateral long tract, in this case the pyramidal tract. She does have upgoing toes, but that's all. There *is* something wrong with her pyramidal tracts, but the pyramidal tract signs are too mild and too symmetrical. Virtually any cerebral insult serious enough to cause stupor and coma can make the toes go up. You'd like to see a true left hemiparesis to diagnose a structural pyramidal tract lesion.

It's very important to decide if she has a left hemiparesis, because without a hemiparesis, her third nerve palsy is unlikely to be inside the midbrain. Which means her coma is not due to a structural lesion of the reticular activating system, but rather to a supratentorial lesion. Furthermore, without a hemiparesis or decerebration, transtentorial herniation (which damages the peripheral IIIrd nerve and the midbrain) is also unlikely. The stiff neck (meningeal inflammation) argues that whatever has affected both hemispheres has done so by way of the CSF. So whatever etiology you consider must affect the meninges and the oculomotor nerve.

Now let's look at the more frequent etiologies for acute extra-axial oculomotor nerve palsy:

Botulism: Perhaps 50% or more of cases of botulism don't fix the pupils, so don't reject the diagnosis if the pupils do react to light.[7]

	Extra-axial Proximal to Cavernous Sinus	Cavernous Sinus and Superior Orbital Fissure
Drugs		
Infection	Chronic basilar meningitis	Cavernous sinus thrombophlebitis Burst pituitary abscess
Genetic/Degenerative		
Immunologic		Tolosa Hunt
Tumor		Pituitary tumor Metastatic tumor
Trauma		Blunt head trauma
Mechanical	Unruptured posterior communicating artery aneurysm	Internal carotid artery aneurysm
Organ Dysfunction	Ruptured posterior communicating artery aneurysm	Pituitary apoplexy

Which of these illnesses can also cause coma and meningismus? Basilar meningitis, burst pituitary abscess, ruptured posterior communicating artery aneurysm (subarachnoid hemorrhage), and cavernous sinus thrombophlebitis.

What tests would you do now? LP? If she has meningitis, you need to know now, but if she *is* herniating, you can't do the LP. Without a fever, cavernous sinus thrombophlebitis, basilar meningitis, and ruptured pituitary abscess are all very unlikely. If you could get a history of sudden onset of headache and coma (suggesting subarachnoid hemorrhage), you could then safely order the CAT scan without running the risk of an LP.

This particular woman was tapped in the emergency room and found to have a subarachnoid hemorrhage.

CASE #7

A 62 year-old man noted some low thoracic/upper lumbar back pain during the day prior to admission. He was awakened that night by marked back pain—so severe it prevented him from standing. An ambulance brought him to the hospital where on exam now he is alert and oriented with clear speech and appropriate mentation. Cranial nerves II-XII are normal.

Motor exam reveals inability to stand because of the back pain. Muscle bulk and tone are normal throughout. Strength is normal in the arms. Lifting either leg produces marked back pain. There is modest weakness of the psoas, quadriceps, tibialis anterior, gastroc, hamstrings, and glutei. Rapid alternating movements are normal in the hands and feet. Finger-nose-finger and heel-shin testing are normal. Reflexes are 2+ and symmetrical in the arms, 1+ at the knees and ankles. The toes are probably downgoing.

Sensory exam reveals modest diminution of vibration and pin in the legs with a sensory level at about T10. Rectal sphincter tone is also somewhat diminished. What else would you look for on the exam? What are your thoughts and what would you do now?

Here's a man with back pain, sudden paraparesis, and a T10 sensory level. The sensory level certainly points to a lesion in the thoracic cord; why aren't there pyramidal tract signs in the legs? Two reasons: acute spinal cord lesions often don't

produce the typical pyramidal tract signs of more chronic cord lesions, and second, the lesion may be extending caudally into the lumbosacral cord to involve the anterior horn cells.

	Thoracic Spinal Cord	Vascular
Drugs		
Infection	Epidural abscess	
	SBE with embolic cord infarction	
Genetic/Degenerative	Ruptured AVM of the cord	
Immunologic		Arteritis of the anterior spinal artery
Tumor	Epidural metastasis	
	Subdural metastasis	
	Intramedullary metastasis	
	Bleed into primary spinal cord tumor	
Trauma		Aortic dissection
Mechanical	Herniated disc	
Organ Dysfunction	Epidural hematoma	
	Anterior spinal artery thrombosis	

The strongest arguments against aortic dissection, SBE with embolic occlusion of the anterior spinal artery, and thrombosis of the anterior spinal artery is that the patient does not have the anterior spinal artery syndrome (sparing of the posterior columns). Keep these diagnoses in mind but consider other, more likely ones first.

Which of the remaining diagnoses is the most dangerous? The epidural abscess. Every time you see a patient with back pain, especially back pain which strikes without a precipitating cause, you must, must check the patient's temperature. A synaptic connection in your brain needs firm soldering: fever and back pain, fever and back pain, fever and back pain.* Until proven otherwise, this paraparetic patient has a spinal epidural abscess which requires your full, uninterrupted attention. Firmly thump—don't just tap—each spinous process for focal tenderness. He'll tell you if there's an abscess there (though he may be up in the chandelier). Plain spine films, blood cultures*, bone scan* (if there's time) and a myelogram are in the offing. Spinal epidural abscess, which is what this patient had, is a relatively easy diagnosis to make if you keep it in mind.

Even if the patient doesn't have focal tenderness of a spinous process, don't discard an infectious etiology. Negative findings may lean you away from a diagnosis, but don't get pulled off balance. Epidural abscess is too explosive to forget about just because the patient didn't have spine tenderness at the onset of his illness. In general,

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Blood Culture: The internal body fluids—blood, urine and CSF—should be sterile. Bacterial infections frequently elude leukocytic pursuit by escaping into the bloodstream where the bacteria can be detected with blood cultures.

Bone Scan: A radioactive chemical (technetium) injected into the patient's bloodstream settles in the patient's bones. A huge geiger counter scans the bones to detect 'hot spots' of excessive uptake—areas of high metabolic turnover—reflecting tumor, infection (osteomyelitis), fracture, arthritis, etc.

it's dangerous to draw positive conclusions (no infection) from negative information (no spinal tenderness); you'll be on much safer ground drawing positive conclusions from positive information.

CASE #8

A 65 year-old man with a history of hypertension is brought to the emergency room in a stuporous state. His family says that this afternoon while working in the garden he experienced a sudden headache, staggered into the house, vomited some twenty minutes later, and then complained of double vision.

On examination his blood pressure is 190/110. The patient follows simple commands after you arouse him by pinching his sternocleidomastoid. He knows the year, the month, and the correct city, but not that he is in a hospital. Speech is garbled and slurred, but comprehensible. Cranial nerves reveal no field cut to threat, flat discs, and no hemorrhages. The right eye is deviated slightly downward at rest, and remains below the level of the left eye when he looks left, up, and down with both eyes. On right gaze there is mild weakness of the right lateral rectus. The pupils are 3mm and reactive; there is no ptosis or nystagmus. Corneal reflexes are symmetrical, and facial grimacing to pain is symmetrical. Gag is present.

Motor exam reveals a markedly unsteady gait, requiring assistance even to stand. Bulk and tone are normal throughout. There is mild symmetrical weakness in the arms and legs with a moderate intention tremor of the right arm. Reflexes are 2+ and symmetrical with downgoing toes. He feels pain bilaterally. What are your thoughts and what would you do now?

A catastrophic event has caused sudden headache, vomiting, stupor, ataxia, ophthalmoplegia, and dysarthria without hemiplegia. The persistent downward deviation of the right eye—skew deviation—indicates brainstem (usually pontine) dysfunction, an anatomic diagnosis reinforced by the right VIth nerve palsy. The man can't even stand, yet isn't hemiplegic. Even if his toes were upgoing, you couldn't blame the pyramidal tracts for the patient's inability to stand. After all, a Babinski sign alone won't make him weak. Of the choices—pyramidal, extrapyramidal, cerebellar, and proprioceptive—cerebellar is the most likely explanation for his sudden inability to stand.

Etiologically, the explosive onset, crescendoing within minutes to maximal deficit, points to an intracerebral or subarachnoid hemorrhage. Combining the anatomic site (cerebellum) with etiologic pathophysiology, we quickly come up with this man's diagnosis: cerebellar hemorrhage. This is an important diagnosis to recognize. Operative drainage will allow him to exit the hospital walking, talking, and feeding himself, but will likely kill him if missed.

The constellation of past hypertension, sudden headache (usually occipital), vomiting, ataxia, progressing stupor, ophthalmoplegia, skew deviation, dysarthria, and either flaccid or stiff limbs, but without early hemiplegia, is a cerebellar hemorrhage until proven otherwise.[9] The relative absence of pyramidal tract signs is due to the wide separation between the pyramidal tracts in ventral pons and the cerebellar hemorrhage situated well behind the 4th ventricle. The patient's coma has two sources: the hemorrhage may be directly compressing the upper pontine reticular activating system, or obstructing the 4th ventricle causing acute, non-communicating hydrocephalus.[10]

An emergency CAT scan in this situation may be life-saving (yours and the patient's) if it shows the signs of posterior fossa mass effect. Look carefully for these signs; they harbor catastrophic consequences if ignored. First try to find the 4th ventricle; a cerebellar mass may obliterate it or else push the 4th ventricle forward and lateral from its normal midline position. An expanding cerebellar mass also obscures the perimesencephalic cisterns and compresses the prepontine cistern by shoving the pons against the clivus. In a young person non-communicating hydrocephalus (from the 4th ventricular obstruction) may not manifest as massively dilated lateral ventricles. Look instead for the temporal horns; they shouldn't be visible in a young person, so if you see the temporal horns, your patient has hydrocephalus. Can you clearly make out the sulci over the hemispheres, or are they compressed up against the skull by increasing intracranial pressure?

Let the neurosurgeons know early about any patient with a suspected cerebellar hemorrhage. If the patient is progressing rapidly into coma, rapid intubation, mannitol, and, most importantly, operative decompression of the posterior fossa may still save him.

CASE #9

A 48 year-old man is wheeled into the emergency room convulsing. By the time you get his vital signs and start an IV, his seizure has stopped. On exam he has a BP of 150/95, pulse 110, respirations 20, and a temp of 103° rectally. Intermittently, his neck, arms, and legs become extended and stiff. He follows no commands and stiffens when you pinch his sternocleidomastoid. The discs are hyperemic without hemorrhages. Lifting up his eyelids, you note the right eye deviated laterally, but both eyes move conjugately when you rock his head from side to side. Both pupils are 3mm and reactive. Corneals are present bilaterally, but he won't grimace. He does swallow spontaneously.

Motor exam (between the bouts of stiffening) reveals a floppy right leg, but some tone in the right arm. He has only occasional spontaneous movements of his right arm and no spontaneous movements of his right leg. He moves his left side more than his right side, and he reacts more to his left sternocleidomastoid being pinched than he does to his right one. Deep tendon reflexes are diminished on the right side and the toes go up bilaterally.

A seizure suddenly begins again in the right leg, marching up the right side and finally generalizing. Where is his lesion and what's the matter with this patient?

Since the seizure began in the right leg, the seizure focus must lie along the medial motor strip of the left hemisphere where the legs drape into the interhemispheric fissure. This locus is supported by the observation that he moves his right leg less than his right arm.

Fever, stupor, and stiff neck point to an infectious etiology, and the spontaneous decerebration suggests increased intracranial pressure. What kind of infectious diseases collect in the interhemispheric fissure? Number one consideration is subdural empyema, a collection of pus spreading from an infected frontal sinus backward through the dura into the interhemispheric fissure. A brain abscess within the medial frontal lobe, and cortical vein thrombosis amidst a raging bacterial meningitis are two other likely considerations. Superior sagittal sinus thrombosis will also raise the intracranial pressure and, by obstructing venous drainage of the medial motor strip,

precipitate focal leg seizures and a hemiparesis worse in the leg (often bilateral hemipareses).

Should you tap a patient who's spontaneously decerebrating even if you suspect an intracranial infection? Not before the CAT scan; an LP may precipitate herniation. Have someone draw blood, urine, and sputum cultures while you call the neurosurgeon to discuss starting antibiotics without first culturing potential intracranial pus*. Get an urgent CAT scan and look for that black sliver of pus along the falx. Be sure the CAT scan cuts through the sinuses so you can rule out a sinus infection.

CASE #10

A 20 year-old male walks into the emergency room claiming he cannot use his right arm. He had been drinking heavily two days ago when he and his friend fired heroin. On awakening this morning, he could neither move his arm nor feel anything touching it.

On exam the right arm is swollen up to shoulder. The biceps, triceps, and forearm muscles feel markedly indurated. Tone is stiff at the elbow because of the swollen tissues. He cannot move his fingers, wrist, or elbow, but he can abduct his shoulder with moderately good strength. Biceps and triceps reflexes are absent in the right arm. He says that he cannot feel when you touch his hand or forearm until you get up to mid-humerus, and that sensations don't become perfectly normal until you reach the shoulder.

What is the anatomic explanation for the paralyzed, anesthetic arm? The marked induration and weakness should immediately point you to the muscle itself. The most common cause of an acutely paralyzed and swollen muscle is ischemia, either from lying on the muscle for a prolonged period or embolic infarction. This can be an explosive situation, because infarcted muscle releases myoglobin into the circulation which may precipitate renal failure from acute tubular necrosis. The severe sensory loss probably results from peripheral nerve compression by the swollen, indurated muscles.

CASE #11

You are asked to see a 65-year-old alcoholic admitted three weeks ago for acute abdominal pain which, at laparotomy, was due to a perforated gastric ulcer eroding into the pancreas. Ten days ago he developed gram negative sepsis, and two days ago he became stuporous with disconjugate gaze.

On exam, his blood pressure is 170/105, pulse 95, temperature 102° rectally, and he is intubated. The patient is drowsy, requiring shaking and pinching to keep him awake. He makes only brief eye contact but will follow most simple commands when they are repeated loudly. His neck is modestly stiff.

Intracranial Pus: It's always better to culture a site of infection before beginning antibiotics, because antibiotics kill only a selective range of bacteria. If in a day or so the antibiotic you choose doesn't work, you can switch to another antibiotic that *will* kill the bacterium. But you can only choose the correct antibiotic by first identifying the bacterium and testing its vulnerability against a number of different antibiotics.

It is unclear if he reacts to threat. There is no Marcus Gunn and the disc are flat without retinal hemorrhages. He does not fully abduct his left eye on left gaze, nor his right eye on right gaze. He seems able to look up and down well but there is modest bilateral ptosis. No nystagmus. Pupils are 3mm and briskly reactive. Corneals are present; grimacing to pain is symmetrical but you can easily lift open his clenched eyelids.

Tone in the arms and legs is normal. He uses both arms and legs symmetrically, but his grip, biceps, and deltoids are moderately weak bilaterally. He is only able to keep his arms elevated for five seconds before they drift. In the legs he can only lift his feet 6-8 inches off the bed and foot dorsiflexion is moderately weak bilaterally. Finger and toe tapping are (within the limits of testing) probably normal.

Reflexes are 1+ and symmetrical throughout. Toes are downgoing.

Sensory exam in intact to pin bilaterally.

First the abnormalities: mild stupor, bilateral lateral rectus weakness, bilateral ptosis, and weakness of the proximal and distal muscles in the arms and legs. Bilateral lateral rectus weakness indicates a lesion somewhere between the lateral rectus muscles and the VIth nerve fascicles (but not in the VIth nerve nuclei; lesions here would produce bilateral gaze palsies). One critical question is the nature of the weakness in his arms and legs. If he has pyramidal tract weakness, the VIth nerve palsies are intra-axial. If the weakness is peripheral, the VIth nerve palsies are more likely due to an extra-axial lesion. Another important question is whether the stupor is related to the lateral rectus weakness, ptosis, and weakness of the extremities, or instead to sepsis or other blood-borne problem.

Except for the weakness in his proximal and distal muscles, there are no other pyramidal tract signs: the tone in his arms and legs is normal, rapid alternating movements are performed reasonably well, the reflexes are not increased, and the toes are downgoing. But acutely, pyramidal tract lesions may not produce spasticity, hyperreflexia, and upgoing toes. In addition, it would be very dangerous to assume that his stupor is *not* resulting from the same neurologic insult causing his other neurologic signs. Because he may have pyramidal tract lesions, and because the stupor may be related to his weakness, we are stuck having to include intra-axial lesions in our etiologic differential diagnosis of bilateral lateral rectus weakness.

Lateral Rectus Muscles	Abducens Nerves in Cavernous Sinus or Orbit	Abducens Nerves in Subarachnoid Space	Abducens Nerve Fascicles
Drug-induced myasthenia gravis	Septic thrombophlebitis	Tuberculous meningitis	Wernicke's encephalopathy
Myasthenia gravis	Botulism	Cryptococcal meningitis	Cerebellar hemorrhage
	Miller Fisher variant of Guillain Barre	Syphilitic meningitis	Cerebellar abscess
		Bilateral Gradenigo's syndrome	
		Increased intracranial pressure	

The combination of ptosis, bilateral lateral rectus weakness, and weakness below the shoulders could well be primary myasthenia gravis or drug-induced myasthenia from aminoglycoside antibiotics.

Bilateral septic thrombophlebitis is possible but higher fever, deeper coma, more ophthalmoplegia, and proptosis with severe chemosis would make this diagnosis more tenable.

To seriously consider botulism, you ought to see more ophthalmoplegia than this man has (considering the degree of his peripheral weakness), and the pupils should be at least somewhat sluggish to light. Still, botulism is a consideration.

The Miller Fisher variant of Guillain Barre is possible. Against this diagnosis is its apparent confinement to the VIth nerves without involvement of III or IV.

Tuberculous and cryptococcal meningitis could entrap the VIth nerves or stretch the VIth nerves by raising intracranial pressure. Even without papilledema, raised intracranial pressure is a serious contender because not every patient with elevated intracranial pressure has papilledema. Syphilitic meningitis (stage II) would be more likely if the patient also had a maculopapillary rash. Gradenigo's syndrome (abducens palsy secondary to inflammation in the apex of the petrous bone) amidst sepsis could conceivably cause stupor and weakness, but bilateral Gradenigo's must be distinctly rare.

Wernicke's encephalopathy and cerebellar masses are also causes of brainstem, cortical, and mild long tract signs, as discussed in previous cases.

Now what? You can administer thiamine, but you still have a patient who needs to be tapped to rule out meningitis. However, you're considering a diagnosis of raised intracranial pressure and at this point you should be wondering if his hypertension might be an early Cushing response. Is there really enough room between the patient and his brainstem to risk doing a spinal tap before the CAT scan?

Unfortunately, this postoperative patient is too encumbered with tubes and wires to be conveniently transported to CAT scan. Unless you enlist extraordinary help in transporting him, you have little choice but to tap him with a neurosurgeon ready to do a second tap into the lateral ventricle (to equalize pressures above and below the brainstem) if the patient begins to deteriorate after the spinal tap. What you must weigh in making your decision is the likelihood of the patient deteriorating after the tap versus the likelihood of harm resulting from the two hour delay in getting the CAT scan or some catastrophe occurring while transporting him to CAT scan.

This patient was tapped without a CAT scan. His CSF had an opening pressure of 320mm, 75 lymphocytes/mm^3, protein 105mg%, and glucose 40mg% (serum glucose 130mg%). Acid fast stain of the centrifuged spinal fluid was positive, and the patient was begun on antituberculous medication. Mycobacterium tuberculosis was positively identified from cultures a month later.

CASE #12

A 50-year-old laborer has suffered for a number of years with low back pain radiating into his right leg. In the past few months the pain has become more severe, but three days prior to admission his back pain suddenly disappeared. Since then, however, the patient has noted numbness around his buttocks and difficulty walking, especially up stairs.

On exam his mental status and cranial nerves are normal. He has significant trouble getting up from a chair. He can walk with caution, but cannot climb stairs without pulling himself up by the railing. There is no ataxia. His arms are entirely normal. In the legs there is no atrophy or fasciculations and the tone is normal. He has moderate (grade 4-) weakness of the gastrocs, hamstrings, and glutei bilaterally; modest weakness (grade 4) of both tibialis anterior muscles; and mild weakness (grade 4 +) of both (grade 4 +) of both psoas and quadriceps muscles. He cannot stand on either leg alone, but he can toe tap rapidly with either foot. Heel-shin is normal. Rectal tone is diminished and he cannot tightly squeeze your finger with his anal sphincter.

Reflexes are 2 + in the arms and 1 + at the knees and ankles. Toes are downgoing.

Sensory exam reveals moderately severe diminution of pin sensation around the anus with gradual improvement as you march the pin up the buttocks and back, reaching normal skin at about L5.

The major problem in this case is anatomic localization and recognition of the urgency of the situation. This man has the cauda equina syndrome: weakness in a relatively symmetrical pattern from about L1 down (psoas is L1,2,3), maximally involving the lower lumbar and sacral regions. This anatomic distribution is confirmed by the sensory loss, also maximal in the lower sacral dermatomes. Whatever the etiology, an acute cauda equina syndrome is an urgent problem requiring emergency myelography to define the anatomy of the involved region. Etiologically, this man has almost certainly extruded his lumbar disc into the caudal spinal canal, compromising the cauda equina.

LABORATORY TESTS

THE LAB IS A HANDY but expensive way to narrow the anatomic diagnosis and track down etiologies. Some lab tests, like the urinalysis, tell you which organ system is not working, but not why. Other lab tests (like a positive blood culture) give you an etiology without telling you where the problem is. The more powerful lab tests tell you both.

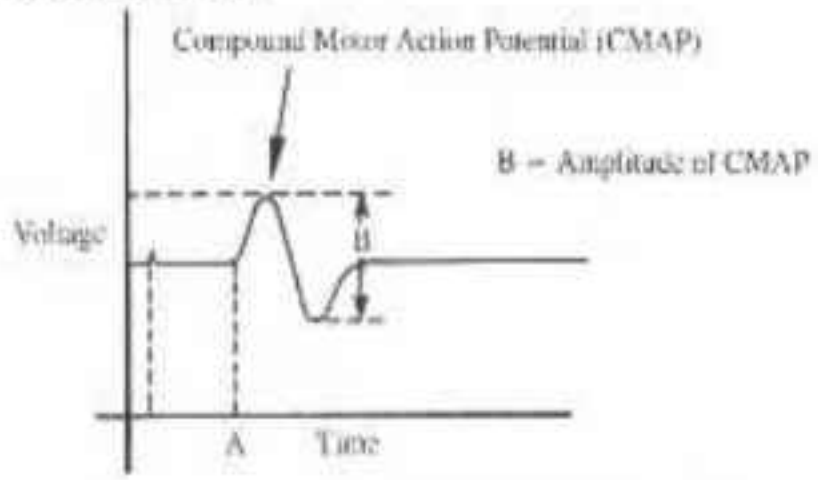
Which lab tests to order and when to order them is something learned and refined over years of practice. In ordering lab tests, ask yourself several things.[1] First, are you at a therapeutic crossroads? Do you really need the information to make a therapeutic decision? Second, is the risk/benefit ratio low enough? That is, should the patient risk the morbidity (complications) of the test for the amount of information likely to be learned from the test?

Some of the more commonly used neurologic tests include nerve conduction velocity (NCV), repetitive nerve stimulation, muscle biopsy, electromyography (EMG), electroencephalography (EEG), brainstem auditory evoked response (BAER), visual evoked response (VER), sensory evoked response (SER), and blood gases. Each of these is powerful if you don't demand more of them than they can deliver.

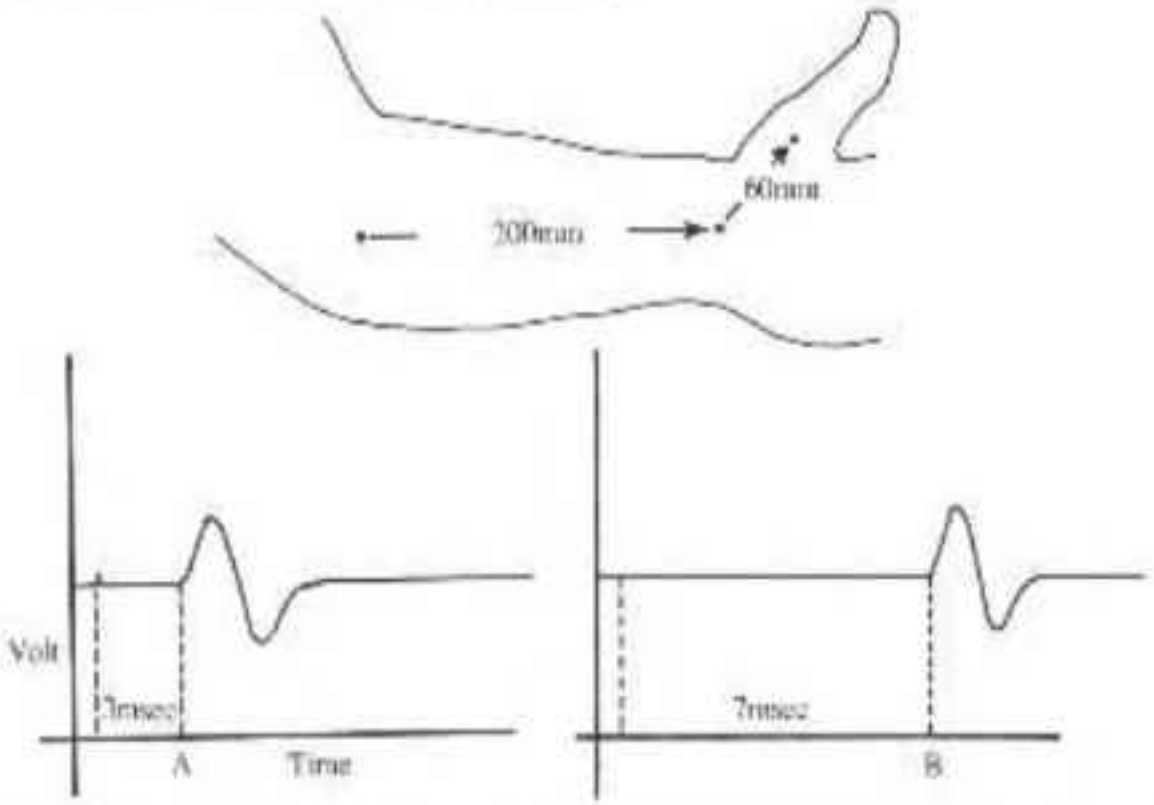
Nerve Conduction Velocity: Radiculopathies

Nerve conduction velocities and electromyography are very effective ways to ferret out the site of peripheral weakness: nerve cell body, root, peripheral nerve, neuromuscular junction, or muscle. But both tests require some background understanding to use them optimally.[2]

First of all, nerve conduction velocity measures only the *fastest* axons. The reason for this is inherent to the method of measurement. Nerve conduction velocity is measured in two steps. Using the median nerve as an example, the first step is to electrically stimulate the median nerve at the wrist, producing a brief contraction of the thumb muscles. This mechanical movement is also an electrical event, the compound motor action potential, recorded by a pickup electrode taped to the thumb and displayed on an oscilloscope screen.



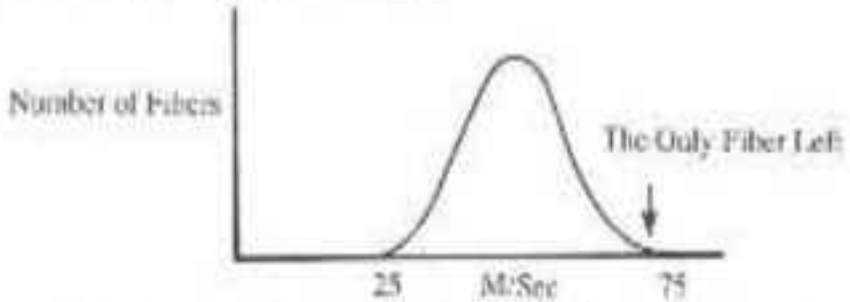
The first electrical impulse to reach the muscle does so at point A, the point from which nerve conduction velocity measurements are taken. By measuring the distance from the stimulating point at the wrist to the recording electrode over the thumb, we can calculate the nerve conduction velocity for the fastest axons—those arriving at point A: velocity = distance/time. For example, if the distance is 60 mm and it took 3 msec, then the velocity is 20 meter/sec. The fly in the ointment is that this 3 msec includes the time it took electricity to travel down the peripheral nerve, stimulate the terminal boutons to release acetylcholine, for acetylcholine to be released from their packets and diffuse across the synaptic cleft, then stimulate the postsynaptic receptor, and for that receptor to send an electrical impulse into the muscle to begin the contraction. The 3 msec, representing all these steps, is called the terminal latency. To determine the true nerve conduction velocity, repeat the terminal latency measurement from a place upstream in the antecubital fossa. Suppose this new terminal latency is 7 msec, which means it took 4 msec for electricity to travel from the antecubital fossa to the wrist. This distance, which you measure on the patient at say 20 cm (200 mm), now gives us distance/time = velocity, or 200 mm/4 msec = 50 meters/sec, the true nerve conduction velocity.



The limitation of nerve conduction velocities is that only the fastest fibers are measured; ignored are all the other axons in that peripheral nerve conducting over a spectrum of velocities. A cross section of any nerve reveals axons of varying diameter which conduct at varying velocities—the larger the diameter, the faster the velocity. By measuring the diameter of each myelinated axon*, the number of myelinated axons of each size can be tabulated, and since the velocity is directly determined from the axonal diameter, the number of axons conducting at any given velocity can be depicted. As a rough estimate, the fastest myelinated fibers conduct at 75 m/sec, the slowest at 25 m/sec, and the commonest ones at about 50 m/sec.

Myelinated Axon: Most axons within a peripheral nerve are unmyelinated, conducting routine information slowly, less than 25 meters/sec.

If we begin poisoning the nerve with a toxin that destroys the slowest axons first, we eventually reach a point where only a single axon remains, the one that conducts at 75 m/sec. We've produced a 99+% peripheral neuropathy, but what is the nerve conduction velocity? Still 75 m/sec! You'd know something was wrong if you looked at the amplitude of the compound motor action potential which, in this example, would be a mere blip on the oscilloscope[6]. The take-home message is not to rely solely on the nerve conduction velocity.



This problem becomes important when you order common peroneal nerve conduction velocities for a low back pain patient with a recent foot drop. You expect a dramatic slowing of nerve conduction velocity to confirm his L5 radiculopathy, but instead the nerve conduction velocity is normal.[3] Here's why. In the worst possible case, let's suppose the L5/S1 disc completely severed the L5 root. What happens to the nerve conduction velocity? Nothing, because a peripheral nerve is made up of several different roots, and as long as there are normal fast axons from an uninvolved root, the nerve conduction velocity will be normal. So when you order a nerve conduction velocity to confirm a radiculopathy, you should *expect* the nerve conduction velocity to be normal. If the common peroneal nerve conduction velocity *were* abnormal, then you would need to consider focal compression of the common peroneal nerve at the fibular head.

Nerve Conduction Velocity: Mononeuropathies

Nerve conduction velocity is most helpful in pinpointing focal compression of a nerve. Because focal nerve compression causes focal demyelination, nerve conduction slows as it crosses the site of compression, but then picks up speed beyond the compression.[4] In certain places, like the carpal tunnel at the wrist, a terminal latency cannot be accurately measured beyond the carpal tunnel, so you can't determine the nerve conduction velocity across the carpal tunnel.[5] To document focal compression of the median nerve at the carpal tunnel, only a prolonged terminal latency is used. A normal terminal latency across the carpal tunnel is less than 3.5 msec. Severe carpal tunnel compression can prolong the terminal latency to 6 msec or more.

Sensory Nerve Conduction Velocity

Sensory nerves in the hand are stimulated by wires wrapped around one of the fingers. The impulse is recorded along the proximal median (or ulnar) nerve. As long as the sensory axon is attached to its cell body in the dorsal root ganglion, the axon remains alive and well. Suppose you find *severe* sensory loss in the hand and arm, but the sensory nerve conduction velocity is normal. The lesion must then be on the spinal

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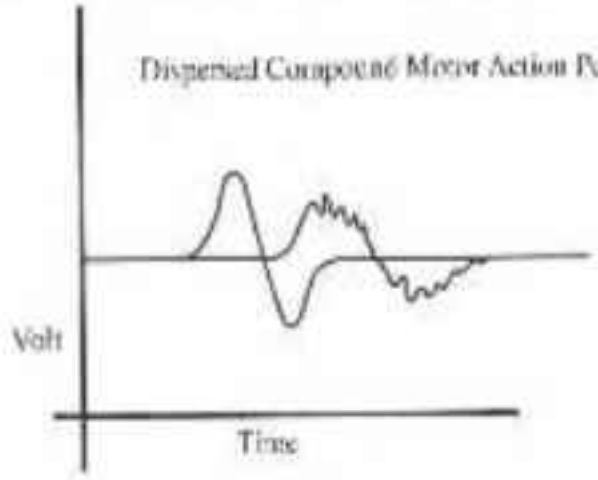
Blip on the Oscilloscope: The compound motor action potential may remain reasonably large if, as individual axons are being destroyed, neighboring intact axons sprout new axonal terminals to reinnervate the muscle fibers being destroyed (see text below).

cord side of the dorsal root ganglion, either in the root or in the cord itself. This situation becomes important after serious neck trauma that leaves the patient's arm flail (completely paralyzed) and anesthetic (absolutely no sensation). Is there any chance the arm will recover? If the sensory nerve conduction is normal, no, but if the sensory nerve conduction is abnormal, yes! An abnormal sensory nerve conduction velocity means that the lesion is likely in the brachial plexus and that the nerves may still regrow. A normal nerve conduction velocity means that the C6,7, and 8 (and probably C5 and T1, too) roots have been avulsed (torn) from the spinal cord, meaning no recovery.[6] Syringomyelia is another good example of non-traumatic sensory loss in the arm with normal sensory nerve conduction velocities.[7]

Nerve conduction Velocity: Polyneuropathies

Peripheral nerve insults tend to preferentially attack either the axon or the myelin jacket. Nerve conduction velocity measurements can sometimes distinguish between these two types of peripheral neuropathies.

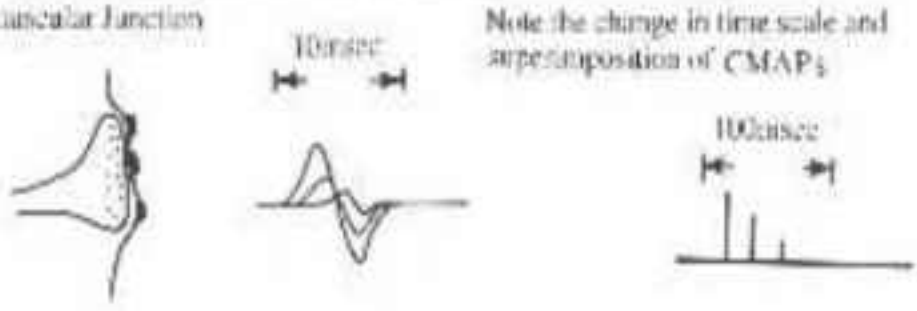
A normal nerve conduction velocity depends on intact myelin which, in turn, depends on intact axons.[8] If we progressively destroy the fastest axons in a peripheral nerve, we will eventually reach the slowest myelinated fiber at about 25 m/sec. If the nerve conduction report, however, returns with a nerve conduction velocity of 15 m/sec, what conclusion do you draw? The most severe, purely axonal neuropathy conducts at 25 m/sec, so less than this must mean the neuropathy is demyelinative.[9] Above 25 m/sec, you can't be sure if the neuropathy is demyelinative or axonal. A strong clue, though, is dispersion of the compound motor action potential. Demyelination slows some axons to 40 m/sec, some to 30 m/sec, 20 m/sec, and 10 m/sec. Instead of all the nerve impulses reaching the muscle at roughly the same time (which would produce a smooth and narrow compound motor action potential), the slower demyelinated axons arriving later spread out (disperse) the compound motor action potential.



Nerve Stimulation: Neuromuscular Blockade

Nerve stimulation can help assess acute weakness. If you discover an abnormally small but undispersed compound motor action potential, then the block must be somewhere between stimulating electrode and the muscle itself. A muscle paralyzed by an intramuscular lesion, such as hypokalemia, won't contract to direct electrical stimulation of the muscle. Other causes of acute weakness with a small compound motor action potential are shellfish poisoning (saxitoxin) which blocks conduction along peripheral nerves, tick paralysis which blocks conduction in terminal axonal twigs, and botulism, myasthenia gravis, and drug-induced myasthenia which block transmission in the neuromuscular junction.

Neuromuscular blockade is better detected by repetitively stimulating the peripheral nerve two or three times a second. After the first few impulses, the amount of acetylcholine released for the next few impulses decreases, even in normals.[10] Normal muscles don't care; they have so many acetylcholine receptors that if a few less are stimulated, there'll always be enough to fire off the muscle[*]. Not so in myasthenia gravis in which acetylcholine receptors are already being destroyed by an antibody mediated attack. In some neuromuscular junctions the number of acetylcholine receptors may be so critically reduced, that without maximal acetylcholine delivery, the neuromuscular junction may not fire off its particular myofibril (sliver of muscle). After those first few robust nerve stimuli, then, each electrical impulse fires fewer myofibrils until, three or four impulses later, the amount of acetylcholine released with each impulse improves again. On the oscilloscope the compound motor action potential becomes smaller for a few impulses.



Fortunately, after those few weaker nerve impulses, neuromuscular transmission improves again,[12] probably because of local accumulation of calcium in the terminal bouton with each new impulse. Calcium facilitates the release of acetylcholine, improving neuromuscular transmission and thereby returning the compound motor action potential to its previous amplitude.[13]

This increase in the compound motor action potential is even more evident with rapid nerve stimulation which allows calcium to accumulate rapidly in the terminal bouton. But if repetitive stimulation is attempted again after a few minutes, the decremental response is even *more* prominent than it was the first time around, called "post tetanic exhaustion."[14]

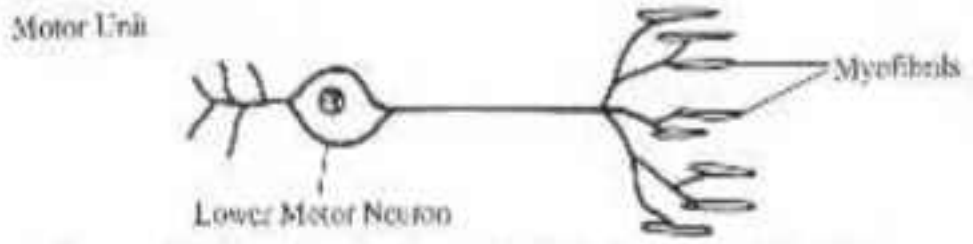
Rapid nerve stimulation is particularly effective in temporarily overriding the neuromuscular block caused by botulism or the Eaton Lambert syndrome, two conditions which prevent the release of acetylcholine from the presynaptic junction.[15] Interestingly enough, every muscle in the body demonstrates the characteristic incremental response to repetitive stimulation, even those muscles with normal strength. This is quite unlike myasthenia gravis in which only the weak muscles demonstrate a defect in neuromuscular transmission.

Fire Off the Muscle: Daube speculates that neuromuscular junctions above the shoulder have less of a 'safety factor' than those below, explaining why illnesses of the neuromuscular junction preferentially affect the cranial nerves.[11]

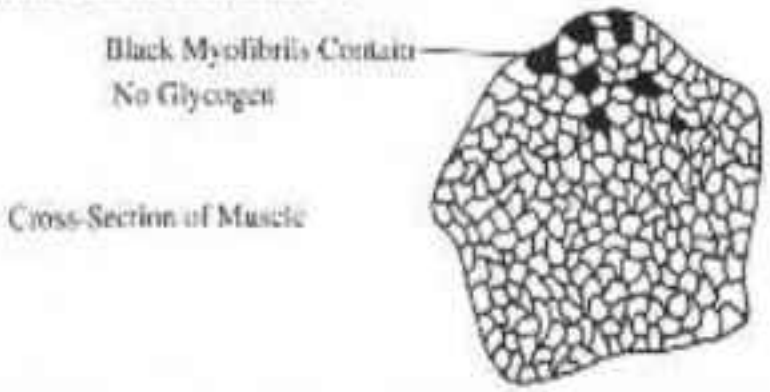
The initial decrease in the compound muscle action potential is not the physiological correlate of myasthenic weakness. Myasthenic muscles weaken after a minute or more because of some poorly understood failure of neuromuscular transmission. The weakness is not because all the neuromuscular receptors have become occupied by acetylcholine (in which case Tensilon, the drug that strengthens myasthenic muscles, would worsen the weakness by overwhelming the receptors with even more acetylcholine).

Electromyography

Electromyography, like the nerve conduction velocity measurement, can be very helpful with a little physiological background. Every muscle is made up of thousands of individual myofibrils which are divvied up into groups, each group innervated by a single lower motor neuron. Some lower motor neurons, like ones to the eye muscles, exert accurate control by governing only a few myofibrils, while other lower motor neurons, to the quadriceps for example, simultaneously innervate hundreds of myofibrils. A lower motor neuron and all of its myofibrils, taken together, constitute a motor unit.



How are the myofibrils of a single unit situated: clumped together or scattered throughout the muscle? Kugelberg ingeniously sorted this problem out in the 1960's by vigorously stimulating a single axon in order to deplete the glycogen within the motor unit. He then removed the muscle, cross-sectioned it, and stained for glycogen. He found that single motor units are scattered across about one fifth of the cross-section of a muscle fascicle*.[15]



You can monitor a single motor unit's electrical activity by means of a recording needle stuck into the muscle. Displayed on an oscilloscope, each motor unit has both an amplitude and a duration. The more myofibrils in a unit, the higher the amplitude; the more widely scattered the myofibrils, the longer the duration.

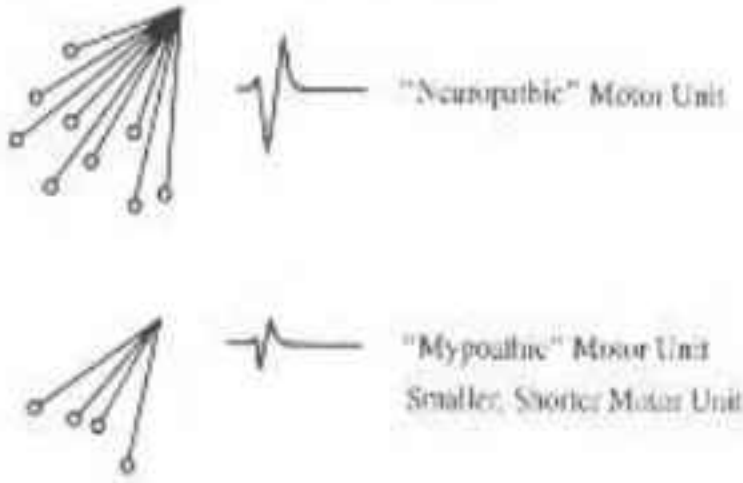
What happens to the myofibrils in a motor unit if we cut the axon innervating them? Without axonal domination, myofibrils are now free to contract at will. The oscilloscope records these spontaneous contractions as positive sharp waves and fibrillations, neither of which are visible under the skin to the naked eye (only fasciculations are). Once positive sharp waves and fibrillations develop, indicating that the axon has separated from its myofibrils, what happens to the muscle now? In a rather touching physiologic gesture, the orphaned myofibrils are adopted by neighboring axonal sprouts, making the new motor unit—now with all those extra myofibrils—that much larger.

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*Fascicle: A bundle of myofibrils. Fascicles are separated from one another by a thin covering of connective tissue. The fascicular structure of beef is well seen in corned beef.



As you'd expect, the oscilloscope reads these new motor units as large amplitude. Since the motor unit area is larger, it takes longer for all the myofibrils to report to the recording needle, so the units also become longer in duration. If the EMG report, then, describes the motor units as large amplitude and long duration, there must have been, at some point, a neuropathic insult to the muscle and subsequent reinnervation. A myopathic illness, in contrast, damages individual myofibrils, making each unit smaller. Electromyography in myopathic weakness will then report small amplitude, short duration units.



Muscle Biopsy

Muscle biopsies distinguish myopathies from neuropathies and frequently uncover the etiologic diagnosis too. Muscles are made up of two types of myofibrils: type I and type II. Type I is akin to the dark meat of chicken, and type II, the white meat. Dark (red) meat in the leg is used for low-key activities like milling around. White breast meat is needed for sudden bursts of activity to flee enemies or attack dinner. This functional distinction adds an extra label to muscles—Type I, red, slow ("IRS"); Type II, white, fast.

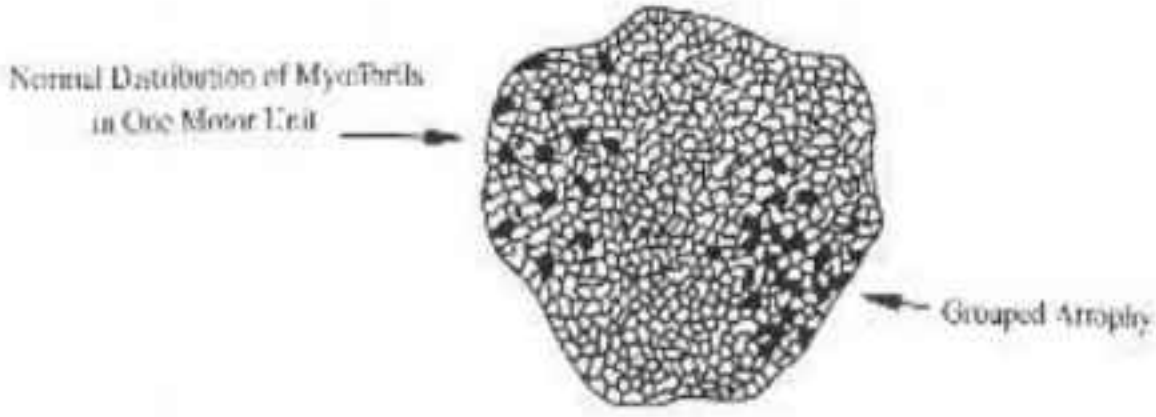
Some people favor dark meat because it's juicier (greasier) than white meat. The grease in red meat is fat for energy, an energy source which white meat does not depend on. Fat is metabolized to a long-chain lipid called palmityl CoA, which is shunted into the mitochondria of red muscle. Inside the mitochondria palmityl CoA is broken down into fragments of acetyl CoA for the Kreb's cycle. Meanwhile, oxygen captured by muscle myoglobin* (hence the dark red color) also enters the mitochondria to crank the cytochrome cycle. The net result of this slow but dependable machinery is that fat becomes converted to a large supply of ATP.

Myoglobin: Animals that don't have ready access to air—seals and whales—have a particularly high concentration of myoglobin.[1]

White meat doesn't produce a slow steady supply of ATP and therefore has relatively few mitochondria and minimal supporting machinery: blood vessels, myoglobin, and fat. For that sudden burst of breast beating, though, white meat *can* produce a lot of ATP in a hurry via the glycolytic pathway, but only at the expense of lactic acid buildup, a debt which must be paid later when the animal can rest.

In humans, type I and type II fibers are randomly scattered throughout each muscle of the body instead of the bulk separation of fowl. Since each muscle fiber type is determined by the type of axon innervating it (!), if a type II axon dies and a neighboring type I axon adopts the orphaned myofibrils, the new larger motor unit will be a type I unit.[18] If you then biopsy the muscle and stain it for mitochondria (type I fiber), you'll see 'fiber type grouping' instead of the random distribution of type I and II myofibrils.

If that type I axon—the one innervating the larger unit—becomes injured before the biopsy, you'll see a cluster of atrophic type I fibers called 'grouped atrophy.' So fiber type grouping and grouped atrophy indicate a neuropathic process. Myopathic processes, in contrast, damage individual myofibrils without altering the basic mosaic of fiber types[*].[19]

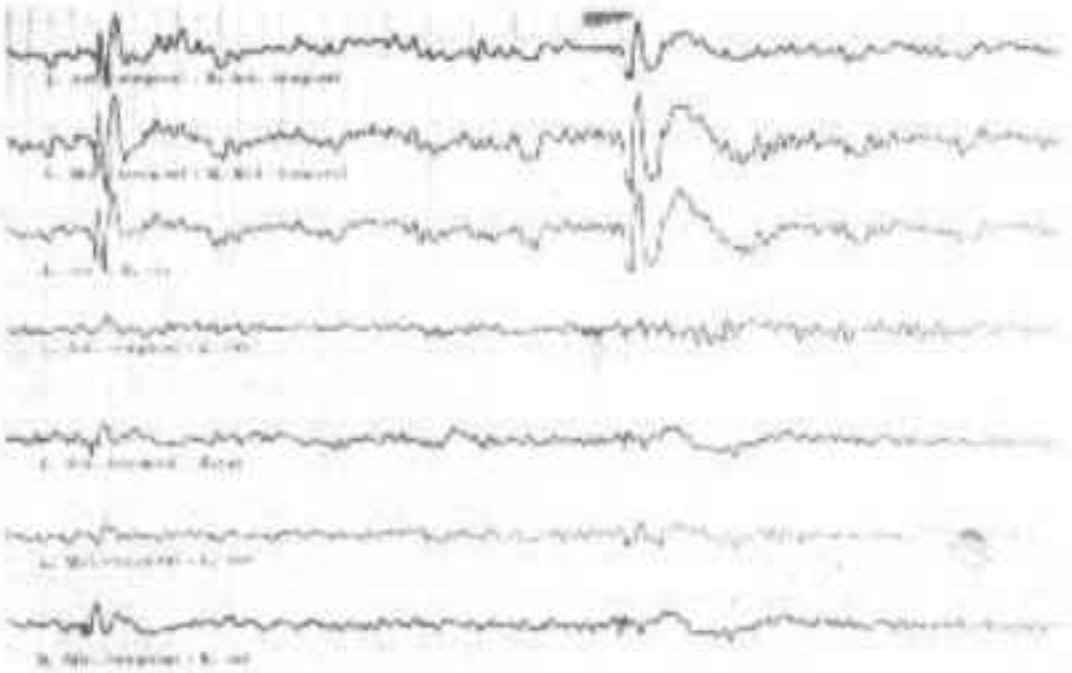


Electroencephalography (EEG)

Unlike the CAT scan which measures anatomy, the EEG measures function. But without an acknowledgement of its limitations, the EEG can assume greater significance than it deserves. The most common misuse of the EEG is to tell if a patient has epilepsy. Epilepsy is a clinical diagnosis, not an EEG diagnosis. You ought to know *before* you do the EEG whether the patient is having seizures. In unwitnessed spells of unconsciousness, the EEG can, admittedly, make you very suspicious of seizures if there are 'epileptiform' discharges on the record, but be sure the discharges are epileptiform. It's common for curious or suspicious, but clinically insignificant, blips and squiggles to occur in the EEG of a normal person.[20] You've sent the patient to the EEG lab for evaluation of an uncertain spell. If you then superimpose an uncertain lab finding on that uncertain spell, your diagnosis of a seizure disorder rests on rather shaky ground.

Mosaic of Fiber Types: Other important pathologic features of myopathies include: migration of muscle nuclei into the interior of myofibrils, marked variation of fiber size (neuropathic myofibrils are either normal size or small and atrophic), and rounding up of myofibrils (in neuropathic atrophy the myofibrils are angulated).

Optimally, an epileptiform discharge should have the following features:[21] 1) the discharge should be a spike (less than 80 msec in duration, or it should hurt if you sat on it); 2) the spike should have a slow wave following it; 3) the spike and wave complex should stand out from the background (be greater than 50% of the background amplitude); and 4) the discharge should be discernible in an entire region of the head, not in just a single electrode; that is, the discharge should be maximal in one electrode and taper off in electrodes further and further from the site of origin. Obviously, there are bonafide epileptiform discharges which meet only one or two (and occasionally none) of these criteria, but be cautious about overinterpreting the EEG if these features are not seen.[21]



In known seizure patients, the EEG helps distinguish focal from non-focal seizure foci. Seizures which appear nonfocal clinically may actually begin on the EEG from a specific cortical area (signifying focal cortical pathology) and activate the opposite hemisphere, called secondary bilateral synchrony*. Even when the EEG discharges appear symmetrical in the two hemispheres, go back and check carefully for two EEG features suggesting an origin in one hemisphere: 1) the *first* spike consistently beginning in one hemisphere, or 2) a 'recruiting rhythm' in one hemisphere culminating after several seconds in a synchronous bihemispheric discharge.[23]

The other major misuse of the EEG is to determine how much brain damage there is or to see if a patient's stroke or other cerebral lesion is improving. Both of these questions are more accurately answered clinically.

You can minimize misuse of the EEG by posing a specific question for the EEG each time you order one. This forces you to question whether the EEG can realistically answer the question you pose for it.

Secondary Bilateral Synchrony: Primary bilateral synchrony is a discharge that begins truly synchronously in both hemispheres. One explanation for the synchrony is that the epileptic focus begins in a deep midline structure and spouts the discharge upward to both hemispheres. Another explanation is that the cortical focus, unseen by the EEG, projects its discharge across the corpus callosum or south into deep midline structures, and then synchronously back up to both cerebral hemispheres.[22]

Electroencephalography is occasionally helpful in assessing stupor, coma, and confusion.[22] I use the word occasionally because an EEG usually just demonstrates widespread slowing of the background frequency*. Bihemispheric slowing only means that the cortex in both hemispheres is not working normally, a fact you already knew before the EEG. A normal EEG, on the other hand, will help uncover pseudodementia—patients so depressed they appear demented.

The unexpected finding in stuporous or comatose patients, one that won't show up on CAT scan or lumbar puncture, is ongoing epileptic activity. Once in a while a confused or stuporous patient will have ongoing electrical seizure activity without concomitant clinical jerking. These patterns are not common, but they do narrow the anatomic and etiologic differential diagnosis when present. We've already mentioned (chapter 38) runs of petit mal and psychomotor status. Bihemispheric *periodic* complexes (repetitive bursts of epileptiform discharges) suggest certain hihemispheric cortical diseases like herpes simplex encephalitis, subacute sclerosing panencephalitis, and Jakob Creutzfeldt disease.[4,23]

Another periodic discharge—this time from only one hemisphere—is called periodic lateralized epileptiform discharges (PLEDS), a pattern seen in all sorts of cerebral insults including herpes simplex encephalitis, tumors, subdurals, and strokes. The patients are frequently in coma, but whether PLEDS contribute to the coma or are only associated with the coma is still unclear. In any case PLEDS tend to disappear after several weeks regardless of therapy.[26] A relatively common pattern seen in stuporous or confused patients is triphasic waves, characteristic of liver or renal failure.[27]

The EEG does help predict the severity and outcome of coma. A monorhythmically slow EEG, one without changes in frequency corresponding to changing levels of consciousness and sleep, indicates a serious disruption of normal physiology.[28] Once in a while you may come across 'alpha coma,' a pattern that, because of good-looking alpha activity, looks surprisingly normal until you spot that the alpha activity is better in the *frontal* instead of the occipital head regions, and that the alpha activity doesn't attenuate to stimulation the way normal alpha activity does. Patients with this pattern have usually suffered a severe cortical or brainstem insult.[29]

Brainstem Auditory Evoked Response

The brainstem auditory evoked response (BAER) is an offspring of electroencephalography. Instead of recording electrical activity from the cerebral cortex, the auditory evoked response records electrical impulses ascending through the brainstem auditory pathway. A series of clicks is introduced through earphones worn by the patient. Beginning at the cochlea, the electrical response to each click travels up a strictly organized brainstem pathway, making mandatory synaptic connections at specific brainstem nuclei. Footprints left by electrical impulses along the brainstem auditory pathway are recorded by an electrical tracing as specific, dependable peaks, each electrical peak corresponding to a brainstem level. By measuring the latency to each peak, you can readily detect a delay between brainstem levels.[30] Despite its exquisite

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Background Frequency: Brain wave activity is measured in cycles per second, or Hertz (Hz). Normal background frequency in the awake state is 8–13Hz (alpha). Slower frequencies range from 4–7Hz (theta) to 1–3 Hz (delta). Above 13Hz is called beta activity.

Jakob-Creutzfeldt Disease: An idiopathic, rapidly (months) fatal infection of the brain producing dementia, myoclonus, and seizures.[31]

sensitivity to subtle abnormalities, the auditory evoked response is limited by its narrow view of the brainstem. Significant lesions outside the auditory pathway will go undetected unless pressure or edema affect the auditory pathway.

Visual Evoked Response

The same principle used for auditory evoked responses is used for the visual evoked response. Instead of clicks, flashes of light in each eye stimulate an electrical response which is recorded by wires over the occiput.[31] Delayed electrical peaks indicate a lesion within the visual system. The VER is far more sensitive to lesions in the optic nerve than to lesions in or behind the chiasm.[32] Don't be intimidated by the VER; despite its sensitivity, the VER is not that much better than a good neuroophthalmologic exam.[33]

Sensory Evoked Potential

Sensory evoked potentials record the electrical response to peripheral nerve stimulation. Depending on where the recording electrodes are placed, the sensory evoked response may be used to detect delay within peripheral nerves (especially within the thoracic outlet where nerve conduction measurements are notoriously difficult to obtain[34]), the posterior columns, or even higher up in the hemispheres.[35]

Blood Gases[36]

Any change in serum pH is met by an immediate compensatory response from the lungs and kidneys which return the pH about halfway to normal by manipulating the serum pCO_2 and HCO_3.

Blood gases allow you to interpret at what stage (acute or chronic) and by what means (pCO_2, HCO_3, or both) the lungs and kidneys are correcting the serum pH. Blood gases measure the pO_2, pH, pCO_2, and HCO_3 in arterial blood. Approaches vary, but the following is one useful way to approach the blood gases.

First, check the pO_2 to make sure the patient is receiving enough oxygen. Next, look at the pH: is the patient acidotic or alkalotic? Decisions from here on depend on whether the patient is acidotic or alkalotic.

Acidosis: If the *pCO_2 is high*, the patient's acidosis is respiratory, and the only question then is whether the respiratory acidosis is acute or chronic. A chronic respiratory acidosis gives the kidneys time to respond (by retaining HCO_3), so the HCO_3 will be high; otherwise, in acute respiratory acidosis, the HCO_3 will remain near normal, 25 meq/L.

How high should the kidneys raise the HCO_3 in chronic respiratory acidosis? The kidneys raise the serum HCO_3 about 40% of the rise in pCO_2. So, a pCO_2 of 60mm, 20mm above normal, should raise the serum HCO_3 by 8 meq, to 33 meq/L. If the HCO_3 is higher than 33 meq/L, the patient must also be suffering a simultaneous metabolic alkalosis, like gastric suction which removes H^+ and KCl.

If, in a chronic respiratory acidosis, the HCO_3 is significantly less than 40% of the pCO_2 elevation, then there must also be a metabolic acidosis. Combined metabolic and respiratory acidosis commonly occur in pulmonary patients who walk around with chronic respiratory acidosis, and who suddenly develop a superimposed, acute metabolic acidosis due to insults like sepsis, renal failure, or methanol intoxication.

If the *pCO_2 is low*, the patient's acidosis is metabolic, the low pCO_2 merely representing the lungs' attempt to compensate by creating a mild respiratory alkalosis. Unfortunately, there is no way, looking at the HCO_3, to distinguish an acute metabolic acidosis from a chronic one, because a metabolic acidosis strips the kidney of its only compensatory defense against acidosis, namely HCO_3.

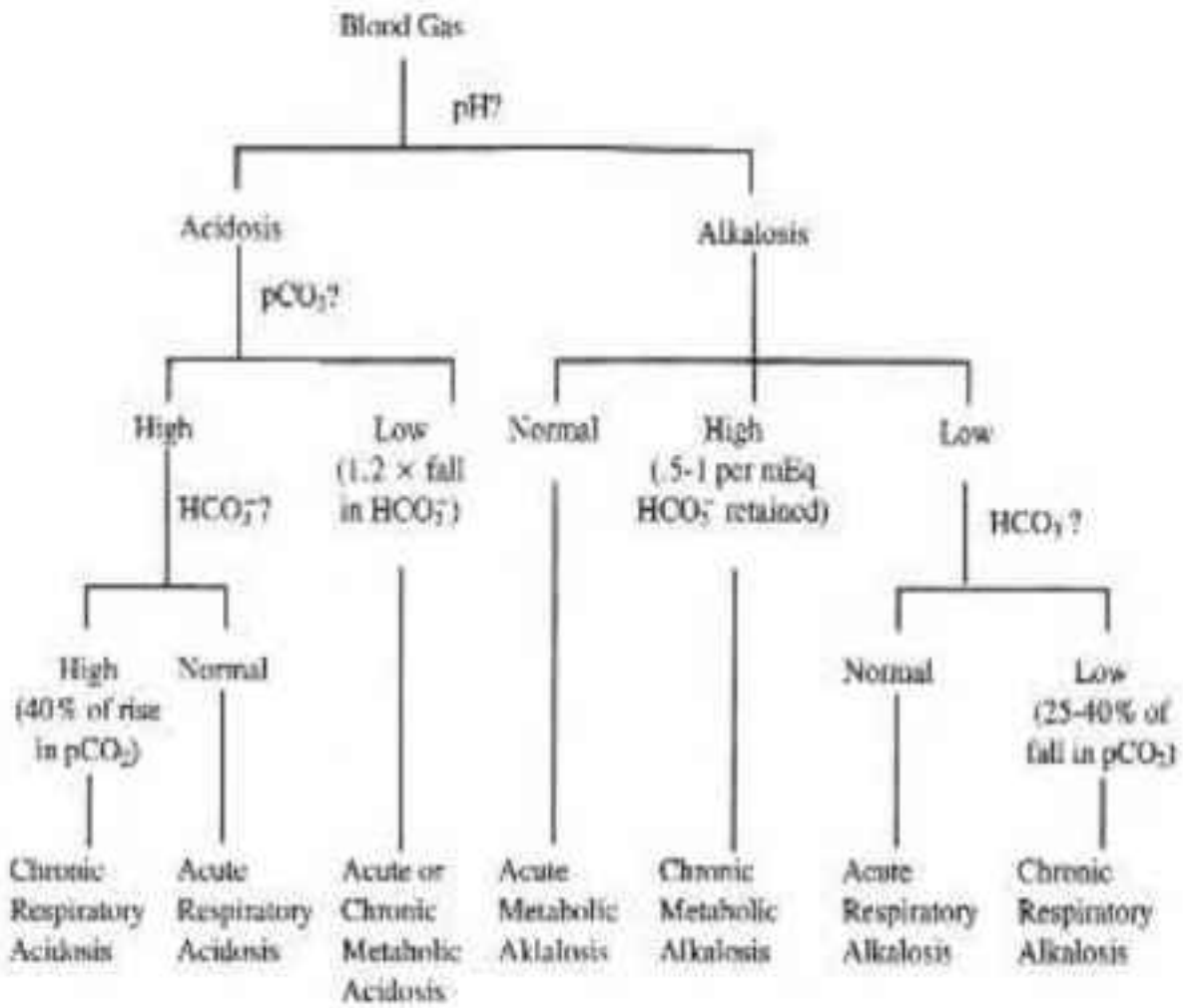
How much of a compensatory response (pCO_2 exhalation) should normal lungs make to a metabolic acidosis? The lungs lower the pCO_2 1.2 times greater than the fall in HCO_3. So, when the HCO_3 is 15 meq/L, a pCO_2 of 20mm is 'overcompensated': the lungs only needed to lower the pCO_2 to 28mm (25 meq - 15 meq = 10meq; 1.2 X 10 = 12mm). The disproportionately low pCO_2 means, therefore, that the lungs are breathing *too* well, that there is a simultaneous respiratory alkalosis. Common examples of combined metabolic acidosis and respiratory alkalosis include gram negative septicemia (lactic acidosis and hyperventilation), sepsis (lactic acidosis) with liver failure (hyperventilation), and aspirin overdose (salicylic acid and hyperventilation).

Alkalosis: If, in the face of alkalosis, the pCO_2 is low, then the cause of the alkalosis is respiratory (hyperventilation). As in respiratory acidosis, the HCO_3 ion is the clue to chronicity. A normal HCO_3 means the kidneys haven't had time to respond (by dumping HCO_3)—acute respiratory alkalosis. A low bicarbonate means the kidneys have had time to compensate by dumping HCO_3. So a low HCO_3 in a respiratory alkalosis means the alkalosis is chronic (compensated).

In respiratory acidosis, you recall, the kidneys compensate by retaining 40% of the rise in pCO_2. In chronic respiratory alkalosis, the kidneys dump HCO_3 with almost the same vigor—25–40% of the drop in pCO_2, but only rarely does the kidney compensate by lowering the HCO_3 below 15 meq/L. So a HCO_3 of 17–20 meq/L is the appropriate renal response for a pH of 7.50 and a pCO_2 of 20mm (40mm - 20mm = 20mm; .25 X 20mm = 5 meq HCO_3). A HCO_3 lower than 15 meq/L is overcompensated, meaning there's a simultaneous metabolic acidosis.

Conversely, an inadequate renal response means there must be an associated metabolic alkalosis, like hyperventilation and gastric suction. Combined respiratory and metabolic alkalosis would also occur with overly vigorous HCO_3 therapy to correct a metabolic acidosis. Despite making the serum suddenly alkalotic, IV HCO_3 doesn't penetrate cells rapidly enough to immediately correct the *intra*cellular acidosis, which is the stimulus that drives the respiratory center in the medulla. So in addition to (and despite) the newly created metabolic alkalosis, the patient continues to hyperventilate himself into a respiratory alkalosis.

If, instead of a low pCO_2, an alkalotic patient has a normal pCO_2, then the cause of his high pH must be a high serum HCO_3—a metabolic alkalosis. That the lungs have failed to respond by retaining CO_2 (to compensate with a respiratory acidosis) means the metabolic alkalosis is acute; pCO_2 retention (.5–1 mm pCO_2 per extra meq of HCO_3 retained) means the metabolic alkalosis is chronic.


Blood Gas
pH?
Acidosis
Alkalosis
pCO_2?
High
Low
(1.2 × fall in HCO_3^-)
Normal
High
(.5-1 per mEq HCO_3^- retained)
Low
HCO_3^-?
HCO_3^-?
High
(40% of rise in pCO_2)
Normal
Normal
Low
(25-40% of fall in pCO_2)
Chronic Respiratory Acidosis
Acute Respiratory Acidosis
Acute or Chronic Metabolic Acidosis
Acute Metabolic Alkalosis
Chronic Metabolic Alkalosis
Acute Respiratory Alkalosis
Chronic Respiratory Alkalosis

DOCTORING

Talking to Patients

AFTER THE HISTORY, PHYSICAL, LABORATORY INVESTIGATION, and synthesis of all these into a diagnosis, comes one of the most difficult tasks of doctoring—talking to the patient about his illness. It will require, believe me, common sense, finesse, tact, and sensitivity to the patient's unspoken needs. Some patients may not be emotionally ready to hear that they have a crippling or fatal illness.[1] Other patients may be more upset by the uncertainty of their illness and its prognosis than by its seriousness.

Rather than bluntly blurting out ominous diagnoses, and also to help clarify misconceptions a patient may have about his illness, ask the patient what he thinks is wrong with him. Remain silent after he finishes his reply. If he wants to know more, he'll break the silence and ask your opinion. *Then* you can correct any misconceptions and explain the nature of his illness. At this point, consciously avoid impatience, complicated vocabulary, and most importantly, a patronizing attitude. Having spent so much time studying medicine, having acquired such an abundant fund of medical knowledge which the patient cannot hope to master, it is only natural that you slip into a paternalistic or authoritative role. Unfortunately, this only fosters patient dependency on the doctor, and sets you up as the fall guy if anything goes wrong.

Try to avoid this situation by bridging the sea of medical knowledge separating you from the patient. Do this by viewing yourself as a textbook of medicine in lay language, an interpreter of a foreign language for the patient. Take whatever time is necessary to explain to the patient the nature of his illness using common, simple English. If you think it's easy to talk plainly, surprise yourself at the end of your discussion by asking the patient what she's going to tell her hubby when he asks "What did the doctor say?" Sure it takes time to explain things to patients, but as one Chief of Neurology said, "You'll never get rich taking care of sick patients."

Talking plainly does not mean talking down. Do not short-change people's intelligence. A large section of the population could be where you are now if they had had better guidance, more encouragement, and larger finances. Given the same information about an illness that you have, many patients can make as intelligent a decision as you about which future steps to take. More importantly, it's their right.[2]

When you need to perform invasive tests* or must choose among several possible therapies, discuss the risks and benefits with your patient. Unless the patient is demented, he and his family should help decide about any potentially dangerous tests or about future therapies. Many patients don't want that responsibility and respond with "You're the doctor; what do you think?" or "You do what's best, doc." Fine, but withhold your advice unless it is specifically asked for. Together you, the patient, and his family can agree on a course of action, but the final decision is the patient's. If he wants to take a riskier course, that's his business. You're not his father or some hand-wringing mentor. Your job is to give the patient enough information to make an

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Invasive Test: A test, using needles or knives, which puts the patient at some risk.

intelligent decision. An illness does not mean that a patient must relinquish control of his own life*. Once he's made his decision, even if it's against your advice, carry out his wishes to the best of your medical ability. This will help save your coronary arteries and minimize antagonizing the patient—maybe even prevent a malpractice suit.

Naturally, being a doctor is more than being a textbook in lay language, more than being compassionate, understanding, perceptive, and wise. Accepting the role of a doctor means you accept responsibility for the patient. You are not simply performing a service for the patient; you are guarding the patient's best interests and welfare when the patient is vulnerable because of a medical illness. When you think the patient's CBC, chest film, EKG, and electrolyte results can all wait until you have had a decent night's sleep, remind yourself that you have voluntarily accepted responsibility for this patient's medical defense.

Organizing Diagnoses

We've obviously spent a good deal of time on organizing symptoms and signs into a matrix of etiologic categories for a comprehensive differential diagnosis, a task that may seem difficult, which it *is* considering all the different diseases. But if doctoring were merely a matter of matching up symptoms and signs with their proper organ system, and then dredging up a list of, albeit organized and consistent, differential diagnoses, we wouldn't need doctors. Computers could do the bulk of this logical thinking, and probably more thoroughly than harried, distracted doctors. The hard part of doctoring, what computers cannot yet do, is judge—judge which diagnoses need to be immediately ruled out and which can wait until tomorrow or next week.

A doctor must know not only the possible diagnoses, but also those diagnoses that have the explosive potential for unexpected deterioration. In the marketplace of diseases, each potential disease will be hawking its attributes and clamoring for attention. Your first job is to attend to those diagnoses which need to be ruled out or treated now, today, not tomorrow or next week. The first time you see the patient, your diagnosis doesn't have to be right. Instead, you must rule out (or treat) those diseases which, if missed, may greet you in the morning with a heart-thumping "remember that patient you saw yesterday? Well, now he's .... (you fill in the catastrophe)." You have to weigh each diagnosis and, just before demoting it to the bottom of your differential diagnosis, judge the consequences of your being wrong—that this unlikely disease is indeed the correct diagnosis. Establishing priorities of diagnostic and therapeutic urgency is what makes doctors doctors. This skill, studied during the stressful years of internship and residency—after learning in medical school how to structure a comprehensive differential diagnosis—takes years, maybe decades, to master as mistakes and successes chisel your maturity and hone your judgment.

Which diseases need to be urgently ruled out or treated presumptively depends greatly on how ill the patient is and whether (and how fast) the patient's clinical state is deteriorating. Let me emphasize that you cannot glean that information from the chart—you must, must determine it for yourself by your own interview and your own examination of the patient *at the bedside*.

Own Life: Sometimes there is only one therapeutic avenue open—like stopping smoking. In that case, encourage, cajole, flatter, berate, or even demand that the patient follow your recommendations. But after you've explained the risks and made your sales pitch, the final decision is still the patient's. Don't let your strong recommendations back you into an adversarial relationship with your patient. No patient is worth your coronary arteries.

When it comes to interpreting laboratory tests, establish *first* how sick the patient is, what symptoms and signs limit him most. *Then* judge whether the test results have anything to do with what's bothering the patient. You won't have any trouble finding abnormal laboratory tests—normal patients walk around with them all the time[3]—but how you connect those tests to the patient depends on your firsthand assessment of the patient. The answer is not in the chart. It's at the bedside.

Handling Patients

It's a good idea at some point—either in the initial history-taking, review of symptoms, or after the physical exam—to ask the patient how he's holding up under the strain of his illness. You don't have to be a psychiatrist to inquire into how tightly a person's head is screwed on. Patients respond appreciatively to a genuine interest in their mental wellbeing. Medical illness is one of the times that the mind-body dichotomy takes on practical significance. When the mind can no longer depend on the body, they must be looked at, if not treated, separately. Your ability to effectively handle patients, separate from their illness, helps determine how much satisfaction you derive from the day to day routine of everyday doctoring. Much has been written about the aloof physician unable to relate humanely to his patients, something patients often interpret as callous unconcern or haughty condescension. Unfortunately, but understandably, the patient who regards his know-it-all doctor as arrogant will be less pleasant to care for than one who feels his physician is treating him as a neighbor and fellow human being. Without rushing to the medical profession's defense, it's been my experience that sick patients do receive the warmth, understanding, compassion, and all the other genuinely humane qualities that doctors are supposed to project.

The criticism leveled at doctors for being too brusque and not enough like Marcus Welby is most vocally expressed by patients with the least organic illnesses. Most middle-class, well-adjusted medical students are unaware of how much psychopathology lies in wait for them. It's amazing how many patients need to be sick. The reasons stem from procuring supplemental disability income, to manipulating family and friends, to excusing themselves for not meeting the responsibilities of self care, to establishing a dependency relationship with someone like their friendly local doctor, to neurotic expectations of a painless, symptomless existence. Doctors may be less than sympathetic with such patients because, in general, doctors resent being sent on wild goose chases looking for the cause of someone's neurotic complaints, or fulfilling someone's dependency needs, or paying taxes to support another person's hysterical or malingering illness. Moreover, the anxiety produced from wanting to call a patient neurotic or hysterical but afraid of missing an organic diagnosis upsets doctors and disrupts a healthy doctor-patient relationship. I can't tell you how to handle your feelings about such patients (other than to go into pathology or radiology), but awareness of these patients and awareness of your feelings toward them may help you enough to handle them both appropriately.

Another way to forestall problems with patients, even though it's a royal pain sometimes, is to tell them to call *before* the next clinic visit if problems arise with their medications, or if particular symptoms (spell them out) occur. Let patients know they have access to you. If their problem is organic, you'll want to know of side effects or new symptoms. If their problem is functional, merely the knowledge that someone cares is often enough for an effective cure. If you're called every other day with trivia, either redefine the symptoms you want to hear about, or else refer the patient to psychiatry for better treatment of his anxiety.

Notwithstanding all I've said about the integrity of the doctor-patient relationship, there is nothing that interferes more with it than discovering you've been treating the wrong disease. First and foremost, be a good clinician and the doctor-patient relationship will usually take care of itself. But don't get caught in the trap of believing that a good clinician is one who always knows the right answer. There will be countless instances when the symptoms, signs, and laboratory results are too nonspecific for you to be certain of either the anatomic site or the etiologic insult. It's very easy, in the midst of your (and especially the patient's) frustration to feel a natural urge to bring order out of chaos, to calm a distressed patient, to feel in command of disease, to be knowledgeable, competent, and confident. Recognize these feelings and be honest with yourself, the patient, and the primary doctor. Admit that you don't know. Clearly differentiate what you think might be going on from what you know is happening.

But once you're satisfied that likely treatable diagnoses have been ruled out, a straightforward way to handle your and your patient's anxiety about the uncertainty of a diagnosis is to tell the patient that his symptom is like a piece of ice in the ocean. Most of the time it's just that—a piece of ice—which will eventually melt away. Sometimes, though, the piece of ice is actually the tip of an iceberg and only continued observation will tell the difference. You don't have to commit yourself. You're not on trial; follow the patient along. As long as the patient's problem is stable or improving, and you've ruled out those illnesses that need urgent decisions, sit tight. If the patient progresses, you progress—with more sophisticated tests or tests which may pose a risk to the patient. You're not a quarterback directing the patient's illness. You're a middle linebacker waiting to see which way the play is developing before taking action.

Death

There will be times when, for any number of reasons, you accidentally kill a patient. The ensuing guilt is almost impossible to prepare for. But if you expect to look after patients and bear responsibility for them, expect to make mistakes, sometimes serious mistakes. It's part of the job, something to be avoided, but still an intrinsic part of doctoring. If you don't want to strike out, get out of the batter's box now.

That you killed someone is actually less important than your reaction to it. A cavalier shrug of the shoulders won't help you avoid similar mistakes, but neither will morbid concern that someone will find out how stupid you really are. So you blundered. Okay, accept it as part of being human, learn from it, and go on, grateful that you're still on your feet and mentally capable of helping someone.

Dying

There are two types of patients for whom you must make decisions without their permission: the hopelessly unconscious patient and the terminally dying patient. In such situations, be guided by the physician's job description—to relieve suffering.[1] You are not a technician who knows the correct dosage of medications and IV rate. You are a physician who must make judgments about immeasurables. Is the patient a source of cohesion for the family, or a disruptive wedge? Illnesses can drain a family's attention and efforts (including financial resources) away from normal members of a family, especially children. You may feel that you must defend your patient's right to live, but you must also defend the family's right to a normal life. Your job is not to mindlessly save lives, but to relieve unnecessary suffering by both the patient and his

family.[5] With all the high-powered technical equipment, it is within our power to drag a patient and his family through the muddy agony of a prolonged, drawn-out terminal illness. Families suffer as much as patients; you simply can't treat a patient separate from his family, even patients without life-threatening illnesses.

As early as possible, with the patient's permission, incorporate the family into your discussions about the patient's illness, especially if he has a potentially life-threatening illness. Let them know what your thoughts are, be it concern that the patient's life may be in jeopardy or that death is imminent. The family must be forewarned of a patient's potential or likely death as early as possible. An unexpected death robs the family of a most primitive human emotion—grieving over someone they love. To deny a family this fundamental emotion is almost immoral. Let them know early on that the patient is in the woods and that you're concerned about him. Let them stay with the patient as long as they like, even if it means moving the patient to a private room to avoid disturbing other patients. If necessary, even try to prolong a terminal illness until you feel the grieving process is over or at least well under way.

When death becomes inevitable, or it becomes obvious that the patient will be left with a subhuman existence after hospitalization, it's time to stop treating the patient and to begin treating the family, even to begin withholding treatment. When to start withholding therapy is one of the most difficult judgment questions a doctor must face. How do you decide when to let nature take its course? Obviously, you cannot ask the family, but you can take your cues from them. Approaching the subject of death or serious disabilty is most gently done by asking the family how they think the patient is doing. Your silence after their response usually elicits a request from the family for your opinion about the patient's condition. At this point you can correct any misconceptions and begin to make the family understand either that the patient's life is in jeopardy, or that his future life will no longer even resemble what it was prior to hospitalization. Carefully assess the family's reaction. If the family accepts the idea of the patient's imminent death with nodding understanding, and if they feel that you've done everything you can, then reassure the family that you are making their loved one as comfortable as possible. You can then focus on ferrying the patient across the river Styx, providing him every dignity and comfort you would want for your own family member.

If instead of accepting the patient's imminent death with aplomb, the family becomes upset and insists that all efforts be made regardless of the outcome, then do what the family wants until they accept the patient's death as an inevitable part of life. Even if you do not feel that prolonged therapeutic efforts are in the family or the patient's best interests, you should still follow (at least for a while) their spoken and unspoken wishes. Don't decide what is best for the family before they have had a chance to come to grips with the realization that they will never see that person again. Hopefully, with frequent contact, you can lead the family to recognize that the patient himself would prefer to be allowed to die rather than linger in a twilight zone of pain, confusion, bed confinement, incontinence, bed sores, and tube feedings, all without meaningful communication with those around him. I am not asking you to play God. In fact, I'm asking you not to. God is trying to tell you something: listen. He has opened his arms to your patient, and you have no right to stand between them. Your only job is to make that transition as noble as you can for the patient and his family.

REFERENCES

ABBREVIATIONS:

ActaMS = Acta Med Scand
Acta Neurochir = Acta Neurochir
Adv IM = Adv Intern Med
AdvN = Adv Neurol
AJEmMed = Amer J Emerg Med
Anesth = Anesthesiol
AnEA = Anesth Analg
AnEM = Ann Emerg Med
AnIM = Ann Intern Med
Annals = Annals Otology
AnN = Ann Neurol
Ann Rev NSci = Annu Rev Neurosci
ArGPsy = Arch Gen Psychiatry
ArIM = Arch Intern Med
ArN = Arch Neurol
ArOto = Arch Otolaryngol
ArOph = Arch Ophthalmol
ArPMR = Arch Phys Med Rehabil
BRBull = Brain Res Bull
BrJOph = Br J Ophthalmol
CJNSci = Can J Neurol Sci
Circ = Circulation
Clin MNS = Clin Neurol Neurosurg
Clin Neurpharm = Clin Neuropharmacol
Clin Oto = Clin Otolaryngol
CMAJ = Can Med Assoc J
CORR = Clin Orthop
Ear N = Ear Neurol
Exp N = Exp Neurol
HrA = Headache
Hum Neurobiol = Hum Neurobiol
JN = J Neurol
JNNP = J Neurol Neurosurg Psychiatry
JNS = J Neurosurg
JNeurphys = J Neurophysiol
JNSci = J Neurol Sci
Laryngo = Laryngoscope
MCNA = Med Clin North Am
M&N = Muscle & Nerve
N = Neurology
NEJM = N Engl J Med
Neuph = Neuro-Ophthalmology
Nprot = Neuroprotection
Nrad = Neuroradiology
NS = Neurosurgery
ObGyn = Obstet Gynecol
Opthal = Ophthalmology
OtoHNS = Otolaryngol Head Neck Surg
PCNA = Pediatr Clin North Am
Prog CV Dis = Prog Cardiovasc Dis
Sem N = Semin Neurol
Stro Recom = Stroke Recurrence
SMJ = South Med J
Surg N = Surg Neurol

Italicized Number = Volume

GENERAL REFERENCE:

HA Skinner. *The Origin of Medical Terms*. Williams and Wilkins Co, Baltimore, 2nd ed., 1961

FOREWORD:

1. AR Damasio, et al (1982) Aphasia with nonhemorrhagic lesions in the basal ganglia and internal capsule, *AnN 39 15*

1a. MA Naeser, et al (1982) Aphasia with predominantly subcortical lesion sites. Description of three capsular/putaminal aphasia syndromes, *AnN 39 2*

1c. O Tanridag, RS Kirshner (1985) Aphasia and agraphia in lesions of the posterior internal capsule and putamen, *N 35 1797*

1d. CW Wallesch, et al. (1983) Lesions of the basal ganglia, thalamus, and deep white matter: differential effects on language functions. *Br and Lang 20 286*

2. S Nigeongale, R. Wilcox (1982) Psychometric assessment in absence status, *AnN 39 516*

3. RD Rees, RM Stewart (1981) Akinetic mutism from hypothalamic damage: successful treatment with dopamine agonist, *N 31 1435*

4. RD Hoopes, et al (1979) Amnesia in focal brain lesions, *AnN 36 705*

4a. V Isnil, et al (1976) Mutism amnesia. *AnN 6 362*

4b. JR Duval (1980) Unilateral amnesia due to thalamic hemorrhage. *N 30 83*

4c. EW Massey, et al (1979) Unilateral agraphia, motor impersistence dysmetria on focal vascular disease, *N 29 1188*

4d. S Nocks, H Ulmerain (1985) Bilateral amnesia in frontal lobe tumor. *AnN 19 366*

5. DA Greenberg, RP Simon (1982) Phenytoin and carbamazepine in status epilepticus: drug induced coma, *N 32 448*

6. PI Lavin, et al (1983) Downbeat nystagmus with supratentorial disease, *Neuph 3 233*

7. AL Bennett, et al (1981) Hyperalbuminemia and sensory loss due to parietal lobe arteriovenous malformation, *AnN 38 122*

8. KD Mantritz, et al (1979) Quantitative analysis of ataxia in late cortical atrophy of the anterior lobe and other forms of cerebellar ataxia, *Brain 102 461*

9. T Brandt, RB Daroff (1980) The multisensory physiological and pathological vertigo syndromes, *AnN 7 195*

10. GB Gwaltney, DL Skinner (1982) Ileocecum. A case with associated vascular abnormalities, *AnN 39 55*

11. C Coers, N Timerman-Topper (1979) Differential diagnosis of limb-girdle muscular dystrophy and spinal muscular atrophy, *N 29 957*

12. W Markesbery, et al (1977) Distal myopathy: electron microscopic and histochemical studies, *N 27 727*

12a. RG Miller, et al (1979) Sporadic distal neuropathy with early adult onset, *AnN 5 320*

13. WH Caposio, et al (1985) CuCl entrapment from S-1 radiculopathy. Report of two cases, *JNS 62 442*

13a. R D'Alessandro, et al (1982) Benign familial spinal muscular atrophy with hypertrophy of the calves, *ArN 39 657*

13b. E Valenstein, et al (1978) Myokymia, muscle hypertrophy and percussion "myotonia" in chronic motoneuron polyneuropathy, *N 28 1130*

13c. P Montagna, et al (1984) Muscular hypertrophy after chronic radiculopathy, *AnN 41 397*

CHAPTER 1:

1. MC Houston, et al (1984) Shock, diagnosis and management, *AcIM 144 1453*

1a. RF Wilson (1985) Science and shock: a clinical perspective, *AnIM 14 711*

2. JE Holt, GB Holt (1984) Reconstruction of the lacrimal drainage system, *AcOto 110 211*

3. A Wright (1954) The internal rectifier, how does it work? (editorial), *ClinOto 8 73*

4. AJ Hudspeth (1983) The hair cells of the inner ear, *SciAm 248 (1) 54*

5. LJ Deftos (1978) Calcitonin in clinical medicine, *AdvIM 21 159*

6. J Tepperman (1968) *Metabolic and Endocrine Physiology*, p. 158, 4th Ed. Yearbook Medical Publishers, Chicago

7. RH Unger, L Orci (1981) Glucagon and the A cell: physiology and pathophysiology, *NEJM 304 1518, 1576*

8. DA Oakes, et al. The anterior pituitary gland, in PK Bondy, LE Rosenberg (eds) *Metabolic Control and Disease*, 8th ed., WB Saunders, Phila, 1980, p. 1108
9. CP Abbott, LR Laws Jr (1979) Clinical endocrinological approach to hypothalamic-pituitary disease. INJM *51* 271
10. JH McAnulty, SD Schimmoeller (1984) Bundle branch block, Prog CV Dis *26* 533
11. AA Jackson (1983) Amino acids: essential and non-essential? *Lancet I* 1084
12. HJ McGee, et al (1993) Why whip eggs in copper bowls? *Nature 308* 667
13. GH Ballantyne (1984) The meaning of ileus. Its changing definition over three millenia, *ArS 198* 252
14. P Matzinger (1981) A one-receptor view of T-cell behaviour, *Nature 292* 497
14a. JA McIntyre, et al (1978) Human leukocyte antigens (HLA), *BMJ 71* 1268
15. RS Geha (1981) Regulation of the immune response by idiotypic and alloteypic interactions, *NEJM 305* 25
15a. P Leder (1983) Genetic control of immunoglobulin production,*Hosp Prac 18* (2) 73
16. M Goldberg (1984) Systemic reactions to intravascular contrast media. A guide for the anesthesiologist, *Anesth* 56 66
17. SA Klotz, et al (1984) Typhoid fever. An epidemic with remarkably few clinical signs and symptoms, *AnIM 144* 533
18. AS Rosenthal (1980) Regulation of the immune response—role of the macrophage, *NEJM 303* 1353
18a. DS Nelson (1981) Macrophages: progress and problems, *Clin Exp Imm 45* 225
19. DL Rebhun, ME Gershwin (1978) Identification and characterization of lymphocyte subpopulations, *Sem A&R 7* 245
20. FW Ruscetti, RC Gallo (1981) Human T-lymphocyte growth factor: regulation of growth and function of T lymphocytes, *Blood 57* 379
20a. HW Murray, et al (1984) Impaired production of lymphokines and immune (gamma) interferon in the acquired immunodeficiency syndrome, *NEJM 310* 883
21. CA Alper, FS Rosen (1975) Clinical applications of complement assays, *AdvIM 20* 61
21a. RH McLean, JA Winkelstein (1984) Genetically determined variation in the complement system: Relationship to disease, *J Path 143* 179
22. AN Theofilopoulos, FJ Dixon (1980) Detection of immune complexes: techniques and implications, *Hosp Prac 15* (5) 150
23. RN Sacks (1981) The oxyhemoglobin dissociation curve, *Int Anes Clin 19* (3) 39
24. JT Edsall (1970) Hemoglobin and the origins of the concept of allosterism, *Fed Proc 29* 226
25. C Merskey (1980) DIC: identification and management, *Hosp Prac 15* (12) 83

CHAPTER 2:

1. TC Lee (1981) Van Gogh's vision. Digitalis intoxication?, *JAMA 245* 727
2. JA Blau (1982) How to take a history of head or facial pain, *BMJ 285* 1259

CHAPTER 4:

1. JK Uscinski, BM Middleton III (1983) Normal liver function. A basis for understanding hepatic disease, *AnIM 143* 2291
2. VF Fleshman, et al (1983) Tests for pernicious anemia: the "Schilling Test," *Mayo* 58 54)

CHAPTER 5:

1. WI Kilman, RX Goyal (1976) Disorders of pharyngeal and upper esophageal sphincter motor function, *AnIM 226* 592
2. CE Bamatt, et al (1984) Retropharyngeal abscess—a ten year experience, *Laryngo 94* 455
3. SM Seibel (1983) Dysgeusia, *AffinMed 1* 342
3a. JA Warner, WF Finlay (1985) Fulminating epiglottitis in adults. Report of three cases and review of the literature, *Anesth 40* 348
4. *JW Powers*, P Connell (1979) Remyelination in multiple sclerosis, *AnN 5* 52
5. VD Sisto, et al (1984) Factors predicting development of renal involvement in progressive systemic sclerosis, *AJM 76* 779
5a. HA Schneider, et al (1984) Scleroderma esophagus: a nonspecific entity, *AnIM 100* 858
6. FW Gerrache Jr, RM Vanston (1980) Hypertrophic cervical osteophytes causing dysphagia. A review, *J NJS 55* 536
6a. C Yue, et al (1985) Two cases of dysphagia due to cervical spine osteophytes successfully treated surgically, *UMAJ 53* 810
6b. G Brandstrup, LG Lellbach (1968) Dysphagia and dysphonia secondary to anterior cervical osteophytes, *Neurog 169*
7. J Edelman., EG Stewart Wynne (1981) Respiratory and bulbar paralysis with relapsing hyperthyroidism, *BMJ 283* 716
7a. GM Kamrin, CR Hamilton Jr (1974) Acute bulbar muscle dysfunction and hyperthyroidism. A study of four cases and review of the literature, *AJM 56* 464
8. KH Merkel, et al (1976) Cerebrovascular disease in sickle cell anemia: a clinical, pathological and radiological correlation, *Stroke 9* 45
8a. HH Wood (1978) Cerebrovascular complications of sickle cell anemia, *Stroke 9* 73

CHAPTER 6:

1. PF Schwartz, et al (1982) Post operatory sepsis and mortality in adults, *JAMA 248* 2279
2. HK Koh, et al (1984) Late neurologic (beyond ten years) of cutaneous malignant melanoma. Report of two cases and a review of the literature, *JAMA 251* (8)993
3. D Enzmann, WR Scott (1977) Intracranial involvement of gonococcal infection, *N 27* 794
4. P Delaney, M Fahn (1980) Intracranial hemorrhage with amphetamine abuse, *N 30* 1125
4a. LR Caplan, et al (1982) Current concepts of cerebrovascular disease—stroke: stroke and drug abuse, *Stroke 13* 868
4b. H Marsh, et al (1983) Cerebral vasculitis associated with oral amphetamine overdose, *ArN 40* 233
5. MP Vessey, et al (1984) Oral contraceptives and stroke: findings in a large prospective study, *BMJ 289* 530
5a. WT Longstreth Jr, PD Swanson (1984) Oral contraceptives and stroke, *Stroke 15* 347
5b. S Gordon Hardy, et al (1985) Ischemic strokes and oral contraceptives, *N/mid 27* 568
6. NS Irey, et al (1978) Oral contraceptives and stroke in young women: A clinicopathologic correlation, *N 28* 1216
6a. NS Irey, HJ Nowo (1973) Luminal vascular lesions associated with female reproductive steroids, *ArPath 96* 227
7. S Picker, et al (1981) Glial membrane potentials and their relationship to [K+]o in rat and guinea pig. A comparative study of microelectrode measurements, and morphologic glia, *J NS 53* 347
8. S Dell (1982) Asymptomatic carotid aneurysm: assessment of its risk of rupture, *N/S 29* 162
8a. LN Sekhar, RC Heros (1981) Origin, growth, and rupture of saccular aneurysms: A review, *N/S 8* 248
9. WE Dandy (1938) Intracranial aneurysm of the internal carotid artery. Cured by operation, *ArS 367* 664
10. JE Welsh, et al (1979) Chronic cerebral hematoma presenting transient neurologic deficits, *Stroke 10* 564
11. MS Pessin, et al (1980) Mechanisms of acute carotid stroke, *AnN 8* 245
11a. TS Olsen, NA Lassen (1984) A dynamic concept of middle cerebral artery occlusion and cerebral infarction in the acute stage based on microprobe screen hypoxemia as a sign of embolic migration, *Stroke 15* 458
11b. JD Easton, DG Sherman (1980) Progress in cerebrovascular disease. Management of cerebral embolism of cardiac origin, *Stroke 11* 433
12. BL Thiele, et al (1980) Correlation of arteriographic findings and symptoms in cerebrovascular disease, *N 30* 1041

13. PA Wolf, et al (1985) Duration of atrial fibrillation and imminence of stroke: the Framingham study, Stroke *16* 661
13a. JD Fisher, DG Sherman (1980) Progress in cerebrovascular disease. Management of cerebral embolism of cardiac origin, Stroke *11* 435
13b. DS Sherman, et al. (1984) Thromboembolism in patients with atrial fibrillation, AnN *41* 708
14. JD Easton, DG Sherman (1980) Progress in cerebrovascular disease. Management of cerebral embolism of cardiac origin, Stroke *11* 435
15. MR Hansen, et al (1980) Brain events associated with mitral valve prolapse, Stroke *11* 499
15a. AC Jackson, et al (1984) Mitral valve prolapse and cerebral ischemic events in young patients, N *34* 754
15b. DR Humphner, JD Barnett (1985) The enigma of the link of stroke to mitral valve prolapse, Stroke *16* 175
15c. GA Barletta, et al (1985) Cerebral ischemic attacks in a comparison of aortic and mitral valve prolapse, Stroke *16* 219
16. S Arnon (1984) Mural thrombi in coronary artery disease. Recent advances in pathogenesis, diagnosis, and approaches to treatment, AnIM *144* 113
16a. UC Keating, et al. (1982) Mural thrombi in myocardial infarction. Prospective evaluation by two dimensional echocardiography, AJM *74* 989
16b. WS Konrad, et al (1984) Myocardial infarction and stroke, N *34* 1013
17. KW Min, et al (1980) Multiple pulmonary arteriovenous anastomoses: formation, distribution, and histologic pathogenesis with long term study, Cancer *45* 2774
18. RA Sanders, et al (1980) CNS embolism due to atrial myxoma, AnN *27* 485
18a. AL Descotes, et al (1978) Atrial myxoma, a review of the neurological complications, treatment, and recurrences, JNNP *41* 1119
19. SG Meister, et al (1972) Paradoxical embolism. Diagnosis during life, AJM *53* 291
20. J Olesen, et al (1972) Spreading cerebral ischemia in classical and normal cerebral blood flow in common migraine, JRA *22* 242
20a. JW Lance (1981) Headache, AnN *10* 1
21. PD Drummond, JW Lance (1984) Extracranial vascular changes and the source of pain in migraine headache, AnN *13* 32
21a. JW Lance (1981) Headache, AnN *10* 1
21b. O Appenzeller (1978) Cerebrovascular aspects of headache, MCNA *62* 467
22. JF Castaldo, et al (1982) Mobile cerebral artery occlusion with migraine, Stroke *13* 308
23. JD Bastianson (1984) Transient neurological manifestations of migraine, Stroke *15* 383
24. AJ Fairlie, et al (1976) Systemic embolism in chronic rheumatic disorder, NEJM *295* 190
25a. J Bolter, et al (1978) Embolism in rheumatic disease, AnnMS *204* 1
25b. PA Wolf, et al (1978) Epidemiologic assessment of chronic atrial fibrillation and risk of stroke: The Framingham Study, N *28* 973
26. M Fisher (1975) Holter cardiac monitoring in patients with transient focal cerebral ischemia, Stroke *9* 514
26a. PJ Kinkbaner, et al (1986) Holter monitoring in patients with transient and focal ischemic attacks of the brain, stroke *17* 192
26. DM Hurley, et al (1981) Atrial fibrillation and arterial embolism in hyperthyroidism, Ann NY *3* Med *71* 361

CHAPTER 10:

1. EW Massey (1980) Joseph Bell, MD, FRCS—Mr. Sherlock Holmes?, SMJ *73* 1635
2. MH Maxwell, et al (1982) Intermittent blood pressure measurements due to cuff use in obese patients, Lancet *2* 35
3. RJ Polinsky, et al (1981) Pharmacologic distinction of different orthostatic hypotensive syndromes, N *31* 1
3a. MG Ziegler, et al (1977) The sympathetic nervous system defect in primary orthostatic hypotension, NEJM *296* 293
4. CA Dinarello, SM Wolff (1982) Molecular basis of fever in humans, AJM *72* 799
4a. E Atkins (1982) Fever: new perspectives on an old phenomenon, editorial, NEJM *307* 958
5. KL Donington (1981) Skin temperature over supraorbital vessels, Lancet *1* 256
6. AS Gross Jr (1975) Documentation of exophthalmos, NEJM *292* 1008
6a. MR Smigel Jr, CS MacCarty (1975) Subject review. Exophthalmos. The most commonly encountered neurological lesions, Mayo *50* 345
7. D McLeod, et al (1977) The role of anaphylactic transport in the pathogenesis of retinal cotton-wool spots, BJOph *61* 177
8. JR Guarino (1980) Auscultatory percussion of the chest, Lancet *1* 1332
9. ND Fowler (1982) Constrictive pericarditis: new aspects, AJC *50* 1014
10. RL Van Horn, GF Solomon (1979) Whitecoat neural hemorrhages: a sign of intracranial hemorrhage, N *29* 236
11. J Dorros, et al (1982) Validity of the hepatojugular reflux as a clinical test for congestive heart failure, AJC *52* 1295
12. JL Heckman, et al (1982) Fuzzy set analysis approach to recognition of the first and second heart sounds, AHJ *104* 1307
13. M Kapur (1983) Aortic valve closure and cardiac cineradiography in the genesis of the second heart sound, AJC *52* 152
14. Y Dotan, et al (1953) Origin of the third heart sound. II. Studies in human subjects, Circ *67* 369
15. JD Harkonen, et al (1983) Controlled trial of fecal occult blood testing in the detection of colorectal cancer, Lancet *2* 1
16. JD Wirtschafter, et al (1976) A stereological analysis of vessel sizing errors in retinal arteriovenous crossings, AnOph *8* 619
17. S Pegh, RL Gordon (1975) Ultrasound scan contact scatter and carotid occlusive disease, JAMA *233* 450

CHAPTER 11:

1. A Rutherun, AL Goldberger (1985) Aids to cardiac auscultation, AnIM *99* 346

CHAPTER 12:

1. JT Rosenbaum, RA Nozik (1985) Uveitis: many diseases, one diagnosis, AJM *79* 545

CHAPTER 13:

1. JW Prineas, F Connell (1979) Remyelination in multiple sclerosis, AnN *5* 22
2. KI Swett, et al (1981) The restoration of conduction by central remodulation, Brain *104* 583

CHAPTER 14:

1. S Polyak (1957) *The Vertebrate Visual System*, The University of Chicago Press, Chicago, pp. 779–783
2. BM Michel, BT Thomas (1980) Palinopsia: cerebral localization with computerized tomography, N *30* 887
2a. RP Lucas (1983) Palinopsia: rare but ominous symptom of cerebral dysfunction, N/S *12* 318
2b. M Russo (1960) Visual disturbances caused by focal brain damage, Arch N *4* 208
3. JW Lance (1975) Simple formal hallucinations confined to the area of a specific visual field defect, Brain *98* 719
3a. BI Ludwig, CA Mamat (1972) Clinical field patterns in epileptic patients with occipital electroencephalographic foci, N *23* 481
3b. T Deonna, et al. (1984) Paroxysmal visual disturbances and benign epilepsy in children, N/ped *15* 151
3c. GS Brindley (1982) Effects of electrical stimulation of the visual cortex, Hum Neurol *1* 281
3d. DH Rosenbaum, et al. (1986) Cortical-evoked seizures in occipital epilepsy: Case report and review of the literature, N *36* 281
4. L Bellugi, et al (1983) Brain organization for language: clues from sign language, Hum Neurol *2* 155
4a. C Chiarelli, et al (1982) Aphasia in a prelingually deaf woman, Brain *105* 29

4b. Ak Buchsbaum (1985) Apraxic dysgraphia of braille in a congenitally blind man, *Neuropsychologia 23:127*

4c. RP Lesser, et al (1986) Electrical stimulation of Wernicke's area interferes with comprehension, *N 36:658*

5. EW Sweet, et al (1984) Crossed Wernicke's aphasia, *N 84:475*

5a. DA Hinshaw, et al (1984) Persistent Broca's aphasia after right cerebral infarction in a right hander, *N 34:387*

6. D Kimura (1982) Speech representation in an unbiased sample of left-handers, *Hum Neuro 2:147*

6a. Y Ivanstone, et al (1987) Language in right handers with right hemisphere lesions: a preliminary study including anatomical, genetic, and social factors, *Brain Lang 29:213*

7. GA Dorsan (1979) Stuttering as a manifestation of ataxia, *Mot 1 Ass 1 44*

7a. J Rosenbek, et al (1978) Stuttering following brain damage, *Brain Lang 5:82*

7b. NA Helm, et al (1978) Acquired stuttering, *N 28:1159*

7c. PT Quinn, G Andrews (1977) Neurogenic stuttering—A clinical entity?, *JNNP 40:969*

7d. AE Miller (1985) Cessation of stuttering with progressive multiple sclerosis, *N 45:1341*

8. D van Cramon (1981) Traumatic aphasia and the subsequent reorganization of speech functions, *N/psychol 19:803*

8a. AS David, I Hone (1991) Mutism following left hemisphere infarction, *JNNP 47:1347*

9. C Chaplin, et al (1981) Speech production mechanisms in aphasia: a delayed auditory feedback study, *Brain Lang 14:106*

10. N Geschwind (1975) The apraxias: neural mechanisms of disorders of learned movement, *Am Sci 63:188*

10a. N Geschwind (1965) Disconnexion syndromes in animals and man, *Brain 88:237*

11. KM Heilman, et al (1979) Wernicke's and global aphasia without alexia, *Arch 36:129*

11a. S Sevush, et al (1983) Preserved oral reading in Wernicke's aphasia, *N 33:916*

11b. ID Kertzer, et al (1981) Word features in Wernicke's aphasia, *JNNP 44:192*

12. J Graham, et al (1980) Cortical deafness—a case report and review of the literature, *J N/Sci 48:35*

12a. WT Dauglerty, et al (1984) Hearing loss in multiple sclerosis, *Arch 40:33*

12. GA Ojemann (1979) Individual variability in cortical localization of language, *J N/S 50:164*

13a. JP Wolz (1982) The evaluation of aphasia, *Stroke 13:209*

13b. DS Knopman, et al (1984) Recovery of naming in aphasia. Relationship to fluency, comprehension and CT findings, *N 34:1461*

14. S Wyyland, JC Taylor (1985) Knowledge categorization in fluent and nonfluent atomic aphasics, *Brain Lang 16:87*

15. R Mayeux, et al (1980) Intellectual memory and language impairment in temporal lobe epilepsy, *N 30:120*

15a. DS Knopman, et al (1984) Recovery of naming in aphasia. Relationship to fluency, comprehension and CT findings, *N 34:1461*

16. AK Ojemann, et al (1981) Aura in temporal lobe epilepsy: clinical and electroencephalographic correlation, *JNNP 46:1009*

16a. S Currie, et al (1971) Clinical course and prognosis of temporal lobe epilepsy. A survey of 666 patients, *Brain 94:173*

17. P Gloor, et al (1982) The role of the limbic system in experiential phenomena of temporal lobe epilepsy, *AnN 12:129*

17a. L Halgren (1982) Mental phenomena induced by stimulation in the limbic system, *Hum Neuro 1:251*

18. RL Gilmore, KM Heilman (1981) Speech arrest in parietal seizures: evidence of an associative language disorder, *N 31:1016*

18a. MG Hamilton, T Matthews (1979) Aphasia: The sole manifestation of focal status epilepticus, *N 29:395*

19. GA Smith, JL DeVito (1954) Central neural integration for the control of autonomic responses associated with emotion, *Ann Rev N/Sci 7:43*

20. IM Jackson (1982) Thyrotropin releasing hormone, *NEJM 306:145*

20a. PW Kalivas, et al (1983) Substantia nigra-mesencephalic tectal projection: hemiparkinsonian behavioral asymmetry following electrolytic lesions of the substantia nigra pars reticulata, *Brain Res 274:305*

21. RM Restak, RB Pape (1978) Can the pituitary secrete directly to brain? (Affirmative anatomical evidence), *Endocrinology, 102:1325*

21a. DT Krieger, AS Liotta (1979) Pituitary hormones in brain: where, how, and why, *Science 205:366*

22. J Kievit, HG Kuypers (1975) Basal forebrain and hypothalamic connections to frontal and parietal cortex in the Rhesus monkey, *Science 187:660*

22a. MB Carpenter, J Sutin (1983) *Human Neuroanatomy*. Williams and Wilkins, Baltimore, 8th edition, pp. 570-575

23. GW Van Hoesen (1982) Neural systems of the non-human forebrain implicated in memory, *Ann NY Acad Sci 444:97*

23a. C Duyckaerts, et al (1985) Bilateral and limited amygdalohippocampal lesions causing a pure amnesic syndrome, *AnN 18:314*

24. A Reinmberg (1979) Participation of brain stimulation reward substrates in memory: anatomical and biochemical evidence, *Fed Proc 38:2646*

24a. JL DeVito (1980) Subcortical projections to the hippocampal formation in squirrel monkey (*Saimiri Sciureus*), *BBJ9:1289*

25. JW Papez (1937) A proposed mechanism of emotion, *AMA Arch Psych 38:725*

26. KM Heilman, GW Speer (1977) Kinsbourne's syndrome resulting from bilateral cortex lesions, *N 27:490*

26a. MB Carpenter, J Sutin (1983) *Human Neuroanatomy*. Williams and Wilkins, Baltimore, 8th edition, pp. 630-632

27. GW Van Hoesen, et al (1981) Widespread corticostriate projections from temporal cortex of the Rhesus monkey, *J Comp N 199:205*

27a. GW Van Hoesen (1985) Neural systems of the non-human forebrain implicated in memory, *Ann NY Acad Sci 444:97*

28. RG Fry (1981) Control of complex conation and emotion in the neocortex by the limbic mesolimbal, subcallosal, and cingulate cortices and the hypothalamus, mammillary body, and thalamus, *Int J N/Sci 15:1*

28a. F Halgren, et al (1978) Mental phenomena evoked by electrical stimulation of the human hippocampal formation and amygdala, *Brain 101:83*

28b. P Gloor, et al (1981) The role of the amygdala in the expression of psychic phenomena in temporal sclerosis, in Y Ben Ari (ed) *The Amygdaloid Complex*. Elsevier/North-Holland Biomedical Press, Amsterdam, pp. 489-497

29. YK Kim, W Umbach (1973) Combined stereotactic lesions for treatment of behavioral disorders and severe pain, *Surgical Approaches in Psychiatry*, ed by LV Laitinen and KE Livingston, University Park Press, Baltimore, p. 182-195

30. AV Delgado-Escueta, et al (1981) Special Report: Current status of basic seizure mechanisms, *NEJM 305:711*

30a. JH Pincus (1981) Violence and epilepsy (editorial), *NEJM 303:696*

30b. V Ramani, RJ Gumnit (1981) Interictal monitoring of epileptic patients with a history of episodic aggression, *AnN9:520*

30c. O Devinsky, D Bear (1984) Varieties of aggressive behavior in temporal lobe epilepsy, *AJPsy 141:651*

31. CB Blakemore, MA Pelmutter (1967) Long term effects of unilateral temporal lobectomy in certain cognitive functions, *JNNP 30:364*

31a. B Milner (1968) Visual recognition and recall after right temporal-lobe excision in man, *N/psychologia 6:191*

31b. GA Ojemann, CB Dodrill (1985) Verbal memory deficits after left temporal lobectomy for epilepsy. Mechanism and intraoperative prediction, *J N/S 62:101*

32. W Penfield, B Milner (1958) Memory deficit produced by bilateral lesions in the hippocampal zone, *A M.A. Arch Psych 79:475*

32a. B Milner (1970) Memory and the medial temporal regions of the brain, in *Biology of Memory*, ed. by KH Pribram, DE Broadbent, Academic Press, New York, pp. 29-50

33. W Penfield, H Jasper (1954) *Epilepsy and the Functional Anatomy of the Brain*, Little, Brown, and Co., Boston. p. 123–143, 452–482

33a. E Halgren, et al (1978) Mental phenomena evoked by electrical stimulation of the human hippocampal formation and amygdala, Brain *101* 83

33b. P Gloor, et al (1982) The role of the limbic system in experiential phenomena of temporal lobe epilepsy, AnN *12* 129

34. BT Woods, et al (1982) Are hippocampal lesions sufficient to cause lasting amnesia?, JNNP *45* 243

34a. S Zola-Morgan, et al (1982) The neuroanatomy of amnesia: amygdala-hippocampus versus temporal stem, Science *218* 1337

35. JA Hirst (1978) The neuroanatomy of amnesia. A critique of the hippocampal memory hypothesis, Brain *101* 403

36. LJ Sperati, KM Heilman (1981) Anterograde memory deficits for visuospatial material after interction of the right thalamus, AnN *40* 153

36a. LR Squire, RY Moore (1979) Dorsal thalamic lesion in a noted case of human memory dysfunction, AnN *6* 503

36b. S Zola-Morgan, LR Squire (1985) Amnesia in monkeys after lesions of the mediodorsal nucleus of the thalamus, AnN *17* 558

36c. DY von Cramon, et al (1986) A contribution to the anatomical basis of thalamic amnesia, Brain *109* 1089

37. MI Albert, et al (1979) The anatomic basis of visual agnosia, N *29* 826

38. The role of memory (editorial), Lancet *2* 1981 p. 237

38a. RM Bauer (1982) Visual hypoemotionality as a symptom of visual-limbic disconnection in man, AdN *20* 702

39. AR Damasio, et al (1982) Prosopagnosia: anatomic basis and behavioral mechanisms, N *32* 331

40. ML Albert, et al (1979) The anatomic basis of visual agnosia, N *29* 870

40a. AJ Cermak, GA Reed (1984) Visual agnosia without alexia, N *34* 947

40b. JE Dobe, RM Bauer (1980) Serine lies on recognizing, Surv Ophth *30* 378

41. ED Rios (1980) Sensory-specific and fractional disorders of recent memory in man. I. Isolated loss of visual recent memory, AdN *37* 193

41a. ED Rios (1980) Sensory-specific and fractional disorders of recent memory in man. II. Unilateral loss of tactile recent memory, AdN *37* 267

41b. [illegible] Chen, et al (1979) The pattern of memory loss resulting from intravenously administered diazepam, AdN *36* 296

42. S Corkin (1984) Lasting consequences of bilateral medial temporal lobectomy: clinical course and experimental findings in H.M., Sem N *4* 249

43. RL Isaacson, Experimental brain lesions and memory. In M Rosenzweig and EL Bennett (eds.) *Neural Mechanisms of Learning and Memory*, Cambridge, Mass.: MIT Press 1976, pp. 521 543

43a. [illegible] Clark, et al (1979) On patterns of memory loss resulting from intravenously administered diazepam, AdN *36* 296

44. GW Van Hoesen, DN Pandya (1975) Some connections of the entorhinal area (area 28) and perirhinal (area 35) cortices of the rhesus monkey. I. Temporal lobe afferents, Br Res *95* 1

44a. FH Lopes da Silva, DL Arnolds (1978) Physiology of the hippocampus and related structures, Ann Rev Physiol *40* 155

44b. DG Amaral, et al (1983) Evidence for a direct projection from the superior temporal gyrus to the entorhinal cortex in the monkey, Br Res *275* 263

45. FH Lopes da Silva, DL Arnolds (1978) Physiology of the hippocampus and related structures, Ann Rev Physiol *40* 185

45a. GW Van Hoesen, et al (1979) Subicular input from temporal cortex in the Rhesus monkey, Science *205* 608

45b. TJ Teyler, P DiScenna (1985) The topological anatomy of the hippocampus: a clinical perspective, JNNP *12* 711

45c. BT Hyman, et al (1984) Alzheimer's disease: Cell-specific pathology isolates the hippocampal formation, Science *225* 1168

46. P Gloor, et al (1981) The role of the amygdala in the expression of psychic phenomena in temporal lobe seizures, in Y Ben-Ari (ed) *The Amygdaloid Complex*, Elsevier/North-Holland, Biomedical Press, Amsterdam, pp 489-497

46a. JA Gray (1983) A theory of anxiety, the role of the limbic system, J Psychiatr *9* (4 Suppl *2*) 1618

46b. JL Marx (1985) Anxiety peptide in brain, Science *227* 935

47. P Gloor, et al (1982) The role of the limbic system in experiential phenomena of temporal lobe epilepsy, AnN *12* 129

47a. M Sarter, HJ Markowitsch (1985) The amygdala's role in human memory processing, Cortex *21* 7

48. H Eichenbaum, et al (1983) Selective olfactory deficits in case HM, Brain *106* 459

48a. SS Schiffman (1983) Taste and smell in disease (first of two parts), NEJM *308* 1275

49. T Engen (1982) The human uses of olfaction, AdOto *4* 298 49b. DC Rubin, et al (1984) Olfactory cuing of autobiographical memory, Am J Psychol *97* 493

50. S Gates, et al (1977) The seizures of frontal lobe epilepsy. A study of clinical manifestations, N *27* 95.

50a. T Rasmussen (1983) Characteristics of a pure culture of frontal lobe epilepsy, Epilepsia *24* 482

51. H Ludwig, et al (1975) Cerebral seizures of probable extratemporal origin, Epilepsia *16* 161

52. AV Delgado Escueta, et al (1982) Complex partial seizures on closed-circuit television and EEG: a study of 691 attacks in *N* patients, AnN *12* 292

53. JK Penry, et al (1975) Simultaneous recording of absence seizures with video tape and electroencephalography. A study of 374 seizures in 48 patients, Brain *98* 427

53a. AV Delgado Escueta, et al (1985) Type I complex partial seizures of hippocampal origin. Excellent results of anterior temporal lobectomy, N *35* 143

54. GD Welch, et al (1985) Type II complex partial seizures. Poor results of anterior temporal lobectomy, N *34* 1

55. AV Escueta, et al (1977) Lapse of consciousness and automatisms in temporal lobe epilepsy. A videotape analysis, N *27* 144

55a. BT Desai, et al (1982) Psychogenic seizures. A study of 42 attacks in six patients, with intensive monitoring, AnN *39* 202

55b. FE Dreifuss (1981) Proposal for revised clinical and electroencephalographic classification of epileptic seizures, Epilepsia *22* 489

56. AV Delgado-Escueta, et al (1982) Complex partial seizures on closed-circuit television and EEG: a study of 691 attacks in 79 patients, AnN *11* 292

56a. RC Collins, et al (1983) Functional anatomy of limbic seizures: Focal discharges from medial entorhinal cortex in rat, Br Res *280* 25

57. R Mayeux, et al (1979) Pantomime, N *29* 1646

58. KL Casey (1982) Neural mechanisms of pain: an overview, Acta Anaes Scand Suppl *74* 12

58a. D Bowsher (1979-80) Central mechanisms of referred pain, Br J Oral Surg *17* 185

59. JP Lee, et al (1981) Neuropathological findings following temporal ablations related to surface and deep EEG patterns, Epilepsia *22* 519

59a. J Engel Jr, et al (1982) Pathological findings underlying focal temporal lobe hypometabolism in partial epilepsy, AnN *12* 518

60. PK Seitz, TN Rao (1976) Gelastic, quiritarian, and narrow epilepsy. A clinicopathological appraisal, JNNP *39* 823

60a. DP Jacome, et al (1980) Perioral reflex epileptic seizures, AnN *37* 349

60b. GN Bruninghaus (1985) Ictal tonic seizures, preictal pallor, and hypothalamic hamartoma, N *35* 1180

61. AV Delgado-Escueta, et al (1982) Complex partial seizures on closed circuit television and EEG: A study of 691 attacks in 79 patients, AnN *12* 292

61a. BT Desai, et al (1982) Psychogenic seizures. A study of 42 attacks in six patients, with intensive monitoring, AnN *39* 202

61b. WH Theodore, et al (1984) Complex partial seizures: clinical characteristics and differential diagnosis. *N 35* 1115

62. MA Falconer, JL Wilson (1958) Visual field changes following anterior temporal lobectomy: their significance in relation to "Meyer's loop" of the optic radiation. *Brain 81* 1

62a. R Marino, Jr, T Rautenstrauss (1968) Visual field changes after temporal lobectomy in man. *N 18* 825

63. NR Miller, Walsh and Hoyt's *Clinical Neuro-Ophthalmology*. Williams and Wilkins, Baltimore, 1982. Fourth edition, p. 135

63a. JD Trobe, et al (1977) Bilateral homonymous hemianopia. A review of 104 cases. *Arch Opht 95* 371

64. DP Rucklidge, et al (1983) Pure Gerstmann's syndrome from a focal lesion. *ANN 40* 461

64a. HH Morris, et al (1984) Transient neuropsychological abnormalities (including Gerstmann's syndrome) during cortical stimulation. *N 34* 877

65. A Damasio, et al (1980) Central achromatopsia: behavioral, anatomic, and physiologic aspects. *N 30* 1064

65a. AL Pearlman, et al (1979) Central color blindness. An acquired defect in hue discrimination. *ANN 5* 253

66. JC Meadows (1974) Disturbed perception of colours associated with localized cerebral lesions. *Brain 97* 615

66a. JM Ostrin, et al (1988) Varieties of color anomia. *Brain 93* 847

67. W Penfield, H Jasper (1954) *Epilepsy and the Functional Anatomy of the Human Brain*. Little, Brown & Co., Boston

68. CN Woolsey, et al (1979) Localization in somatic sensory and motor areas of human cerebral cortex as determined by direct recording of evoked potentials and electrical stimulation. *J NPS 51* 476

69. M Critchley (1953) *The Parietal Lobes*. Edward Arnold and Co., London, p. 108

69a. RJ Joynt, MN Goldstein (1975) Middle cerebral hemisphere. *AdvN 7* 147

70. PE Roland (1976) Acromegaly. Tactile discrimination after localized hemispheric lesions in man. *ANN 33*

70a. B Boivie, F Perbeng (1953) Studies on the cervical cord of man. Sensory patterns after interruption of the posterior columns. *N 5* 90

71. F Mauguière, J Courjon (1978) Somatosensory epilepsy. A review of 127 cases. *Brain 101* 307

72. RA Lende, AJ Papp (1976) Sensory Jacksonian seizures. *J NS 44* 206

73. PE Roland, et al (1980)Supplementary motor area and other cortical areas in organization of voluntary movements in man. *J Neurophys 43* 118

73a. U Jurgens (1984) The efferent and afferent connections of the supplementary motor area. *Br Res 300* 63

74. JR Crosa, et al (1980) Significance of the supplementary motor area in partial seizures and in cerebral localization. *N/S 5* 66

74a. JM Van Buren, P Fedio (1976) Functional representation on the mesial aspect of the frontal lobes in man. *J N/S 44* 225

75. DA Lee (1981) Paul Broca and the history of aphasia. Roland P. Mackay Award Essay. 1980. *N 11* 600

75a. A Meyer (1974) The frontal lobe syndrome, the aphasias and related conditions. A contribution to the history of cortical localization. *Brain 97* 565

76. RP Lesser, et al (1984) The localization of speech and writing functions in the frontal language area. Results of extraoperative cortical stimulation. *Brain 107* 275

77. BJ Ansell, CK Flowers (1982) Aphasic adults' use of thematic and situational linguistic cues for semantic analysis. *Brain Lang 16* 61

77a. M Zimmerman, S Halperin (1982) Apraxics' selective deficits in appreciating grammatical agreements. *Brain Lang 16* 109

77b. HB Coslett, LJ Rubi, KM Heilman (1984) Reading: selective sparing of closed-class words in Wernicke's aphasia. *N 34* 1038

78. JP Mohr, et al (1978) Broca aphasia: pathologic and clinical. *N 28* 311

79. SH Aarabath, et al (1982) Pure word deafness. Analysis of a case with bilateral lesions and a defect at the prephonemic level. *Brain 105* 271

80. S Geschwind (1970) Subangular alexia without agraphia or hemianopsia. *Brain Lang 3* 229

80a. SH Greenblatt (1973) Alexia without agraphia or hemianopsia. Anatomical analysis of an autopsied case. *Brain 96* 307

81. SH Greenblatt (1976) Subangular alexia without agraphia or hemianopsia, *Brain Lang 3* 229

82. KM Heilman, et al (1983) Transcortical sensory aphasia with relatively spared spontaneous speech and naming. *ANN 28* 236

83a. F Benson (1979) *Aphasia, Alexia, and Agraphia*. Churchill Livingstone, New York, p. 88

83. DF Benson (1977) The third alexia. *ArN 34* 327

83a. HS Kirshner, WG Webb (1982) Word and letter reading and the mechanism of the third alexia. *ArN 39* 84

83b. S Sevush, KM Heilman (1984) A case of literal alexia: evidence for a disconnection syndrome. *Brain Lang 22* 92

84. GG Celesia (1976) Organization of the auditory cortical area in man. *Brain 99* 403

84a. S Locke, et al (1962) Projection of the diencephalic medial geniculate nucleus in man. *Brain 85* 519

84b. AB Ruben (1984) The anatomy of disorders of auditory comprehension. *Sem N 4* 174

85. DL Woods, et al (1984) Bitemporal lesions disconnect auditory evoked potentials and perception. *NEUCNP 57* 208

85a. DR Upenieuxm, F Newcombe (1976) Clinical and anatomic findings in a case of auditory agnosia. *ANN 33* 712

85b. HF Hoffman, RS Hoffman (1986) Hearing loss in japanese macaques following bilateral auditory cortex lesions. *J Neurophys 55* 256

86. HB Coslett, et al (1984) Pure word deafness after bilateral primary auditory cortex infarcts. *N 34* 347

87. HS Kirshner, WG Webb (1981) Selective involvement of the auditory-verbal modality in an acquired communication disorder: benefit from sign language therapy. *Brain Lang 13* 161

88. SH Auerbach, et al (1982) Pure word deafness. Analysis of a case with bilateral lesions and a defect at the prephonemic level. *Brain 105* 271

88a. HB Coslett, et al (1984) Pure word deafness after bilateral primary auditory cortex infarcts. *N 34* 347

89. HB Coslett, et al (1984) Reading: selective sparing of closed-class words in Wernicke's aphasia. *N 34* 1038

89a. KM Heilman, et al (1981) Comprehension of affective and nonaffective prosody. *N 34* 917

89b. LJ Rubi, et al (1982) Conduction aphasia, syntactic alexia, and the anatomy of syntactic comprehension. *ArN 39* 232

90. A Kertesz, et al (1982) Localization in transcortical sensory aphasia. *ArN 39* 475

90a. KM Heilman, et al (1981) Transcortical sensory aphasia with relatively spared spontaneous speech and naming. *ArN 38* 236

90b. M Bartlo, et al (1980) Mechanisms of repetition in transcortical sensory aphasia. *BNNP 43* 200

91. KM Heilman, et al (1979) Wernicke's and global aphasia without alexia. *ArN 36* 129

91a. H Kinsbourne, et al (1981) Word deafness in Wernicke's aphasia. *JNNP 44* 107

92. LJ Rubi, et al (1982) Conduction aphasia, syntactic alexia, and the anatomy of syntactic comprehension. *ArN 39* 232

92a. OA Selnes, et al (1985) The critical role of Wernicke's area in sentence repetition. *AnN 17* 549

92b. H Damasio, AR Damasio (1980) The anatomical basis of conduction aphasia. *Brain 103* 337

93. JP Mohr, et al (1978) Broca aphasia: Pathologic and clinical. *N 28* 311

93a. CL Ludlow, et al (1986) Brain lesions associated with nonfluent aphasia fifteen years following penetrating head injury. *Brain 109* 57

94. SE Freedman, et al (1984) Anatomic basis of transcortical motor aphasia. *N 34* 409

94a. ED Bost (1980) Left medial parietal lobe and receptive language functions: Mixed transcortical sensory after left anterior cerebral artery infarction. *N 30* 143

95. HB Scliff, et al (1985) Aphemia. Clinical-anatomic correlations. *ArN 40* 728

95a. RL Ruff, E Adès (1981) Apraxia resulting from a left frontal lesion sparing. N 31 553
95. KM Heilman, et al (1981) Transcortical sensory aphasia with word-level sound confusion: speech and naming. Arch 38 229
96a. KM Heilman, et al (1979) Memory and global aphasia without alexia. Arch 36 129
96b. HS Kirschner, WG Webb (1982) Word and letter reading and the midsection of the third ventricle. Arch 39 80
96c. E Zaidel, AM Peters (1981) Phonological encoding and ideographic reading by the disconnected right hemisphere: two case studies. Brain Lang 14 205
97. LJ Rubi, KM Heilman (1981) Alexia and agraphia with spared spelling and letter recognition abilities. Brain Lang 11 1
98. AD Friedman, et al (1981) Mechanisms interfering writing and speech in aphasia. Brain Lang 13 212
99. RT Watson, KM Heilman (1983) Callosal apraxia. Brain 106 391
99a. A Yamadori, et al (1980) Left unilateral agraphia and tactile amnesia. Disturbances were over evidence of the anterior cerebral artery. Arch 37 58
99b. F Geschwind, AR Damasio (1981) Praxis and writing of the left hand may be severed by different callosal pathways. Arch 38 634
99c. RD Seitz, et al (1984) Callosal syndrome: implications for understanding the neuropsychology of speech. Arch 41 806
100. ET Ajax, et al (1977) Alexia without agraphia and the anterior callosum. N 27 685
100a. WW Henderson, et al (1985) Left hemispheric pathways in reading: inferences from pure alexia without hemianopia. N 35 362
100b. FM Vincent, et al (1977) Alexia without agraphia, hemianopia, or colour-naming defect: a disconnexion syndrome. N 27 689
100c. AR Damasio, H Damasio (1983) The anatomic basis of pure alexia. N 33 1573
101. HD Ross (1981) The aprosodias. Functional-anatomic organization of the affective components of language in the right hemisphere. Arch 38 561
101a. S Weinstein, et al (1981) Disturbances in prosody. A right-hemisphere contribution to language. Arch 38 742
101b. FD Ross, et al (1981) How the brain integrates affective and propositional language into a unified behavioral function. Hypotheses based on clinicoanatomic evidence. Arch 38 745
101c. FD Ross (1981) Right hemisphere's role in language, affective behavior and emotion. TINS 7 342
102. KM Heilman, et al (1984) Comprehension of affective and nonaffective prosody. N 34 917
103. DG Cogan (1979) Visuospatial dysgnosia. AJO 88 361
103a. M Critchley (1953) *The Parietal Lobes*. Edward Arnold and Co., London, p. 172-202, 356-358
103b. KM Heilman, et al (1986) Review article. The right hemisphere: neuropsychological functions. J NS 64 693
104. DB Hier, et al (1980) Hemispheral abnormalities after right hemisphere stroke. N 31 337
104a. FW Black, BA Bernard (1984) Constructional spectrum as a function of lesion locus and size in patients with focal brain damage. Cortex 20 111
105. JL Mark, RN Levine (1981) The basis of visual constructional disability with cerebral lesions. Cortex 17 512
105. CM Hutter (1982) Disconnection for praxis. Arch 39 33
106a. DC Cogan (1979) Visuospatial dysgnosia. AJO 88 (3 Pt 1) 361
106. KM Heilman, E Valenstein (1979) Mechanisms underlying hemispatial neglect. Arch 5 166
106a. MM Mesulam (1981) A cortical network for directed attention and unilateral neglect. Arch 10 309
106b. KM Heilman, et al. (1984) Neglect and related disorders. Sem N 14 468
106c. DN Levine, et al (1986) Left spatial neglect: effects of lesion size and premorbid brain atrophy on severity and recovery following right cerebral infarction. N 36 362
107. AF Rocon (1983) Understanding stroke and its rehabilitation. Stroke 14 458

CHAPTER 15:

1. SM Sheridan, et al (1979) Acute confusional states with right middle cerebral artery infarctions. JNNP 39 84
1a. JW Schmidley, RO Messing (1984) Agitated confusional states in patients with right hemisphere infarctions. Stroke 15 813
2. G Trzebiec, et al (1978) Observer variability in assessing impaired consciousness and coma. JNNP 41 609
3. D von Cramon (1978) Consciousness and disturbances of consciousness. JN 219 1
3a. JJ Cairns, RP Simon (1979) The comatose patient: a diagnostic approach and treatment. Int Anes Clin 17(2) 313
4. TW Welsh, C Leonard (1983) Persistent vegetative state. Unknown if the syndrome to include chronic disorders. Arch 40 1045
4a. JR Dougherty Jr, et al (1981) Hypoxic-ischemic brain injury and the vegetative state: Clinical and neuropathologic correlation. N 31 991
5b. CM Prater (1980) Honored guest presentation: Akinetic mutism vs. agitated behavior. Clin N-S 27 9
5. JJ Cairns, et al (1941) Akinetic mutism with an epidermoid cyst of the 3rd ventricle. Brain 64 273
5a. MS Hochman, et al (1985) Syringomyelia in the neurocephalic artery: report of a case with CT and necropsy findings. JNNP 48 1179
5b. LD Ross, RM Stewart (1981) Akinetic mutism from hypothalamic damage: Successful treatment with dopamine agonists. N 31 1435
6. *Diagnostic and Statistical Manual of Mental Disorders*. Washington, D.C.: The American Psychiatric Association; 1968, 1st edition
7. RT Watson, et al (1981) Thalamic neglect. Possible role of the medial thalamus and nucleus reticularis in behavior. Arch 38 501
7a. RT Watson, KM Heilman (1979) Thalamic neglect. N 29 690
7b. AC Papanicolaou, et al (1986) Intracerebral evoked response suppression during speech production. Brain Lang 27 50
8. MM Mesulam (1981) The functional anatomy and hemispheric specialization for directed attention. The role of the parietal lobe and its connectivity. TINS 8 346
8a. KM Heilman, T Van Den Abell (1980) Right hemisphere dominance for attention: The mechanism underlying hemispheric asymmetries of inattention (neglect). N 30 327
8b. BM Direl, BC Collins (1984) The functional anatomy of frontal lobe neglect in the monkey: behavioral and quantitative 2 dimensional studies. Ann N 15 521
8c. DL Woods, RT Knight (1986) Electrophysiologic evidence of increased distractibility after dorsolateral prefrontal lesions. N 36 212
9. A Goldstein (1976) Opioid peptides (endorphins) in pituitary and brain. Science 193 1081
9a. JH Wood (1982) Neuroendocrinology of cerebrospinal fluid: peptides, steroids, and other hormones. NS 11 293
10. GW Terman, et al (1984) Intrinsic mechanisms of pain inhibition: activation by stress. Science 226 1270
10a. AS Markowitz, JC Liebeskind (1983) Neural and neurochemical substrates of pain and pain inhibition. Sem N 3 325
11. PR Yarnell, S Lynch (1970) Retrograde memory immediately after concussion. Lancet 1 863
11a. JA Mandleberg (1976) Cognitive recovery after severe head injury. 3. Amnesia duration and time from injury (1). JNNP 39 1001
12. N Kapur, AK Coughlan (1980) Confabulation and frontal lobe dysfunction. JNNP 43 461
2a. DT Stuss, et al (1978) An extraordinary form of confabulation. N 28 1166
12b. DF Sharpe, et al (1981) Mechanisms of confabulation. N 31 1070
13. N Bowers (1984) Alcoholic Korsakoff's syndrome: An update. Sem N 4 226
13a. WG Muir, et al (1979) Memory recovery in Korsakoff's psychosis: A neuropsychological and neuropsychological investigation of two cases. Brain 102 749
14. KM Heilman, GW Sypert (1977) Korsakoff's syndrome resulting from bilateral fornix lesions. N 27 490
14a. WG Muir, et al (1979) Memory

disorder in Korsakoff's psychosis. An neuropathological and neuropsychological investigation of two cases. Brain 102 749
15. LR Squire, RY Moore (1979) Dorsal thalamic lesion in a noted case of human memory dysfunction. AnN 6 503
15a. G Goldenberg, et al (1985) Amnesic syndrome with a unilateral thalamic lesion: a case report. JN 229 39
15b. LJ Spinnler, KM Hollman (1983) Anterograde memory deficit for visuospatial material after infarction of the right thalamus. AnN 6 140
15c. LJ Spinnler, KM Hollman (1982) Amnestic disturbance following infarction of the left dorsomedian nucleus of the thalamus. Neuropsychologia 20 597
16. AJ Parkin (1984) Amnesic syndrome: a lesion-specific disorder? Cortex 20 479
17. K Butters (1979) Amnestic Disorders. in *Clinical Neuropsychology* ed. by KM Heilman, E Valenstein. Oxford University Press. New York. p. 439–474
17a. LR Squire (1982) The neuropsychology of human *memory*. Ann Rev N/Sci 5 241
18. W Penfield, B Milner (1958) Memory deficit produced by bilateral lesions in the hippocampal zone. AMA ArN Psych 79 475
18a. W Penfield, G Mathieson (1974) Memory. Autopsy findings and comments on the role of hippocampus in experimental recall. AnN 31 145
18b. H Lucien, et al. (1980) Basal temporal language area demonstrated by electrical stimulation. N 36 580
19. AJ Rowan, LM Pontius (1979) Transient global amnesia: Clinical and electroencephalographic findings in 10 cases. N 29 899
19a. JR Shuping, et al (1980) Transient global amnesia. AnN 7 241 (9)
M Regard, T Landis (1980) Transient global amnesia: neuropsychological dysfunction during attack and recovery in two "pure" cases. JNNP 47 668
20. GP Crowell, et al (1984) The transient global amnesia-transient obscuration. ArN 41 75
20a. W Logue, DG Sherman (1982) Transient global amnesia. *Stroke 14* 1005
20b. JL Pierfitte, GA Dumain (1980) Transient global amnesia a hippocampal phenomenon? JNNP 43 785
20c. J Olsen, MB Jorgensen (1986) Leao's spreading depression in the hippocampus explains transient global amnesia. ANS 73 219
21. A Rosa, L Gustafson (1976) Distribution of cerebral degeneration in Alzheimer's disease. A clinico-pathological study. Arch Psych Nervenkr 223 15
21a. MJ Ball (1978) Topographic distribution of neurofibrillary tangles and granulovacuolar degeneration in hippocampal cortex of aging and demented patients. A quantitative study. Acta Neuro 42 73
21b. ET Hyman, et al. (1984) Alzheimer's disease: cell-specific pathology isolates the hippocampal formation. Science 225 1168
21c. MJ Ball, et al (1985) A new definition of Alzheimer's disease: A hippocampal dementia. Lancet 1 14
22. PJ Eslinger, AR Damasio (1985) Severe disturbance of higher cognition after bilateral frontal lobe ablation: Patient EVR. N 35 1731
23. H Gardner, et al (1975) Comprehension and appreciation of humorous material following brain damage. Brain 98 399
24. LW Massey, CE Corley (1984) Delirium: Diagnosis and treatment. SMJ 76 1147
25. PD Harvey, et al (1984) The consistency of thought disorder in mania and schizophrenia. An assessment of acute psychosis. J Nerv Ment Dis 172 458
25a. J Mendlewicz, M Harrow (1984) Thought disorder. A function of schizophrenia, mania, or psychosis? J Nerv Ment Dis 172 35
26. B Shaffer: *Is There No Place On Earth For Me*. Houghton Mifflin, Boston. 1981. Originally in The New Yorker, May 25, p. 109
27. J Pippinbarren, et al (1980) Schizophrenia like psychosis caused by a metabolic disorder. Lancet 1 454
27a. AJ Getenberg (1970) The catatonic syndrome. Lancet 1 1339
27b. GJ Thienhaus, N Khoda (1984) Meningeal cryptococcosis misdiagnosed as a manic episode. AJPsy 141 1439
27c. WH Anderson, JC Knetzke (1981) Diagnosis and early management of acute psychosis. AFM 123 825 1428
27d. DC Owens, et al (1948) Unsuspected organic disease in chronic schizophrenia demonstrated by computed tomography. JNNP 47 1065
28. CB Wells (1982) Refinements in the diagnosis of dementia (editorial). AJPsy 139 62
28a. J Cutting (1979) Memory in functional psychosis. JNNP 42 1091
29. CW Wahl, et al (1952) Toxic and functional psychoses. Diagnosis and treatment in a medical setting. AmJP 66 989
30. RG Robinson, et al (1983) A two-year longitudinal study of post-stroke mood disorders: findings during the initial evaluation. Stroke 14 736
31. HS Silverman, et al (1983) Thinking disorder in depression. Logic and strategy in an attempt to manipulate. AmJPsych 40 775
31a. TW McAllister (1983) Overview: pseudodementia. AJPsych 140 528
31b. DA Plotkin, et al (1985) Subjective memory complaints in geriatric depression. AJPsy 142 1103
32. R Lesbine, et al (1983) Epilepsy from cerebral arteriovenous malformations. CNS(2) 1091
32a. PM Crawford, et al (1986) Arteriovenous malformations of the brain: natural history in unoperated patients. JNNP 49 1
33. EL So, JE Penry (1981) Epilepsy in adults. AnN 9 3
33a. LS Rosen Jr, KH Taddeucci (1984) The diagnostic assessment of single seizures. Is urgent computed tomography necessary? AJN 40 744
33b. M Ramsey-Lassegues, et al (1984) Value of computed tomographic scan in the evaluation of adult patients after their first seizure. AnN 15 536
34. AC Young, et al (1982) Is routine computerized axial tomography in epilepsy worth while? Lancet 2 1446
35a. JL Loiper, et al (1985) Late onset epileptic seizures. A retrospective study of 250 patients. ANS 72 380
35. RE Hurtough, DR Wilson (1982) Temporolimbic lesions of generalized epilepsy: observations in split-brain patients. N/S 30 735
36. E Gastaut, et al (1960) Lipomas of the corpus callosum and epilepsy. N 30 132
37. P Gloor (1978) Generalized epilepsy with bilateral synchronous spike and wave discharge. New findings concerning its physiological mechanisms. Electroen Clin Neurop (EEG Suppl No. 34) 243
37a. I Dravy, PE Dreifuss (1983) Pyknoepsy: petit mal. ANS 72 583
38. J Engel Jr, et al (1982) Recent developments in the diagnosis and therapy of epilepsy. AnIM 97 584
39. AV Delgado-Escueta, et al (1983) The intractable epilepsies (second of two parts). NEJM 308 1576
39a. L Guan, et al (1982) Controlled trials in epilepsy: a review. Epilepsia 23 491
39b. D Chadwick, DM Turnbull (1985) The comparative efficacy of antiepileptic drugs for partial and tonic clonic seizures. JNNP 48 1073
40. L Gram, et al (1985) Valproate: an updated review. ANS 72 329
40a. N Callahan, et al (1985) A prospective study between carbamazepine, phenytoin, and sodium valproate as monotherapy in previously untreated and recently diagnosed patients with epilepsy. JNNP 48 639
40b. DL Schomer (1984) Partial epilepsy. N(2)34 306 526
40c. J Bruni, P Albright (1983) Valproic acid therapy for complex partial seizures. Its efficacy and toxic effects. AnN 40 135
40d. DM Turnbull, et al (1982) A comparison of phenytoin and valproate in previously untreated adult epileptic patients. JNNP 45 55
41. CW Glasser, AL Fine (1981) Pompeian pharmacokinetics and clinical therapeutics. N/S 8 112
41a. AV Delgado-Escueta, et al (1983) The intractable epilepsies (second of two parts). NEJM 308 1576
42. CM MacLeod, et al (1978) Memory impairment in epileptic patients: selective effects of pharmacological intervention. Science 200 1401
42a. RJ Porter, WH Theodore (1983) Newer drug regimens in the treatment of epilepsy. AnIM 347 945
43. EH Reynolds, et al (1982) Phenytoin

...ion monotherapy for epilepsy: A long-term prospective study, assisted by serum level monitoring in previously untreated patients. Epilepsia 22 443

43a. P Allen[hi], J Bruni (1983) Treatment of polypharmacy in epileptic patients. AnN 40 793

44. CW Illingw..., AL Hunt (1982) Pharmacokinetic pharmacodynamics and clinical therapeutics. Neurosurg 8 132

44a. FC Rubinstein, et al (1944) Predicting individual pharmacologic levels of patients seen in a private office practice. N 231 761

45. FJ Se..., JK Perry (1981) Epilepsy in adults. AnN 9 3

45a. BJ Dunn, WH Theodore (1985) Nonsurgical treatment in the treatment of epilepsy. AnIM 102 943

45b. MJ Ramsay, et al (1980) A double blind study comparing carbamazepine with phenytoin as initial routine therapy in adults. N 33 964

45c. AV Delgado-Escueta, et al (1982) The treatable epilepsies (second of two parts). NEJM 306 1426

46. DM Turnbull, et al (1983) Plasma concentrations of serum valproate: their clinical value. AnN 14 38

46a. RP Loeser, et al (1984) High dose monotherapy in treatment of intractable seizures. N 34 707

47. S Gore, et al (1982) Long term follow up of absence seizures. N 33 1988

48. JH Meakes (1976) Diagnosis and treatment of minor motor seizures. PCNA 23 455

48a. WT Blume, et al (1977) Generalized sharp and slow wave epilepsies. Automated clinical systems and long term follow up. Brain 56 289

49. LL Se..., et al (1980) Misdiagnosis of complex partial seizures. AnN 41 648

49a. SI Lo... (1983) Nonconvulsive status epilepticus. AnN 42 778

49b. J Van Rossum, et al (1985) Psychomotor coma. AnN 17 989

49c. PD Wi...mson, et al (1985) Complex partial status epilepticus: a CT/EEG correlative study. AnN 17 647

50. AV Delgado-Escueta, et al (1982) The treatable epilepsies (first of two parts). NEJM 306 1008

50a. WH Theodore, et al (1983) Complex partial seizures: Clinical characteristics and differential diagnosis. N 33 1115

51. PS Bergman (1957) Cerebral bladders. An analysis of bladder cases with especial reference to the electroencephalogram and pictures of recovery. AMA Arch Psych 78 568

52. BE Schwartz, JC Rose (1964) Arrest syndrome accompanying withdrawal hallucinosis in a chronic psychotic. N 14 986

52a. W Cleveland, et al (1951) Schizophrenic appearance of Amos's syndrome. JAMA 247 1243

53. ML Albert, et al (1978) Use and utility of visual stimuli. N 29 876

53a. AA Gurvich, GA Ilyutchik (1991) Visual agnosia without alexia. N 34 947

53b. JK Trobe, RM Bazer (1985) Seeing without recognizing. Surv Ophth 29 325

54. RW Hamer, JD Trobe (1984) Visual memory and perceptual impairments in psychogenic. J Clin N Ophth 4 29

54a. AR Damasio (1985) Prosopagnosia. TINS 8 132

54b. R Hay, KD Laver (1980) Type III complex partial seizures, association with surgical outcome. Epilepsia 25 657

55. R Rizzo, et al (1992) The group reflex and preservation. Brain 97 181

56. J Tweedy, et al (1985) Significance of cortical distribution signs. N 32 1656a. I Isaacs, VH Cheeman (1980) Three primitive reflexes in normal adults. N 30 184

57. RM Cheetam, et al (1980) Peripheral neuropathy in sleep restricted myelomeningocele patients on sleep quiet diets. AnN 8 416

57a. J Oxford (1990) Sensory-motor bodily echo in falling asleep. Brain 82 92

57b. MA Dimitry, N Villyard (1990) Clomipramine treatment of insomnia due to sleep myoclonus. AnN 27 119

57c. DS Lazarus, et al (1981) Midbrain reticular formation involvement in the inhibition of acoustic startle. Physiol Behav 26 259

58. JC Rothwell, et al (1984) On the significance of giant somatosensory evoked potentials in cortical myoclonus. JNNP 47 33

58a. M Hallett, et al (1979) Cortical reflex myoclonus. N 29 1107

58b. H Kelly Jr, et al (1978) Movement Disorders and cranial See rhythms: An MEG study in reflex myoclonus. N 28 1087

58c. H Schwab, et al (1978) Electroencephalographic studies of myoclonus. Myoclonus-related cortical spikes and high amplitude somatosensory cortical potentials. Brain 101 445

59d. L Rosen, et al (1977) Facial reflex epilepsy with myoclonus: electrophysiological investigation and therapeutic implications. EEGCNP 42 95

59c. GG Sutton (1975) Receptors in facial reflex myoclonus. JNNP 38 905

59f. GG Sutton, RF Mayer (1974) Facial reflex myoclonus. JNNP 37 201

59. CD Marsden, et al (1983) Clinical neurophysiology of muscle jerks, myoclonus, chorea, and tics, in Advances in Neurology 39: Motor Control Mechanisms in Health and Disease, ed by JE Desmedt. Raven Press, New York pp 805 851

59a. D Chadwick, AT Fraser (1979) A mimic myoclonus: an example of reticular reflex myoclonus? JNNP 42 53

59b. M Hallett, et al (1979) Cortical reflex myoclonus: a physiological type of human post-hypoxic myoclonus. JNNP 40 253

59c. M Hallett, et al (1979) Cortical reflex myoclonus. A form of essential myoclonus. Brain 100 239

60. AI Fulton, JJ Townsend (1976) Myoclonus in Alzheimer cirrosis. A confusing sign. AnN 32 278

60a. HE Williams, et al (1984) Physiologic analysis of the myoclonus of Alzheimer's disease. N 34 898

60b. MH Rosen, BA Feldman (1976) Neurologic disorders in renal failure. NEJM 294 143

61. DE Wilkins, et al (1984) Physiologic analysis of the myoclonus of Alzheimer's disease. N 34 898

62. M Hallett, et al (1977) Reticular reflex myoclonus, a physiological type of human post-hypoxic myoclonus. JNNP 40 253

62a. M Hallett, et al (1979) Cortical reflex myoclonus. N 29 1107

63. TW Kanyanaki (1963) Hyperplexia. AnN 40 240

63a. H Stevens (1965) "Jumping Frenchmen of Maine" AnN 12 311

63b. JF Hardison (1980) Are the jumping Frenchmen of Maine passive? JAMA 244 78

64. MM Hebert, M Cherington (1977) Spinal myoclonus. N 27 942

64a. R Levy, et al (1983) Spinal myoclonus related to an arteriovenous malformation. Response to clonazepam therapy. AnN 40 254

65. J Jacobs, et al (1981) Disappearing palatal myoclonus. N 31 748

65a. HF Wolintz-Dekel, et al (1983) Brainstem auditory evoked potentials in 20 patients with palatal myoclonus. AnN 6 155

65b. F Matson, ET Ajax (1979) Palatal myoclonus and corrective upper sensorimotor in the central nervous system. AnN 5 92

66. J Jankovic, S Fahn (1980) Physiologic and pathologic tremors. Diagnosis, mechanism, and management. AnIM 92

66a. AS Wee (1986) Unilateral nasality (see upon and tremors). Ear N 25 205

67. AG Shenfield, et al (1984) Intrusions and consciousness. Brain Lang 22 148

CHAPTER 16:

1. HH Williams (1969) Neurosurgical classics XXI. JN 6 20 814

2. JW Lance (1980) The control of muscle tone, reflexes, and movement: Robert Wartenberg lecture. N 30 1303

3. A Benedetti, et al (1985) Stretch reflexes of triceps surae in patients with upper motor neuron syndrome. JNNP 46 54

4. D Burke, et al (1972) Spasticity, decerebrate rigidity and the clasp-knife phenomenon: an experimental study in man. Brain 95 31

5. M Wiesendanger (1984) Pyramidal tract function and its clinical "pyramidal weakness". Hum Neuro 2 93

6. RJ Schmahmann (1978) A behavioral analysis of complete unilateral section of the pyramidal tract at the medullary level in Macaca mulatta. AnN 4 234

7. G Rushworth (1968) Spasticity and rigidity: an experimental study. *JNNP 23* 99
7a. P Ashby, M Verrier (1976) Neurophysiologic changes in hemiplegia. Possible explanation for the initial disparity between muscle tone and tendon reflexes. *N 26* 1143
8. JW Lance (1980) The control of muscle tone, reflexes, and movement: Robert Wartenberg lecture. *N 30* 1390
9. MR Dimitrijevic, et al (1980) Clonus: the role of central mechanisms. *JNNP 43* 321
10. J Van Gijn (1978) The Babinski sign and the pyramidal syndrome. *JNNP 41* 865
11. VT Meier (1983) Lacunar strokes. A reassessment. *AcN 68* 129
11a. CM Fisher (1982) Lacunar strokes and infarcts: A review. *N 32* 871
11b. JF Meiler (1982) Lacunes. *Stroke 13* 5
11c. A Rascol, et al (1982) Pure motor hemiplegia: CT study of 30 cases. *Stroke 13* 1132. NL Rosenberg, B Kistler (1941) Computerized tomography and pure sensory stroke. *N 31* 317
13. RL Ho (1982) Pure motor hemiplegia due to infarction of the cerebral peduncle. *AcN 59* 525
14. E Clarke, PK Robinson (1956) Cervical myelopathy: a complication of cervical spondylosis. *Brain 79* 483
14a. RH Smith (1988) *Cervical Spondylosis and Its Neurologic Complications*. Charles C Thomas Publ, Springfield, IL, pp. 111-122
15. J Hall, et al (1977) The role of ischemia in the pathogenesis of cervical spondylotic myelopathy: A Review and new microangiographic evidence. *Spine 2* 100
15a. HH Meyer, et al (1984) Benign tumors of the foramen magnum. *J NS 61* 136

CHAPTER 17:

1. DB Calne, et al (1979) Advances in the neuropharmacology of Parkinsonism. *AnIM 90* 219
1a. SD Iversen (1991) Motor Control, Br Med Bull *37* 147
1b. *J Neurol Sci 117* Feb 1993 suppl *S 31*
2. MW Bradbury (1984) The structure and function of the blood brain barrier. *Fed Proc 43* 186
2a. JD Fenstermacher (1985) Current models of blood brain transfer. *TINS 8* 449
3. Y Toyokura, et al (1985) Effects of bromocriptine on Parkinsonism. A nationwide collaborative double-blind study. *ANS 72* 357
4. CN Kurtzke, et al (1984) Blink rates and disorders of movement. *N 34* 627
5. H Tsuboyama, DB Calne (1980) Action tremor in Parkinson's disease. *JNNP 43* 259
5a. JW Lance, et al (1963) Action tremor and the cogwheel phenomenon in Parkinson's disease. *Brain 86* 95
6. *J Laryngol S Falci* (1986) Physiologic and pathologic tremors. Diagnosis, mechanism, and management. *AnIM 95* 468
6a. D Jefferson, et al (1979) Beta-adrenergic antagonists in essential tremor. *JNNP 42* 904
6b. RR Young, RT Shahani (1979) Pharmacology of tremor. *Clin Neuropharm 4* 139
7. U Giovanni, SM Channabasavanna (1986) Is akathisia a forerunner of tardive dyskinesia? A clinical report with brief review of literature. *Clin NS 25* 86 187
7a. T van Putten, et al (1980) Akathisia with haloperidol and thiothixene. *ArGPsych 37* 1036
7b. E Szobadi (1986) Akathisia: a new entity. *NMJ 2* 92 (1)
8. RP Granacher Jr (1981) Differential diagnosis of tardive dyskinesia: an overview. *AJPsych 138* 1288
9. AC Peters, et al (1979) ECHO 25 focal encephalitis and subacute hemichorea. *N 29* 678
9a. CS Kaw, et al (1983) Hemichorea hemiballism and bizarre infection in the basal ganglia. *N 33* 452
9b. WG Ironson, S Fahn (1977) Treatment of vascular hemiballismus and hemichorea. *N 27* 634
10. M Hallett, N Alvarez (1983) Attempted right elbow flexion movements in patients with athetosis. *JNNP 46* 345
10a. *J Foley* (1983) The athetoid syndrome. A review of a personal series. *JNNP 46* 280
10b. CD Marsden, MJ Harrison (1974) Idiopathic torsion dystonia. *Brain 97* 793
11. K Burns, et al (1984) Lesions of the putamen and dystonia: CT and magnetic resonance imaging. *N 34* 960
11a. D Denny-Brown: Clinical symptomatology of diseases of the basal ganglia, in Yahr MD (edit), Handbook of Clinical Neurology. Vol 6: Diseases of the Basal Ganglia. Amsterdam, North Holland, 1968 pp. 133-143
12. S Lal (1979) Pathophysiology and pharmacotherapy of spasmodic torticollis: a review. *Can J Neurol Sci 6* 427
12a. AJ Stoessl, et al (1986) PET studies of cerebral glucose metabolism in idiopathic torticollis. *N 36* 853
12b. S Gardner (1986) Idiopathic spasmodic torticollis: pathophysiology and treatment. *Can J Neurol Sci 13* 88
13. GB Koelle (1979) New drugs and the brain. Discoveries in brain chemistry are leading to a more rational search for new psychotropic drugs. *Science 205* 751
14. VA Bohn (1980) The causes of cerebral palsy. A contemporary perspective. *JAMA 247* 1473
14a. *J Foley* (1983) The athetoid syndrome. A review of a personal series. *JNNP 46* 280
15. MP Stanley, CD Marsden (1982) Writer's cramp—a focal dystonia. *Brain 105* 461
15a. M Hughes, DJ McLellan (1989) Increased co-activation of the upper limb muscles in writer's cramp. *JNNP 48* 382
15b. J Ravits, et al (1985) Primary writing tremor and myoclonic writer's cramp. *N 35* 1382
16. MD Yahr (1978) A physician for all seasons. James Parkinson 1755-1824. *ArN 35* 185
17. E Krantzon (1972) An analysis of Parkinsonian gait. *Brain 95* 425
18. EM Critchley (1981) Speech disorders of Parkinsonism: a review. *JNNP 44* 751
18a. S Scott, H Caird (1983) Speech therapy for Parkinson's disease. *JNNP 46* 166
18b. RD Kent, JC Rosenbek (1982) Prosodic disturbance and neurologic lesion. *Brain Lang 15* 259
19. MJ Bell (1984) The morphological basis of dementia in Parkinson's disease. *Can J N Sci 11* 181
19a. U Berrylunner, SI Keh (1984) Neurochemical basis of dementia in Parkinson's disease. *Can J N Sci 11* 185
19b. RG Brown, CD Marsden (1984) How common is dementia in Parkinson's disease? *Lancet 2* 1262
20. A Berardelli, et al (1983) Physiological mechanisms of rigidity in Parkinson's disease. *JNNP 46* 45
21. LJ Findley, et al (1981) Tremor, the cogwheel phenomenon and clonus in Parkinson's disease. *JNNP 44* 534
22. J Benson, et al (1983) Comparison of three parkinsonian reflexes in normal elderly patients and in senile dementia of Alzheimer type. *JNNP 46* 160
22a. J Tweedy, et al (1982) Significance of primitive reflexes in normal adult ageing. *N 32* 1689
23. AE Lang, J Weiner (1985) Paroxysmal hemiballismus with lesions outside the subthalamic nucleus. *Can J N Sci 12* 125
24. JJ Melamed, et al (1978) Hemiballismus. Detection of focal lesion by CT scan. *ArN 4* 502
24a. AR Greenman, et al (1984) Experimental hemichorea/hemiballism in the monkey. Studies on the striatonigral site of action in a drug induced dyskinesia. *Brain 107* 579
25. LJ Findley, MA Gresty (1980) Suppression of "static" tremor with levodopa. *BMJ 281* 1043
25a. SJ Bensimon, PP Rubin Rabson Tremor: clinical features and treatment in three cases. In: *Clinical and Experimental Neurology*, ed by JH Tyner and MI Dietz, AIHS Health Science Press, Sydney, 1984, pp. 119-136
26. S Sachs (1982) Chorea caused by cardiac infarction. *ArN 40* 908
26a. M Tatlisumak, et al (1995) Generalized chorea due to bilateral small deep cerebral infarcts. *N 25* 586
27. N Sarmiento, et al (1986) Action induced rhythmic dystonia: an autopsy study. *N 36* 921
27a. DC Dooling, RD Adams (1975) The pathologic anatomy of postencephalitic parkinsonism. *Brain 98* 29
28. R Dominguez, P Rondot (1983) Dystonia caused by putaminal capsulo-

cardiac vascular lesions. JNNP 45 404
28a. J Narbeth, et al (1984) Hemidystonia secondary to localized basal ganglia tumour. JNNP 47 701
28b. N Sasahara, et al (1984) Acromodulated dystonic dystonia. An autopsy case. N 34 32
29. CD Marsden (1984) Movement disorders in basal ganglia disease. Hum Neurol 2 265
29a. CD Marsden (1984) Function of the basal ganglia as revealed by cognitive and motor disorders in Parkinson's disease. Can J Neurol Sci 11 129
29b. MB Shaikh, et al (1985) Forebrain structures regulating flight behavior in the cat. Br Res Bull 14 217
30. IB Petty, AB Young (1983) Speculations on the functional anatomy of basal ganglia disorders. Ann Rev Neurol 6 73
30a. HK Strehlenbert, CD Barnes (1982) Control of substantia nigra pars reticulata neurons by the nucleus accumbens. BRBull 21 259
30b. GJ Mogenson, MA Nielsen (1982) Evidence that an accumbens to subpallidal GABA-ergic projection constitutes to locomotor activity. BRB 11 309
31. MR DeLong, et al (1984) Role of the basal ganglia in limb movements. Hum Neurol 2 135
31a. RG Lee (1984) Physiology of the basal ganglia: an overview. Can J Neurol Sci 11 134
32. HD Caine, J Shoulson (1983) Psychiatric syndromes in Huntington's disease. AJPsy 140 728
32a. MR Hayden (1983) Reflections on the history of Huntington's chorea. TINS 6 122
33. JB Martin (1984) Huntington's disease: New approaches to an old problem. N 311 1059
33a. GA Graveland, et al (1985) Evidence for degenerative and regenerative changes in neostriatal spiny neurons in Huntington's
33b. RA Roos, et al (1985) Neuronal distribution in the putamen in Huntington's disease. JNNP 48 422
34. JH Growdon, et al (1977) Huntington's disease: Clinical and chemical effects of chronic administration. ANN 1 418
34a. D Tarsy, M Baldwin (1977) Drugs in extrapyramidal movement disorders. ANN 34 736
34b. HL Klawans, et al (1980) Tardive dyskinesia: review and update. AJPsy 137 900
35. K Magnup, et al (1985) Pirlindole in the treatment of hyperkinetic extrapyramidal movement disorders. ANS 72 341
36. G Tell, et al (1981) Treatment of Huntington disease with gamma-acetylenic GABA, an irreversible inhibitor of GABA-transaminase: Increased CSF GABA and homocarnosine with no clinical amelioration. N 31 207
36a. DG Owens, et al (1982) Spontaneous involuntary disorders of movement. Their prevalence, severity, and distribution in chronic schizophrenics with and without treatment with neuroleptics. ArGPsy 39 452
36b. JM Kane, JM Smith (1982) Tardive dyskinesia: Prevalence and risk factors, 1959 to 1979. ArGPsy 39 473
37. DR Burt, et al (1977) Anti-schizophrenic drugs: chronic treatment elevates dopamine receptor binding in brain. Science 196 326
37a. AM Marshall, RK Mishra (1980) Dopamine sensitive adenylate cyclase and dopaminergic/neuroleptic receptor binding: effect of neuroleptic drugs. Adv Biochem Psychopharm 24 153
38. SH Snyder (1982) Schizophrenia, Lancet 2 970
38a. J Cross, et al (1982) Dopamine receptors in the central nervous system, Int Rev Neurobiol 23 255 38b. E Richelson (1984) Neuroleptic affinities for human brain receptors and their use in predicting adverse effects, J Clin Psychiatry 45 331
39. F Javoy-Agid, Y Agid (1980) Is the mesocortical dopaminergic system involved in Parkinson disease?, N 35 1326
39a. FX Walsh, et al (1987) Dopamine and homovanillic acid concentrations in striatal and limbic regions of human brain. AnN 22 52
40. GR Uhl, et al (1985) Parkinson's disease: Loss of neurons from the ventral tegmental area contralateral to therapeutic surgical lesions, N 35 1215
41. J Stevens, et al (1974) GABA blockade, dopamine, and schizophrenia: experimental studies in the cat. Psychopharm 39 185
42. JR Stevens, A Livermore Jr (1978) Kindling of the mesolimbic dopamine system: Animal model of psychosis, N 28 39
43. TJ Crow, et al (1977) Do nucleus accumbens penicillin site of antipsychotic action of neuroleptic drugs?, Psychol Med 7 213
43a. G Bartholini (1976) Differential effect of neuroleptic drugs on dopamine turnover in the extrapyramidal and limbic system. J Pharm Pharmacol 28 429
44. AV Mackay, et al (1982) Increased brain dopamine and dopamine receptors in schizophrenia, ArGPsy 39 991
44a. P Seeman, et al (1976) Antipsychotic drug doses and neuroleptic dopamine receptors, Nature 261 717
44b. F Owen, et al (1978) Increased dopamine-receptor binding in schizophrenia, Lancet 2 223
44c. HY Zemlan (1985) Down-regulation of central dopamine receptors in schizophrenia, AJPsy 142 1534
45. J Cross, et al (1983) Dopamine receptors in the central nervous system, Adv Biochem Psychopharm 36 135
45a. JW Kebabian, et al (1984) Pharmacological and biochemical evidence for the existence of two categories of dopamine receptor, Can J Neurol Sci 11 116

CHAPTER 18:

1. AM Smith, D Bouchamma (1981) Neuronal activity in cerebellar cortex related to control of prehensile force, J Neurophys 45 286
2. J Dichgans (1984) Clinical symptoms of cerebellar dysfunction and their pathophysiological significance, Hum Neurol 2 268
3. C Marsden (1978) The mechanisms of physiological tremor and their significance for pathological tremors, in *Physiological Tremor, Pathological Tremors and Clonus*, ed by J Desmedt, S Karger, New York, p 1–16
4. PN Leigh, et al (1983) Beta adrenoreceptor mechanisms in essential tremor, a double blind placebo controlled trial of propranolol, studied and assessed, JNNP 46 730
4a. TA Lamon, DH Calne (1983) Review, Essential tremor, Clin Neuropharm 6 183
4b. RR Young (1982) Essential familial tremor and other action tremor, Sem N 2 369
4c. L Cleeves, LJ Findley (1984) Beta-adrenoreceptor mechanisms in essential tremor: a comparative single dose study of the effect of a non-selective and beta-2 selective adrenoreceptor antagonist, JNNP 47 916
4d. R Travaglini, TA Lamon (1984) Adrenergic beta-receptor sensitivity in essential tremor, JNNP 47 1216
4e. MH Cleeves, A Morgan (1985) Clonidine in essential tremor: preliminary observations from an open trial, JN 232 55
4f. J Elble (1986) Physiologic and essential tremor, N 36 225
5. T Ville, J Ross (1980) Central neural mechanisms contributing to cerebellar tremor produced by limb perturbations, J Neurophys 43 219
6. WC Kolbe, et al (1981) Cerebellar atrophy demonstrated by computed tomography, N 31 605
6a. KH Mumenthaler, et al (1979) Quantitative analysis of stance in late cortical cerebellar atrophy of the anterior lobe and other forms of cerebellar ataxia, Brain 102 461
7. LA Abeli, et al (1980) Square wave oscillation. The relationship of saccadic intrusions and oscillations, N Suppl 4 21
7a. JA Sharpe, WA Fletcher (1984) Saccadic intrusions and oscillations, Can J Neurol Sci 11 476
8. C Wetzenbaker, et al (1983) Opsoclonus—a cerebellar disorder?, Neurol 2 73
8a. V Vignolendo, CD Lim (1977) Electrooculographic analysis of opsoclonus: Its relationship to saccadic and nonsaccadic eye movements, N 27 1129
8b. (1985) AnN 18 623
8c. SN Bellur (1975) Opsoclonus: Its clinical value, N 25 502
9. F Bornheim, et al (1976) Myoclonic encephalopathy of infants or "dancing eye syndrome." Report of 7 cases with long term follow-up and

review of the literature (cases with and without neuroblastoma), Hum Pathol Arch 54 119
9a. MA Mazzarella, et al (1984) Ocular involvement in neuroblastoma: prognostic implications, Ophthal 91 936
9b. B Dimpfel, R Payne (1986) Paraneoplastic opsoclonus-myoclonus. Association with medullary thyroid carcinoma and review of the literature, ArN 43 440
10. DG Cogan, et al (1982) Ocular signs of cerebellar disease, ArOph 100 755
10a. RH Spector, BT Tyson (1981) The ocular motor system, AnN 9 543
10b. DS Zee, et al (1981) Effects of ablations of flocculus and paraflocculus on eye movements in primate, J Neurophys 45 878
10c. DS Zee (1984) New concepts of cerebellar control of eye movements, UtahNS 87 59
11. JA Sharpe, AW Lo (1981) Voluntary and visual control of the vestibulo-ocular reflex after cerebral hemidecortication, AnN 10 164
11a. BO Barber (1984) Vestibular neurophysiology, OtNS 97 53
12. GM Halmagyi, MA Gresty (1979) Clinical signs of visual-vestibular interaction, JNNP 42 934
12a. T Shimazu, H Kwan (1982) Floccular inhibition of the vestibulo-ocular reflex in man, J Clin Neurophys 2 201
13. RD Kent, JC Rosenbek (1982) Prosodic disturbance and neurologic lesion, Brain Lang 15 259
14. J Dichgans (1981) Clinical symptoms of cerebellar dysfunction and their topodiagnostical significance, Hum Neurob 2 269
15. S Gilman (1969) The mechanism of cerebellar hypotonia. An experimental study in the monkey, Brain 92 621
16. J Fenby (1978) Vestibulogenic imbalance, BMJ 1 1244
16a. MR Dix (1969) Modern tests of vestibular function, with special reference to their value in clinical practice, JLO 83 171
17. J Dichgans (1984) Clinical symptoms of cerebellar dysfunction and their topodiagnostical significance, Hum Neurob 2 269
18. DG Cogan, et al (1982) Ocular signs of cerebellar disease, ArOph 100 755
19. P Brodal (1978) The corticopontine projection in the rhesus monkey. Origin and principles of organization, Brain 101 251
20. PM van Buren (1963) Somatic responses from stimulation of the inferior Rolandic and Sylvian regions in man, J NrS 29 119
21. MR DeLong, et al (1984) Role of basal ganglia in limb movements, Hum Neurob 2 235
21a. CD Bucy (1983) The basal ganglia in extrapyramidal dysfunction, BRBull 11 271
22. H Schneider, et al (1983) Dextral hemisphere differences in the kinesthetic perceptual associated with writing and drawing, Hum Neurob 2 197
22a. CD Marsden (1982) The mysterious motor function of the basal ganglia: The Robert Wartenberg lecture, N 32 514
22b. VB Brooks (1981) Comment: on functions of the "cerebellar circuit" in movement control, Can J Phys Pharm 59 776
23. KY Huang, PS Lai (1984) Ataxic-hemiparesis: localization and clinical features, Stroke 15 261
23a. HB Montgomery Jr (1981) Signs and symptoms from a cerebral lesion may suggest cerebellar dysfunction, AJN 40 422
23b. M Kushner, et al (1984) Contralateral cerebellar hypometabolism following cerebral insult: a positron emission tomographic study, AnN 15 425
23c. E Mori, et al (1984) Ataxic hemiparesis from small capsular lacunae. Computed tomography and somatosensory evoked potentials, ArN 41 1050
24. GP Perman, A Rucy (1936) Homolateral ataxia and cranial paresis, Case report, K 59 1013
24a. K Ketterer, Y Stinchem (1981) Ataxic hemiparesis in patients with primary pontine hemorrhage, Stroke 14 982
24b. K Ichikawa, et al (1985) Capsular ataxic hemiparesis. A case report, ArN 39 585
25. CM Fisher (1978) Ataxic hemiparesis. A pathologic study, ArN 35 126
25a. T Sakai, et al (1981) Ataxic hemiparesis with trigeminal weakness, N 31 855
25b. VJ Inacci, CB McCutchen (1982) Capsular ataxic hemiparesis, AnN 39 528
26. PF Hoedemaker, BO Berg (1981) Ataxic hemiparesis from a midbrain mass, AnN 9 405
26a. K Radhakrishnan, et al (1984) Ataxic hemiparesis: clinical, electrophysiologic, radiologic and pathologic observations, Clin NNS 84 91
27. Hale Bassi, et al (1981) Hemiataxia and cranial hemiparesis following capsular infarct, JNNP 46 561
27a. J Bogousslavsky, et al (1991) Frontal ataxic hemiparesis, AnN 47 892
28. KH Maurer, et al (1979) Quantitative analysis of stance in late cortical cerebellar atrophy of the anterior lobe and other forms of cerebellar ataxia, Brain 102 461
28a. WC Kistler, et al (1991) Cerebellar ataxia demonstrated by computed tomography, N 37 401
29. K Lechtenberg, S Gilman (1978) Speech disorders in cerebellar disease, AnN 3 285
29. JD Speelman, J Van Mierlo (1984) Stereotactic thalamotomy for the relief of intention tremor of multiple sclerosis, JNNP 47 596
30a. G Broggi, et al (1983) Long term results of stereotactic thalamotomy for cerebral palsy, NrS 17 195
30b. DF Ballard, BS Nashold Jr (1984) Stereotaxic thalamotomy for treatment of posttraumatic movement disorders, J NrS 61 316
30c. K Matsumoto, et al (1984) Long-term follow-up review of cases of Parkinson's disease after unilateral or bilateral thalamotomy, J NrS 60 1003

CHAPTER 19:

1. PM Black (1982) Neuroscience for the Neurosurgeon. Neuropeptides in cerebrospinal fluid, NrS 11 550
1a. JH Wood (1982) Related Disciplines. Neurochemistry of cerebrospinal fluid: peptides, steroids, and other hormones, NrS 11 203
1b. RW Ciesler, RD Spence (1982) Cerebrospinal fluid: A selective review, AnS 11 1
2. MC Moore-Ede, et al (1983) Circadian timekeeping in health and disease. Part 1. Basic properties of circadian pacemakers, NEJM 309 469
2a. MC Moore Ede, et al (1983) Circadian timekeeping in health and disease. Part 2. Clinical implications of circadian rhythmicity, NEJM 309 530
2b. AA Sadun, et al (1984) A retinohypothalamic pathway in man: light mediation of circadian rhythms, Brain 107 775
3. EGG, ML Apuzzo (1985) The pineal gland: anatomy, physiology, and clinical significance, J NrS 63 321
3a. F Waldhauser, et al (1984) Fall in nocturnal serum melatonin during prepubertal and pubertal years, Lancet 1 362
3. RM Dorsch (1987) Historical aspects of normal and abnormal brain fluids. I. Cerebrospinal fluid, AnN 89 197
5. Y Pamya, et al (1984) Computerized topography of cranial sutures. Part I: Comparison of serum osteocalcin in children and adults, J NrS 61 53
6. CM Fleur (1982) Hydrocephalus as a cause of disturbances of gait in the elderly, N 32 1358
6a. PS Sorensen, et al (1986) Motor disturbances in normal-pressure hydrocephalus, AnN 42 34
7. BV Pollard (1981) Gas agenesis in communicating hydrocephalus, JNNP 44 305
7a. E Knutsson, U Lying Tunell (1981) Gait apraxia in normal pressure hydrocephalus: Patterns of movement and muscle activation, N 35 155
8. V Rajshekhar, TA Chandy (1977) Non-neoplastic stenosis of the aqueduct presenting in adolescence and adult life, Surg Neurol 7 333
8a. MI Herman, et al (1984) Benign aqueductal stenosis in adults, JNNP 37 1327
9. WE Dandy, The Brain, Harper & Row, New York, 1969, pp. 202-265
10. PK Newman, et al (1980) Hydrocephalus and intracranial meningiomas in adults, JNNP 43 188
10a. HW Murray, et al (1941) Ventriculocaval shunting for hydrocephalus complicating tuberculous meningitis, AJM 29 895

10f. M Troost, et al (1986) Computed tomography in CNS tuberculosis, Ital Neurol 25 91
11. J van Gijn, et al (1985) Acute hydrocephalus after aneurysmal subarachnoid hemorrhage, J Neurosurg 63 355
11a. T Dorai, et al (1983) Disturbances of cerebrospinal fluid circulation during the acute stage of subarachnoid hemorrhage, NS 12 435
11b. J van Gijn (1985) Acute hydrocephalus after aneurysmal subarach noid hemorrhage, J Neurosurg 63 355
11c. VK Kelkar, KP Sengupta (1981) Symptomatic hydrocephalus following aneurysmal subarachnoid hemorrhage, Surg N Z 51 402
12. B Gaddell, et al (1985) Meningiomas of the lateral ventricles. Clinical, neuroradiologic and surgical considerations in 19 cases, Surg N 24 364
12a. G Morrison, et al (1984) Intraventricular mass lesions, Radiol 152 435

CHAPTER 20:

1. AJ Patchett (1977) Clinical testing of olfaction reviewed, Brain 100 173
1a. RL Doty, et al (1984) University of Pennsylvania smell identification test. A rapid quantitative olfactory function test for the clinic, Laryngol 94 176
2. L Bakay (1984) Olfactory meningiomas. The missed diagnosis, JAMA 251 53
2a. CL Botero, et al (1983) Supratentorial and olfactory meningiomas. Report on a series of 155 primary cases, Acta NChir 67 181
3. SR Bruesch, LB Arey (1942) The number of myelinated and unmyelinated fibers in the optic nerve of vertebrates, J Comp N 77 631
4. AM Potts, et al (1972) Morphology of the optic nerve. III. Fiber characteristics of the larval outflow, Invest Oph 11 1004
5. WP Hoyt, O Luis (1962) Visual fiber anatomy in the infrageniculate pathway of the primate, ArOph 68 94
6. AA D'Cruz, C Eltenberger Jr (1963) Diagnostic differences in visual field defects. Demyelinating versus compressive optic neuropathy, Neurol 13 239
7. C Fisher (1969) The neurology of visual acuity, Brain 102 639
8. JJ Lieberstein, et al (1982) Effectiveness of a pinhole method for visual acuity screening, ArOph 100 222
9. L Garron, et al (1968) Bilateral central and centrocecal scotomata due to optic lesions, BJOph 68 346
9a. NG Pace, MD Sanders (1984) Bilateral central scotomata due to intracranial tumors, BJOph 68 449
10. C Fisher (1968) The neurology of visual acuity, Brain 102 639
11. JM Siegel, RC Carr (1948) Differential diagnostic and psychophysical testing in retinal disease, Int Ophth Clin 20 21
12. JR Cruysberg, A Friedrich (1982) Acquired color vision defects in compressive optic neuropathy, Neuroph 2 169
12a. J Fiatoni, G Verdaz (1964) Occipital deficiency, stereoscopic vision, with special reference to its detection and classification by means of the test of Farnsworth, Vis Res 2 201
13. JD Trobe, et al (1982) Contrast sensitivity and other vision tests in anterior optic nerve disease, Neurol 32 281
14. JD Trobe, et al (1983) Contrast sensitivity and other vision tests in anterior optic nerve disease, Neurol 33 985
15. JR Thompson, et al (1981) How to measure the relative afferent pupillary defect, Surv Ophth 26 39
16. O Lowenstein, IE Lowenstein, The pupil. In H Davson (ed) *The Eye*, New York, Academic Press 1969 Vol 3 p 255-337
17. JR Thompson, et al (1981) How to measure the relative afferent pupillary defect, Surv Ophth 26 39
18. JR Thompson, et al (1977) Hippocrates' Semantic and historic considerations of the word, AJOph 77 1116
19. JA Stevens, TC Hutton (1980) Measurement of the relative afferent pupillary defect in retinal detachment, AJOph 90 19
20. JR Thompson, et al (1982) The relationship between visual acuity, pupillary defect, and visual field loss, AJOph 93 68
20a. DA Newsome, et al (1981) Afferent pupillary defect in macular degeneration, AJOph 92 396
21. JM Van Buren: *The Retinal Ganglion Cell Layer*, Charles C Thomas, Springfield, IL, p 67
22. L Fisher (1973) A versatile color confrontation test for the central visual field. A comparison with quantitative perimetry, ArOph 89 3
22a. JS Mandel, et al (1983) Visual field testing with red targets, ArOph 101 927
23. TO Paul, WF Hoss (1976) Fundoscopic appearance of papilledema with optic tract atrophy, ArOph 94 461
23a. NM Newman, et al (1982) Ophthalmoscopy of the normal nerve fiber layer. Use in detection of neurologic disease, AnN 39 226
24. NM Newman, et al (1982) Ophthalmoscopy of the normal nerve fiber layer. Use in detection of neurologic disease, AnN 39 226
25. JR Sanders, BR Youngs (1981) Intracerebellar amblyopia, J Clin Neuph 1 213
26. M Rosenberg, *Neuro-Ophthalmology*, in *Neurosurgery*, RH Wilkins, SS Rengachary (eds), 55;Graw Hill, New York, p. 86
27. JD Trobe (1978) Chiasmatic/sellar adhesions presenting with a homonymous temporal arcuate scotoma, AJOph 77 348
28. AJ Mizuniewicz (1982) Causes of optic nerve damage in glaucoma, Robert N Schaffer Lecture, Ophthal 89 743
28a. HA Quigley, et al (1981) Optic nerve head blood flow in chronic experimental glaucoma, ArOph 107 956
28b. HA Quigley, et al (1983) Optic nerve head blood flow in chronic experimental glaucoma, ArOph 107 956
28c. J Sebag, et al (1980) Optic disc cupping in anterior ischemic optic neuropathy resembles galucomatous cupping, Ophthal 87 857
28d. DS Minckler, GL Spaeth (1980) Optic nerve damage in glaucoma, Surv Oph 26 128
29. A Sommer, et al (1977) The nerve fiber layer in the diagnosis of glaucoma, ArOph 95 2140
29a. HA Quigley, et al (1980) Clinical evaluation of nerve fiber layer atrophy as an indicator of glaucomatous optic nerve damage, ArOph 98 1564
30. RA Hitchins, S Anderton (1983) Identification of glaucomatous visual field defects from examination of monocular photographs of the optic disc, BJOph 67 822
30a. HH Hoskins, FC Gelber (1975) Optic disk topography and visual field defects in patients with increased intraocular pressure, AJOph 80 284
30b. GL Portney, AM Roth (1964) Optic cupping caused by an intracranial aneurysm, AJOph 58 77
30c. PJ Airaksinen, et al (1985) Neuroretinal rim area in early glaucoma, AJOph 99 1
30d. (1980) Neurocentral rim, ArOph 98 940 30e. JD Trobe, et al (1980) Nonglaucomatous excavation of the optic disc, ArOph 98 1046
31. HA Quigley, et al (1981) Optic nerve damage in human glaucoma. II. The site of injury and susceptibility to damage, ArOph 99 635
31a. JD Trobe, et al (1980) Nonglaucomatous excavation of the optic disc, ArOph 98 1046
31b. RA Hitchings, GL Spaeth (1976) The optic disc in glaucoma. I. Classification, BJOph 60 778
31c. B Schwartz (1973) Cupping and pallor of the optic disc, ArOph 89 273
32. RF Kinch, DB Anderson (1971) Clinical recognition of glaucomatous cupping, AJOph 71 442
32a. HA Quigley, et al (1982) Optic nerve damage in human glaucoma. II. Quantitative correlation of nerve fiber loss and visual field defect in glaucoma, ischemic neuropathy, papilledema, and toxic neuropathy, ArOph 100 135
32b. HA Quigley (1982) Early detection of glaucomatous damage. II. Changes in the appearance of the optic disk, Surv Oph 30 131
32c. HA Quigley, et al (1981) Optic nerve damage in human glaucoma. II. The site of injury and susceptibility to damage, ArOph 99 635
33. J Berschin, RH Osher (1980) Baring of the circumlinear vessel. An early sign of optic nerve damage, ArOph 98 866
33a. RH Osher, J Berschin (1981) The significance of baring of the circumlinear vessel, ArOph 99 817

33b. G Balazsi, EB Warner (1983) Relationship between tuning of the circumlinear vessels of the optic disc and glaucomatous visual field loss. Can J Ophthalmol 18:333
33c. DR Anderton (1983) Wide segments of the optic disc and retina in glaucoma?. Ophthal 90:766
34. HA Quigley, et al (1980) Clinical evaluation of nerve fiber layer atrophy as an indicator of glaucomatous optic nerve damage. ArOph 98:1564
34a. SM Drance (1972) The glaucomatous visual field. BJOph 56:186
35. L Frisén, WP Hoyt (1974) Insidious atrophy of retinal nerve fibers in multiple sclerosis. Funduscopic identification in patients with and without visual complaints. ArOph 92:91
35a. VH Patterson, JR Heron (1980) Visual field abnormalities in multiple sclerosis. JNNP 43:205
36. PR Lichter, JW Henderson (1978) Optic nerve infarction. AJOph 85:900
36a. DR Bogen, JS Glaser (1975) Ischaemic optic neuropathy. The clinical profile and natural history. Brain 98:689
37. RH Spector, et al (1981) Occipital lobe infarction. Perimetry and computed tomography. N Jt 1:695
38. S Hayreh (1972) Optic disc changes in glaucoma. BJOph 56:778
38a. Y Isayama, et al (1983) Posterior ischemic optic neuropathy. I. Blood supply of the optic nerve. Ophthalmologica 186:197
39. S Hayreh, TA Weingeist (1980) Experimental occlusion of the central artery of the retina. I. Ophthalmoscopic and fluorescein fundus angiographic studies. BJOph 64:896
40. HO Wolbarsht, et al (1982) Ocular pneumoplethysmography and ophthalmodynamometry in the diagnosis of central retinal artery occlusion. Stroke 13:199
41. S Hayreh (1974) Pathogenesis of cupping of the optic disc. BJOph 58:563
41a. S Hayreh, TA Weingeist (1980) Experimental occlusion of the central artery of the retina. I. Ophthalmoscopic and fluorescein fundus angiographic studies. BJOph 64:896
42. S Hayreh, TA Weingeist (1980) Experimental occlusion of the central artery of the retina. I. Ophthalmoscopic and fluorescein fundus angiographic studies. BJOph 64:896
42a. J Arruga, MD Sanders (1982) Ophthalmologic findings in 70 patients with evidence of retinal embolism. Ophthal 89:1536
43. GC Brown, JA Shields (1979) Cilioretinal arteries and retinal arterial occlusion. ArOph 97:84
43a. J Inarez Jr, RP Clemons (1978) Cilioretinal arteries. A study based on review of stereo fundus photographs and fluorescein angiographic findings. ArOph 96:1953
44. S Hayreh (1981) Anterior ischaemic optic neuropathy. ArN 38:655
44a. DR Bogen, JS Glaser (1975) Ischaemic optic neuropathy. The clinical profile and history. Brain 98:689
45. MF Lieberman, et al (1978) Embolic ischemic optic neuropathy. AJOph 86:208
45a. S Hayreh (1981) Anterior ischaemic optic neuropathy. ArN 38:655
45b. MX Repka, et al (1983) Clinical profile and long-term implications of anterior ischemic optic neuropathy. AJOph 96:478
45c. S Hayreh (1981) Anterior ischaemic optic neuropathy. V. Optic disc edema at early stage. ArOph 99:1030
45d. D Gold (1977) Retinal artery occlusion. Ophthal 85:992
46. J Arruga, MD Sanders (1982) Ophthalmologic findings in 70 patients with evidence of retinal embolism. Ophthal 89:1536
46a. R Mas-Morales, et al (1980) Retinal fluorescein angiographic evidence for atherosclerotic vitreoretinal disease. Demonstration of ophthalmoscopically occult emboli and post embolic endothelial damage after cracks of cholesterol plaque. Stroke 11:154
47. GC Brown, JA Shields (1979) Cilioretinal arteries and retinal arterial occlusion. ArOph 97:84–47a. DN Gingwar, et al (1984) Cilioretinal artery occlusion. A case report. ArOph 76:1025–476. GC Brown, et al (1983) Cilioretinal artery obstruction. Retina 3:18
48. GC Brown, LE Magargal (1982) Central retinal artery obstruction and visual acuity. Ophthal 89:14
48a. J Inarez Jr, RP Clemons (1978) Cilioretinal arteries. A study based on review of stereo fundus photographs and fluorescein angiographic findings. ArOph 96:1953
48b. JD Kirkham, et al (1985) The ataxy-oculopathies of Tay-Sachs and other storage diseases. AnN 17:327
49. S Hayreh (1974) Anterior ischaemic optic neuropathy II. Thrombi on ophthalmoscopy and fluorescein angiography. BJOph 58:985
50. H. Smith, SA Cross (1953) Occipital lobe infarction after open heart surgery. J Clin Neurol 3:23
51. MA Sandberg (1980) Hereditary retinitis pigmentosa, vision findings from electroretinography, fundus reflectometry, and psychophysics. In Opt Clin 20:39
52. DM Siegal, RR Cies (1980) Electrodiagnostic and psychophysical testing in retinal disease. Int Opt Clin 20:21
53. MF Marmor (1980) Visual loss in retinitis pigmentosa. AJOph 89:863
53a. RE Cies, KG Noble (1935) Retinitis pigmentosa. Opthal 88:168
54. T Kirkham (1979) Neuroophthalmology: clinical assessment of visual function. Signs and symptoms of primary tumors, in *Clinical Neuroradiology: A Pattern-oriented Approach*, ed by C Dyke, F Labbe, JE Marcus, F Nattelet. Raven Press, New York, p. 185–406
55. SE Young, et al (1976) The tilted disc syndrome. AJOph 82:38
55a. R Eschenbach, et al (1980) Stereoptic visual field defects in the tilted disk syndrome. Neurol 5:229
55b. JM Apple, et al (1982) Congenital anomalies of the optic disc. Surv Opth 27:3
56. JD Trobe, et al (1981) Confrontation visual field techniques in the detection of anterior visual pathway lesions. AnN 10:28
56a. JD Trobe, et al (1981) A screening method for chiasmal visual field defects. ArOph 99:264
57. WF Hoyt, O Luis (1963) The primate chiasm. Details of visual fiber organization studied by silver impregnation techniques. ArOph 70:69
58. JS Glaser, et al (1971) Visual morbidity with chiasmal gliomas. Long-term studies of visual fields in untreated and irradiated cases. ArOph 85:3
58a. L Frisén (1968) The neurology of visual swells. Brain 102:639
59. AD Schwimmer, BA Thompson (1967) Pituitary tumors with central scotomas simulating retrobulbar optic neuritis. N J 7:782
59b. K Sogiti, et al (1965) Scotomatous defects in the central visual field in pituitary adenomas. Neurol 15:197
60. SN Kaul, et al (1974) Relationship between visual field defect and arterial occlusion in the posterior cerebral circulation. JNNP 37:1022
60a. RH Spector, et al (1981) Occipital lobe infarction: Perimetry and computed tomography. N Jt 1:695
61. AB Safran, JS Glaser (1980) Stankiewicz dissociation in lesions of the anterior visual pathways. A reappraisal of the Riddoch phenomenon. ArOph 98:29
61a. JD Trobe, et al (1981) Confrontation visual field techniques in the detection of anterior visual pathway lesions. AnN 10:28
62. JE O'Connell (1975) The anatomy of the optic chiasma and retrochiasmal terminations. JNNP 38:710
63. R Bernard, BS Ray (1969) The arterial supply of the human optic chiasm. J NNS 31:527
63a. Y Isayama, et al (1983) Posterior ischemic optic neuropathy. I. Blood supply of the optic nerve. Ophthalmologica 186:197
64. H. Smith. Additional comments on the neuro-ophthalmological examination, in *The University of Miami Neuro-Ophthalmology Symposium*, ed by H. Smith, Charles C Thomas, Publisher, Springfield, IL, 1964, p. 45
64a. JD Trobe, et al (1984) Chiasmal and tuberculum sellae tumors. Diagnostic and prognostic features. NJM 25:941
65. FR Humphrey, et al (1982) Visual field defects in obstructive hydrocephalus. JNNP 45:59
65a. Oster (1978) Neuroophthalmological complications of enlargement of the third ventricle. BJOph 62:536
66. LW Stepple, et al (1978) Bilateral homonymous hemianopia. AJOph 86:536
66a. RP Newmann, et al (1984) Altitudinal hemianopia caused by occipital infarctions. Clinical and computerized tomographic correlations. ArN 41:413

67. CH Goldenberg, WF Hoyt (1971) Geniculate homonymous homonymous field defects in two patients with partial lesions of the lateral geniculate nucleus. *JNNP 34* 1

68. PJ Saxena, et al (1976) Optic inter syndrome. A review of 21 patients. *ArOph 95* 656

68a. MB Bender, I Bodis-Wollner (1978) Visual dysfunctions in optic tract lesions. *AnN 3* 167

68b. SA Newman, NR Miller (1982) Optic tract syndrome. Neuro-ophthalmologic considerations. *ArOph 100* 1241

68c. DG Stoddon, et al (1984) Congruous and incongruous sectoral visual field defects with lesions of the lateral geniculate nucleus. *AJOpt 98* 283

69. SA Cross, JL Smith (1982) Crossed-quadrant homonymous hemianopsia. The "checkerboard" field defect. *J Clin Neuph 2* 149

70. HW Kupfer, et al (1968) Bilateral homonymous hemianopsia. *AJOph 86* 516

70a. JL Smith (1983) Altitudinal field and. *J Clin Neuph 3* 282 70b. BP Newman, et al (1984) Altitudinal hemianopsia caused by occipital infarctions. Clinical and computerized topographic correlations. *AnN 45* 435

71. JR Keane (1980) Blindness by lowering internal hemianopsia. *AnN 8* 198

72. S Symon, et al (1980) Vision in the temporal crescent in occipital infarction. *Brain 103* 43

73a. JR. McAuley, et al (1979) Correlation of CAT scan and visual field defects in vascular lesions of the posterior visual pathways. *JNNP 42* 799

73. MT Perrin, E Vaclor (1981) Macular sparing hemianopsia by means of Haidinger brushes. *BJOph 65* 429

74. JGL Spector, et al (1981) Occipital lobe infarctions: Parenchymal and computed tomography. *N Jer* 1098

74a. O Meienberg (1981) Sparing of the temporal crescent in homonymous hemianopsia and its significance for visual orientation. *Neuph 2* 129

75. HA Quigley, et al (1982) Quantitative study of optic nerve head capillaries in experimental optic disk pallor. *AJOph 93* 689

75a. RL Radius, DR Anderson (1979) The mechanism of disc pallor in experimental optic atrophy. A fluorescein angiographic study. *ArOph 97* 532

76. S Hayreh (1977) Optic disc edema in raised intracranial pressure. V. Pathogenesis. *ArOph 95* 1553

76a. S Hayreh (1979) Fluids in the anterior part of the optic nerve in health and disease. *Surv Ophth 23* 1

77. L Frisén (1982) Swelling of the optic nerve head: a staging scheme. *JNNP 45* 13

77a. Anon (1978) Editorial: pathogenesis of optic disc swelling. *BJOph 62* 529

78. JA Ruiz (1982) Hazel retinal circulation and visual loss due to papilledema. *AnOph 14* 166

79. MM Newman, et al (1982) Ophthalmoscopy of the retinal nerve fiber layer. Use in detection of neurologic disease. *AnN 59* 226

79a. WF Hoyt, CL Knight (1973) Comparison of congenital disc blurring and incipient papilledema in red free light—a photographic study. *Invest Oph 12* 241

80. MS Hayreh, S Hayreh (1977) Optic disc edema in raised intracranial pressure. I. Evolution and resolution. *ArOph 95* 1237

81. HF Lavin (1908) The clinical significance of spontaneous pulsation of the retinal vein. *ArN 25* 37

81a. TJ Walsh, et al. (1969) Obstruction of retinal venous pulsations during elevation of cerebrospinal fluid pressure. *AJOph 67* 954

82. GG Neele, RE Carr (1983) Diabetic retinopathy. I. Nonproliferative retinopathy. *Ophthal 90* 1263

82a. SA Tenn (1984) Retinal manifestations of vascular disease. *Hosp Pract 19* (5) 60

83. RW Ross Russell, NG Pope (1983) Cortical perfusion of brain and retina. *Brain 106* 619

83a. TP Kearns (1983) Differential diagnosis of CRV obstruction. *Ophthal 90* 475

83b. JB Carter (1985) Chronic ocular ischemia and carotid vascular disease. *Stroke 16* 771

83c. EA Waybright, et al (1982) Anterior ischemic optic neuropathy with internal carotid artery occlusion. *AJOph 93* 42

84. JR Keane (1979) Retinal ischemia: its significance in 100 patients with acute encephalopathy or unknown cause. *AnN 36* 801

84a. PJ Muller, JH Deck (1974) Intraocular and optic nerve sheath hemorrhage in cases of sudden intracranial hypertension. *J N-S 41* 160

85. TP Kearns (1983) Differential diagnosis of central retinal vein obstruction. *Ophthal 90* 475

86. P Arnbjerk (1978) Primary central venous thrombosis in young adults: the diverse manifestations of an unrecognized disease. *AnN 3* 61

86a. MF Beal, et al (1982) Cerebral vein thrombosis and multiple intracranial hemorrhages by computed tomography. *AnN 39* 617

86b. J Chiras, et al (1985) Venous infarctions. *Neurol 27* 389

86c. MG Bousser, et al (1985) Cerebral venous thrombosis—a review of 38 cases. *Stroke 16* 199

87. S Hayreh (1976) So-called 'central retinal vein occlusion' I. Pathogenesis, terminology, clinical features. *Ophthalmologica 172* 1

87a. S Hayreh (1976) So-called 'central retinal vein occlusion' II. Venous stasis retinopathy. *Ophthalm Inquis 172* 31

87b. C Ellenbogen Jr, KH Moseley (1978) Papilopeptebrus benign intracranial hypertension. *AnN 3* 438

88. KA Zakka, et al (1978) Optic-sheath veins in a primary optic nerve sheath meningioma. *AJOph 87* 91

88a. JC Perimutter, et al (1980) Disappearing optic-disc shunt vessels and pseudotumor cerebri. *AJOph 89* 703

88b. RW Hollenhorst Jr, et al (1978) Visual prognosis of optic nerve sheath meningiomas producing shunt vessels on the optic disk. *Mayo 53* 84

88c. PA Sibony, et al (1981) Optic nerve sheath meningiomas. Clinical manifestations. *Ophthal 91* 1313

89. DJ Green, et al (1980) Ischemic optic neuropathy in chronic papilledema. *ArOph 98* 902

89a. JH Atkins, BP O'Neill (1982) Pseudotumor cerebri. *AnIM 97* 349

89b. M Wall, et al (1985) Visual field defects in idiopathic intracranial hypertension (pseudotumor cerebri). *AJOph 96* 854

90. JJ Corbett, et al (1982) Visual loss in pseudotumor cerebri. Follow-up of 57 patients from five to 41 years and a profile of 14 patients with permanent severe visual loss. *AnN 39* 461

90a. S Duke-Elder, GI Scott. Neuro-ophthalmology (1971) S Duke Elder (ed). *System of Ophthalmology 12* CV Mosby Co, St. Louis, p 60

90b. S Hayreh (1977) Optic disc edema in raised intracranial pressure. VI. Associated visual disturbances and their pathogenesis. *ArOph 95* 1566

91. S Hayreh (1977) Optic disc edema in raised intracranial pressure. VI. Associated visual disturbances and their pathogenesis. *ArOph 95* 1566

91a. JC Orcutt, et al (1984) Factors affecting visual loss in benign intracranial hypertension. *Ophthal 91* 1338

91b. AA Sadun, et al (1984) Transient visual obscurations with elevated optic discs. *AnN 16* 486

92. JJ Corbett, et al (1982) Visual loss in pseudotumor cerebri. Follow-up of 57 patients from five to 41 years and a profile of 14 patients with permanent severe visual loss. *ArN 39* 461

92a. AA Sadun, et al (1984) Transient visual obscurations with elevated optic discs. *AnN 16* 486

93. A Garner, et al (1975) Pathogenesis of hypertensive retinopathy. An experimental study in the monkey. *BJOph 59* 3

93a. S Keith, et al. (1945) Fundus lesions in malignant hypertension. II. A pathologic study of experimental hypertensive optic neuropathy. *ArOph 105* 1198

93b. (1978) Hypertensive retinopathy (optic disc swelling) vs hypertensive encephalopathy. *Major Problems in Neurology 7* 229

93c. S Hayreh, et al. (1986) Fundus lesions in malignant hypertension. V. Hypertensive optic neuropathy. *Ophthal 93* 70

94. S Hayreh (1977) Optic disc edema in raised intracranial pressure. V. Pathogenesis. *ArOph 95* 1553

94a. S Hayreh (1977) Optic disc edema in raised intracranial pressure. VI. Associated visual disturbances and their pathogenesis. *ArOph 95* 1566

94b. S Hayreh (1981) Anterior ischemic optic neuropathy. V. Optic disc edema in early sign. ArOph 99 1030

95. EA Cox, et al (1981) Relative afferent pupillary defects in optic neuritis. AJOph 92 685

96. DR Bogber, JS Glaser (1975) Ischaemic optic neuropathy. The clinical profile and natural history. Brain 98 689

96a. WF Hoyt, et al (1973) Malignant optic glioma of adulthood. Brain 96 121

97. E Nikoskelainen, et al (1981) Prognosis of optic neuritis with special reference to cerebrospinal fluid immunoglobulins and measles virus antibodies. AnN 9 545

97a. GC Ebers (1985) Optic neuritis and multiple sclerosis. AnN 42 702

97b. JF Kurtzke (1985) Optic neuritis in multiple sclerosis. AnN 42 704

98. GD Jones, SE Pelden (1982) Clinical and computed tomographic findings in the Foster Kennedy syndrome. AJOph 93 317

98a. EW Mistry, B Schoenberg (1984) Foster Kennedy syndrome. AnN 41 658

99. S Hayreh (1981) Anterior ischemic optic neuropathy. V. Optic disc edema in early sign. ArOph 99 1030

99a. NJ Schatz, JL Smith (1967) Non-tumor causes of the Foster Kennedy syndrome. J NrS 27 37

99b. MR Miller, et al (1979) Giant cell (temporal) arteritis. The differential diagnosis. Surv Oph 23 259

100. NR Miller (1980) Anterior ischemic optic neuropathy: diagnosis and management. Bull NY Acad Med 56 643

101. WH Spencer (1978) Diseases of the optic disk and aberrant axoplasmic transport. The XXXIV Edward Jackson memorial lecture. AJOph 85 1

101a. MO Tso (1981) Pathology and pathogenesis of disease of the optic nervehead. Ophthal 88 1066

101b. T Ishibashi, et al (1986) Formation of drusen in the human eye. AJOph 101 343

102. MA Rosenberg, et al (1979) Analysis of pseudopapilledema I. Population, laterality, acuity, refractive error, ophthalmoscopic characteristics, and coincident disease. ArOph 97 65

102a. PJ Savino, et al (1979) A clinical analysis of pseudopapilledema. II. Visual field defects. ArOph 97 71

102b. E Mustonen (1983) Pseudopapilledema with and without vascular optic disc drusen. A clinical analysis I. Acta Oph 61 181

103. PJ Savino, et al (1979) A clinical analysis of pseudopapilledema. II. Visual field defects. ArOph 97 71

103a. JW Gittinger Jr, et al (1986) Ischemic optic neuropathy associated with optic nerve drusen. J Clin Neuro 6 79

103b. RW Beck, et al (1985) Decreased visual acuity from optic disc drusen. ArOph 103 1155

104. MJ Hanna, et al (1981) Hemorrhagic complications of optic nerve drusen. AJOph 92 70

104a. K Rutnastein, M Ali (1982) Retinal complications of optic nerve drusen. BJOph 66 83

104b. RA Hitchings, et al (1976) Hemorrhages with optic nerve drusen. A differentiation from early papilledema. AnN 32 675

105. RW Britner, AR McPherson (1985) Adverse reactions in intravenous fluorescein angiography. ArOpt 15 1084

105a. RJ Pacumeta (1982) Low incidence of side effects following intravenous fluorescein angiography. AnOph 14 31

106. EM Helveston, et al (1982) The trochlea. A study of the anatomy and physiology. Opthal 89 120

107. FW Kerr, OW Hallowell (1964) Location of pupilomotor and accommodation fibres in the oculomotor nerve: Experimental observations on paralytic mydriasis. JNNP 27 473

108. G Roman-Campos, KR Edwards (1979) Painful ophthalmoplegia: oculomotor nerve palsy without mydriasis due to compression by aneurysm. IJA 19 43

108a. JT Kissel, et al (1982) Pupil sparing oculomotor palsies with internal carotid posterior communicating artery aneurysms. AnN 11 149

108b. JD Trobe 91985) Isolated pupil-sparing third nerve palsy. Ophthal 92 58

108c. PS O'Connor, et al (1983) Pupil sparing third nerve palsies caused by aneurysm (letter) AJOph 95 395

109. PC Gilmore, TJ Corlow (1980) Diabetic oculomotor paresis with pupil fixed to light. N 30 1229

110. SE Nadeau, JD Trobe (1981) Pupil sparing in oculomotor palsy, a brief review. AnN 10 143

110a. S Hall, et al (1983) Pupillary sparing oculomotor palsy from metastatic carcinoma. Surv N 29 363

111. SR Sen (1956) Aneurysms of the posterior communicating artery and oculomotor paresis. JNNP 37 435

112. F Cramsky, H Nathan (1982) The lateral wall of the cavernous sinus. With special reference to the nerves situated in it. J NrS 56 226

112a. LB Klintz, et al (1982) Computed tomographic evaluation of the cavernous sinus. Ophthal 89 374

113. LB Klintz, et al (1982) Computed tomographic evaluation of the cavernous sinus. Ophthal 89 374

113a. JS Dynes (1962) The so-called cavernous sinus: a review of the controversy and its implications for neurosurgery. N/S 31 212

114. JA Kurtz, BE Younge (1981) Paralysis of cranial nerves III, IV and VI. Cause and prognosis in 1,000 cases. ArOph 99 76

114a. BE Younge, F Sumita (1977) Analysis of trochlear nerve palsies: diagnosis, etiology, and treatment. Mayo 52 11

115. A Nouros (1985) Extraocular muscle palsy from minor head trauma: Initial sign of intracranial tumor. Neurol 35 43

116. SB Hopping, et al (1983) Nasopharyngeal masses in adults. Ann Oto Rhino Laryngo 92 137

117. WF Maloney, et al (1980) Evaluation of the causes and accuracy of pharmacologic localization in Horner's syndrome. AJOph 90 394

118. JS Czarnecki, et al (1979) The analysis of anisocoria. The use of photography in the clinical evaluation of unequal pupils. Can J Oph 14 297

119. HL Van der Wiel, J Van Dijk (1982) Localization of Horner's syndrome. Uses and limitations of the hydroxyamphetamine test. J NrSci 39 229

120. WF Maloney, et al (1980) Localization of the cause and accuracy of pharmacologic localization in Horner's syndrome. AJOph 90 394

120a. HS Thompson, SP Pilley (1976) Unequal pupils. A flow chart for sorting out the anisocorias. Surv Oph 21 45

121. MB Nolph, MW Dion (1982) Horner's syndrome associated with internal carotid artery dilation and erosion. Laryngo 92 1344

121a. JG Morris, et al (1984) Facial sweating in Horner's syndrome. Brain 107 751

122. CM Fisher, et al (1978) Spontaneous dissection of cervico-cerebral arteries. Can J NrSci 5 9

122a. HH Ringelstein, et al (1983) The pathogenesis of strokes from internal carotid artery occlusion. Diagnostic and therapeutical implications. Stroke 14 867

122b. S Finkelstein, et al (1980) Delayed stroke following carotid occlusion. N 30 84

122c. S Takagi, Y Shinohara (1981) Internal carotid occlusion, volume of cerebral infarction, clinical findings, and prognosis. Stroke 12 835

123. DS O'Doherty, JB Gucer (1958) Diagnostic value of Horner's syndrome in thrombosis of the carotid artery. N 8 542

123a. TF West, et al (1976) Horner's syndrome and headache due to carotid artery disease. BMJ 1 818

123b. J Zaleski (1981) Preganglionic Horner's syndrome in carotid artery disease. Mt. Sinai J Med 48 456

123c. RO Hart, JD Fawcett (1955) Dissecting internal Stroke 16 975

123d. M.Kal, et al (1986) Spontaneous dissection of the cervical internal carotid artery. AnN 19 126

124. B Miller (1952) Raeder's paratrigeminal syndrome. Original concept and subsequent deviation. ArN 30 395

125. D Wood, et al (1986) Episodic unilateral mydriasis and migraine. AJOph 98 729

126. RE Apple, RJ Stamm (1978) Raeder's paratrigeminal syndrome. AJOph 10 1151

126a. DR Cohen, et al (1975) Raeder's paratrigeminal syndrome. AJOph 79 1044

126b. BS Glasscock, HS Thompson (1980) Raeder's syndrome. A clinical review. Surv Oph 24 199

127. JD Selhorst, et al (1976) Disorders in cerebellar ocular motor control II. Macrosaccadic oscillation. An oculographic, control system and clinicoanatomical analysis. Brain 99 509
127a. G Averbuch, et al (1979) Alterations of ocular motility in cerebellar pathology. An electronystagmographic study. AdN 36 274
127b. JR Hotson (1982) Cerebellar control of fixation eye movements. N 32 31
127c. DG Cogan, et al (1982) Ocular signs of cerebellar disease. ArOph 100 755
128. RH Spencer, BT Tusa (1981) The oculomotor system. AdN 9 517
128a. BT Tusa, et al (1972)Hemispheric control of eye movements. II. Quantitative analysis of saccade pursuit in a hemispherectomy patient. AdN 27 449
129. R Shiromoto, et al (1979) Ocular motor abnormalities in Parkinson's disease. AdN 36 386
129a. B Estanol, et al (1979) Effects of cerebellectomy on eye movements in man. AdN 36 281
129b. OB White, et al (1983) Ocular motor deficits in Parkinson's disease. II. Control of the saccadic and smooth pursuit systems. Brain 106 571
130. HS Mair (1981) Review. Restrictive factors in strabismus. Surv Opht 28 7
131. NR Miller, et al (1982) Unilateral Duane's retraction syndrome (type 1) ArOph 100 1168
131a. MG Hotchkiss, et al (1980) Bilateral Duane's retraction syndrome. A clinical-pathologic case report. ArOph 98 870
131b. RS Baker, WC Robertson Jr (1980) Acquired Duane's retraction syndrome in a patient with rheumatoid arthritis. ArOph 98 1872
131c. EL Raab (1986) Clinical features of Duane's syndrome. J Ped Opt & Strab 23 64
132. JH Lepore, JS Glaser (1980) Misdirection revisited. A critical appraisal of acquired esotropia nerve synkinesis. ArOph 98 2206
133. TA Cox, et al (1979) Primary aberrant oculomotor regeneration due to intraneural microcysts. AdN 36 530
133a. D Bogber, et al (1979) Primary aberrant third nerve regeneration. AdN 5 413
133b. KJ Schatz, et al (1977) Primary aberrant oculomotor regeneration. AdN 34 29
134. JS Overstreet, HS Thompson (1978) The iris sphincter in aberrant regeneration of the third nerve. ArOph 96 1606
134a. PA Sibony, et al (1984) Acquired oculomotor synkinesis. Surv Opht 28 387
134b. J Selga, AA Sadun (1983) Aberrant regeneration of the third nerve following orbital trauma. Synkinesis of the iris sphincter. AdN 40 762
135. W Bozeman (1981) Diplopia of superior oblique palsy. J Clin Neuroph 1 199
135a. EM Helveston (1967) A rectstep test for diagnosing paresis of a single vertically acting extraocular muscle. AJOph 64 914
135b. CF Sydnor, et al (1982) Traumatic superior oblique palsies. Opt dual 89 134
135c. BR Younge, F Sutula (1977) Analysis of trochlear nerve palsies. Diagnosis, etiology, and treatment. Mayo 52 11
136. SG Diamond, et al (1979) Binocular counterrolling in humans during dynamic rotation. Ann Oto 87 490
136a. BJ Kushner, S Kratt (1982) Ocular torsional movements in normal humans. AJOph 93 752
136b. BJ Kushner (1986) Ocular torsional movements in humans with normal and abnormal ocular motility: part II—subjective observations. J Ped Oph & Strab 23 6
137. EJ Selhorst, et al (1976) Disorders in cerebellar ocular motor control. I. Saccadic overshoot dysmetria. An oculographic, control system and clinicoanatomical analysis. Brain 99 497
137a. DG Cogan, et al (1982) Ocular signs of cerebellar disease. ArOph 100 755
137c. DS Zee, et al (1976) Ocular motor abnormalities in hereditary cerebellar ataxia. Brain 99 207
138. TH Kirkham, D Guthrie (1984) A quantitative study of abnormal eye movements in Huntington's chorea using the sclera search coil technique. NOph 4 27
138a. RJ Leigh, et al (1983) Abnormal ocular motor control in Huntington's disease. N 33 1268
139. AE Hanning (1983) Classification of the hereditary ataxias and paraplegias. Lancet 1 1151
140. DS Zee, et al (1976) Slow saccades in spinocerebellar degeneration. AdN 23 243
140a. A Konstantinov (1981) Neurological findings of spinocerebellar degeneration with slow eye movements. Adv Oto Rhino Laryngol 28 214
141. MS Phillips, et al (1984) Neuropathological findings in Miller Fisher syndrome. JNNP 47 482
141a. GA Jamal, WN MacLeod (1984) Electrophysiologic studies in Miller Fisher syndrome. N 34 685
141b. U Meienberg (1985) Lesion site in Fisher's syndrome (letter). AdN 41 250
141c. R Sanino, et al (1984) Miller Fisher syndrome: Clinical and electrophysiologic evidence of peripheral origin in 10 cases. N 34 953
141d. JA Weiss, JC White (1986) Correlation of IA afferent conduction with the ataxia of Fisher syndrome. MdN 9 327
142. ML Zaccaro, et al (1983) Eye-movement abnormalities in ophthalmoplegia, ataxia, and areflexia (Fisher's syndrome). ArOph 101 55
142a. O Malmberg, F Ryffel (1983) Supranuclear eye movement disorders in Fisher's syndrome of ophthalmoplegia, ataxia, and areflexia. Report of a case and literature review. AdN 40 803
143. C Wenzel, et al (1982) Eye movements in cerebellar and combined cerebellobrainstem diseases. Ann Otorhinolaryngol 91 165
143a. D Zee (1984) New concepts of cerebellar control of eye movements. OtoRNS 92 59
144. H Shibasaki, et al (1979) Oculomotor abnormalities in Parkinson's disease. ArN 36 360
144a. AT Bahill, BT Tusa (1979) Types of saccadic eye movements. N 29 1150
145. L Weinfeld, RW Stevens (1938) Horner's syndrome with unilateral accommodative paresis. AJOph 86 214
146. EP Hannan, et al (1984) Transverse myelitis due to meningovascular syphilis. AdN 42 333
146a. SJ McPhee (1984) Secondary syphilis: uncommon manifestations a common disease. WJM 140 35
146b. RP Simon (1985) Neurosyphilis. AdN 47 608,617, 10 Horst, et al (1978) Pineal tumors. A 55-case experience. AdN 35 530
148. SJ Bunce, et al (1980) Ghost cell mitral dysfunction secondary to shunt malfunction in hydrocephalus. NSS 7 333
148a. JE Corbett, et al (1978) Neuro-ophthalmological complications of enlargement of the third ventricle. JAOph 62 536
148b. AS Chemba, GR Delong (1975) Sylvian aqueduct syndrome as a sign of acute obstructive hydrocephalus in children. JNNP 38 258
148c. JR Kranz (1985) Pretectal parakeratolabia. Five patients with "V" pattern convergence nystagmus. ArOph 42 592
149. RA Bell, HS Thompson (1978) Ciliary muscle dysfunction in Adie's syndrome. ArOph 96 638
149a. HS Thompson (1978) Segmental palsy of the iris sphincter in Adie's syndrome. ArOph 96 1615
150. JE Lowenfeld, HS Thompson (1981) Mechanism of tonic pupil defect. AdN 10 235
151. HS Thompson (1978) Segmental palsy of the iris sphincter in Adie's syndrome. ArOph 96 1615
152. R Levy (1967) The tendon reflexes in the Holmes-Adie syndrome. N 17 1213
153. TP Naidich, et al (1983) The Chiari II malformation. Part IV. The hindbrain deformity. Neurol 27 179
153a. RS Paul, et al (1983) Arnold Chiari malformation. Review of 71 cases. J NS 58 183
154. RW Baloh, JW Sprague (1981) Downbeat nystagmus. A type of central vestibular nystagmus. N 31 364
154a. RA Pedersen, et al (1980) Intermittent downbeat nystagmus and oscillopsia reversed by suboccipital craniectomy. N 30 1239
154b. N Shanlin, et al (1972) Downbeat nystagmus as a sign of brainstem involvement in acute meningoencephalitis. N 21 767

154c. LW Lilne, et al (1983) Downbeat nystagmus. A case report of lacunar brain stem encephalitis, J Clin Neuph 3:4 245
154d. GM Halmagyi, et al (1983) Downbeating nystagmus. A review of 62 cases, ArN 40 777
155. BT Tusa, et al (1980) Upbeat nystagmus and internuclear ophthalmoplegia with bruxism gliosis, ArN 37 453
155a. T Nakada, MR Remler (1981) Primary position upbeat nystagmus. Another central vestibular nystagmus?, J Clin N Oph 1 185
155b. A Fetter, et al (1983) Primary position upbeating nystagmus. A variety of central positional nystagmus, Brain 106 949
155c. I Kato, et al (1985) Primary position upbeat nystagmus. Localizing value, ArN 42 819
156. CM Fisher (Your recipe talk), Cerebellum: nuances eccentric gaze.
156a. D Zee (1984) New concepts of cerebellar control of eye movements, OtoHNS 92 59
157. BT Tusa (1980) Dizziness and vertigo in vertebrobasilar disease. Part 1. peripheral and systemic causes of dizziness, Stroke 11 301
157a. MS Hanson, C Onofrio ph (1975) Positional nystagmus, ArOto 101 675
157b. P Wiesen, et al (1981) Positional vertigo and nystagmus of central origin, Can J N Sci 8 133
157c. MJ Harrison (1981) Nystagmus, Br J Hosp Med 26 484
157d. AG Van Vliet (1982) Nystagmus, Doc Oph 52 435
158. RD Yee, et al (1980) Study of congenital nystagmus: optokinetic nystagmus, BJOph 64 836
158a. GK von Noorden, R LaRoche (1983) Visual acuity and motor characteristics in congenital nystagmus, AJOph 95 348
158b. MA Gresty, et al (1984) The differential diagnosis of congenital nystagmus, JNNP 47 936
159. MA Gresty, et al (1982) Acquired pendular nystagmus: its characteristic localizing value and pathophysiology, JNNP 45 331
160. RW Baloh, et al (1980) Optokinetic nystagmus and parietal lobe lesions, AuN 7 299
160a. M Brigell, et al (1984) Hypometric saccades and low-gain pursuit resulting from a thalamic hemorrhage, AuN 15 374
160b. RA Pedersen, BT Troost (1981) Abnormalities of gaze in cerebrovascular disease, Stroke 12 251
160c. RJ Leigh, RJ Tusa (1985) Disturbance of smooth pursuit caused by infarction of occipitoparietal cortex, AuN 17 185
161. LR Caplan (1980) "Top of the basilar" syndrome, N 80 72
161a. JD Trobe, et al (1977) Isolated homonymous hemianopia. A review of 104 cases, ArOph 89 377
162. DS Lawrence, JL Smith (1966) Optokinetic nystagmus and occipital lesions, AJOph 61 753
163. JG Mora, R Joffe (1985) Perineural spread of extracranial basal and squamous cell carcinomas. The clinical appearance of spread into the trigeminal and facial nerves, AJN 40 424
164. RC Schneider, et al (1973) Traumatic spinal cord syndromes and their management, Clin N/S 20 424
164a. RC Schneider (1978) Syringomyelia. Personal observations concerning the neurological diagnosis and the mechanism of treatment by computerized axial tomography, Clin N/S 25 96
164b. D Denny-Brown, N Yanagisawa (1973) The function of the descending root of the fifth nerve, Brain 96 783
165. LB Kline, et al (1982) Computed tomographic evaluation of the cavernous sinus, Ophthal 89 374
165a. LB Kline, et al (1983) The cavernous sinus: a computed tomographic study, AJ Vrnd 3 299
166. DL Daniels, et al (1985) Magnetic resonance of the cavernous sinus, AJNR 6 187 166a. M Chui, et al (1985) High resolution CT of Meckel's cave, N/rad 27 403
167. RO Crisóstomo-Jones, et al (1982) Cavernous sinus thrombosis, JNNP 45 1082
167a. RJ Kadlec, WA Robinson (1984) Septic cavernous sinus thrombosis, AnEmMed 13 449
168. TM Markowitz (1981) Acute palatal cavernous sinus syndrome in unruptured intracavernous aneurysm of the internal carotid artery. Possible pathogenetic mechanisms, J Clin N/ Oph 1 31
168a. HW Barr, et al (1971) Intracavernous carotid aneurysm. A clinical-pathological report, Brain 94 607
169. G Schultz, et al (1983) Treatment of vascular lesions with balloon catheters, AJN/rad 4 395
169a. GM Debrun (1983) Treatment of traumatic carotid-cavernous fistula using detachable balloon catheters, AJ N/rad 4 187
170. TJ Leonard, et al (1984) Ophthalmoplegia incarcerid cavernous sinus fistula, BJOph 68 128
170a. JD Trobe, et al (1978) Meningiomas and aneurysms of the cavernous sinus. Neuro-ophthalmologic features, ArOph 96 1571
170b. A Kastan, P Schwarz (1977) Orbitomeningeal anomalies in sellar and parasellar pathology, Ophthalmologica 175 80
170c. TR Friberg, RL Sergi (1978) Ischemic optic neuropathy in cavernous sinus thrombosis, A Oph 96 453
170d. PM Markowitz (1981) Acute painful cavernous sinus syndrome in unruptured intracavernous aneurysm of the internal carotid artery. Possible pathogenetic mechanisms, J Clin N/ Oph 1 31
170e. H Nohira, et al (1981) Long term observations in cases with spontaneous carotid cavernous fistulae, Surg N 11 542
170f. RF Saul, JK Hilliker (1985) Third nerve palsy: the presenting sign of a pituitary adenoma in five patients and the only neurologic sign in four patients, J Clin N/oph 5 183
171. RK Lala, PJ Jozetta (1977) Glossopharyngeal neuralgia, J N/S 47 316
171a. JG Rushton, et al (1981) Glossopharyngeal (vagoglossopharyngeal) neuralgia. A study of 217 cases, ArN 38 201
171b. C Ulirge, G Braggi (1985) Surgical treatment of glossopharyngeal neuralgia and pain from cancer of the oropharynx. A 20-year experience, J N/S 56 952
172. L Kudrow (1983) Cluster headache: New concepts, Neurol Clin 1 369
172a. CA Pagni (1982) Trigeminal neuralgia, Panminerva Med 24 113
173. SJ Dimond (1980) Abnormal bipolar association in facially distributed trigeminal pain, J N/S 53 634
173a. GH Fromm, et al (1984) Trigeminal neuralgia. Current concepts regarding etiology and pathogenesis, ArN 41 1290
174. ML Lazar, JB Kirkpatrick (1979) Trigeminal neuralgia and multiple sclerosis: demonstration of the plaque in an operative case, N/S 5 711
175. B Breese, RJ Ignelzi (1982) Microvascular decompression for trigeminal neuralgia. Results with special attention to the late recurrence rate, J N/S 57 487
175a. H van Limmen, et al (1982) A 10 year experience in the treatment of trigeminal neuralgia. Comparison of percutaneous stereotaxic thermocoagulation and percutaneous expansion, J N/S 57 757
175b. SJ Haines, et al (1980) Microvascular relations of the trigeminal nerve. An anatomical study with clinical correlation, J N/S 52 381
175c. P Richards, et al (1983) Operative findings on microsurgical exploration of the cerebello-pontine angle in trigeminal neuralgia, JNNP 46 1094
176. MM Cohen, S Lessel (1979) Retraction of the lower eyelid, N 29 586
177. RH Spector, S Shirk (1983) Vercheml facial palsy with sensorineural and learning caused by intrapontine lesion, ArN 40 512
177a. Y Nakajima, et al (1982) Lesions of the lateral distribution of taste due to pontine hemorrhage, JN 229 133
178. D Cohen III, KK Adour (1978) Acoustic reflex and loudness discomfort in acute facial paralysis, ArOto 104 300
179. KK Adour (1976) Cranial polyneuritis and Bell's palsy, ArOto 102 262
180. U Fisch, H Pelz (1984) On the pathogenesis of Bell's palsy, ArOto 93 552
180a. JI Pulec (1981) Facial re-innervation of Bell's palsy. Early decompression of the facial nerve in Bell's palsy, ArOto 90 570
180b. E Stennert (1981) Pathomor-

disease is cell metabolism: A key to treatment of Bell's palsy, *AnOto 80* 577

180. RR Gacek (1981) Comment, *AnOto 90* 581

181. GM Novotny (1970) Gustatory sweating and related syndromes, *J Otolaryngol 5* 251

181a. K Sadjadpour (1975) Postfacial palsy pterygoma: faulty nerve regeneration or ephaptic transmission?, *Brain 98* 403

182. M Van Zandijcke, et al. (1982) Facial myokymia in the Guillain-Barre syndrome: a clinicopathologic study, *N 32* 741

182a. JE Mulder, et al (1983) Myokymia in Guillain-Barre syndrome, *N 33* 574

182b. MF Mendez, et al (1985) Isolated facial myokymia and facial synkinesis: computed tomography and magnetic resonance imaging simulation, *J Clin Neurophys 3* 129

182c. RB Tarlov (1976) Myokymia and facial contraction in multiple sclerosis, *AdNM 126* 61

182d. L Gomarin, et al (1986) Calcium and myokymia of brainstem origin, *N 36* 176

183. JC Marson (1978) Hemifacial spasm. A vascular cause, *AdN 53* 481

183a. JR Mackinnon, CF Reynolds III (1979) Blepharospasm: Successful treatment with clonazepam, *AdN 5* 401

184. RS Diesa (1981) Clinical features of Meige's disease (idiopathic orofacial dystonia): A report of 17 cases, *AdN 35* 147

184a. WJ Weiner, et al. (1981) Meige syndrome: Oromandibular dystonia after long-term neuroleptic therapy, *N 31* 1535

184b. DE Casey (1980) Pharmacology of blepharospasm-oromandibular dystonia syndrome, *N 30* 690

185. J Jankovic, SC Patel (1983) Blepharospasm associated with meningioma lesions, *N 33* 1232

186. A Bernardelli, et al (1985) Pathophysiology of blepharospasm and oromandibular dystonia, *Brain 108* 593

186a. CM Tanner, et al. (1982) Meige disease: Acute and chronic cholinergic effects, *N 32* 783

186b. J Jankovic, et al (1982) Blinking and blepharospasm: Mechanism, diagnosis, and management, *JAMA 249* 1160

186c. J Jankovic, J Ford (1983) Blepharospasm and orofacial cervical dystonia: Clinical and pharmacological findings in 400 patients, *AnN 13* 402

187. RG Auger (1979) Hemifacial spasm: Clinical and electrophysiologic observations, *N 29* 1264

187a. JD Lesser, J Chen (1983) Hemifacial spasm: treatment by microsurgical facial nerve decompression, *N/S 53* (4)

188. P Kim, T Fukushima (1980) Observations on epilepsy in patients with hemifacial spasm. Effect of microvascular decompression and surgical considerations, *J N/S 60* 821

188a. AR Møller, PJ Jannetta (1985) Hemifacial spasm: Results of electrophysiologic recording during microvascular decompression operations, *N 35* 960

188b. VK Nielsen (1985) Electrophysiology of the facial nerve in hemifacial spasm: ectopic-ephaptic excitation, *M&N 5* 305

188c. VK Nielsen (1986) Indirect and direct evidence of ephaptic transmission in hemifacial spasm (letter), *N 36* 591

188d. J Ravits, M Hallett (1986) Pathophysiology of hemifacial spasm (letter), *N 36* 591

189. P Kim, T Fukushima (1984) Observations on epilepsy in patients with hemifacial spasm. Effect of microvascular decompression and surgical considerations, *J N/S 60* 821

189a. T Iwakuma, et al (1982) Hemifacial spasm: Comparison of three different operative procedures in 110 patients, *J N/S 57* 581

189b. D Fazzalari, et al (1983) Hemifacial spasm: results of microvascular relocation, *Can J Neu Sci 10* 107

190. AH Kaye, CH Adams (1981) Hemifacial spasm: a long term follow-up of patients treated by posterior fossa surgery and facial nerve wrapping, *JNNP 44* 1160

190a. A Oki, T Nagao (1986) Resolution of hemifacial spasm after posterior fossa exploration without vascular decompression, *N/S 18* 478.

191. RG Auger (1979) Hemifacial spasm: Clinical and electrophysiologic observations, *N 29* 1264

191a. GC Fabiyi, CB Adams (1978) Hemifacial spasm: treatment by posterior fossa surgery, *JNNP 41* 829

191b. PJ Jannetta, et al. (1977) Etiology and definitive microsurgical treatment of hemifacial spasm. Operative technique and results in 47 patients, *J N/S 47* 321

192. FM. Haughton, JM. Pearce (1982) Observations on the Babinski test, *Lancet 1* 929

193. A Eviatar, L Eviatar (1974) A cranial look at the "cold (clonic)," *AnOto 93* 361

194. RG Hart, J Davenport (1981) Diagnosis of acoustic neuroma, *N/S 9* 450

194a. SG Harsen, ER Lees Jr (1981) Diagnosis of acoustic neurinoma, *N/S 9* 372

195. RG Hart, et al (1983) Acoustic tumors: Atypical features and recent diagnostic tests, *N 33* 211

196. RG Hart, et al (1983) Acoustic tumors. Atypical features and recent diagnostic tests, *N 33* 211

197. RG Hart, J Davenport (1981) Diagnosis of acoustic neuroma, *N/S 9* 450

198. RG Hart, J Davenport (1981) Diagnosis of acoustic neuroma (1981) *N/S 9* 450

199. LM Flood, et al (1984) Pitfalls in the diagnosis of acoustic neuroma, *Can Otolo 9* 165

199a. J Thompson, et al (1981) Acoustic neuromas. Diagnosis and recovery of various new combinations, *AnOto 107* 601

200. SG Harner, ER Lees Jr (1981) Diagnosis of acoustic neurinoma, *N/S 6* 371

200a. DM Batts, et al (1985) Changing concepts of acoustic neuroma diagnosis, *AnOto 111* 17

201a. A Hakuba, et al (1979) Jugular foramen neurinomas, *Surg N 11* 83

204b. AH Kaye, et al (1981) Jugular foramen schwannomas, *J N/S 60* 1045

202. RP Green, M Brien (1985) Accessory nerve latency to the middle and lower trapezius, *ArPMR 66* 23

203. S Balagura, RG Katz (1980) Unilateral innervation to the sternocleidomastoid muscle: a misstatement, *AnN 7* 86

203a. N Geschwind (1981) Nature of the decussated innervation of the sternocleidomastoid muscle (letter), *AnN 10* 605

204. TA Wright (1975) Accessory spinal nerve injury, *CORR 108* 15

204a. A Uzun, G Bernard (1972) Isolated accessory nerve palsy of spontaneous origin. A clinical and electromyographic study, *AnN 27* 496

205. BD Shore, et al (1981) Shoulder pain and function after neck dissection with or without preservation of the spinal accessory nerve, *AJS 140* 478

206. LW Massey, et al (1984) Cranial nerve paralysis following carotid endarterectomy, *Stroke 15* 157

206. B Theodosiou, MS Mahaley Jr (1985) Injury of the peripheral cranial nerves during carotid endarterectomy, *Stroke 16* 864

207. A Lieberman, DF Benson (1977) Control of confusional expression in pantothenic palsy. A personal experience, *AnN 34* 717

CHAPTER 21:

1. HW Tapdon (1981) Posterior internuclear ophthalmoplegia of Lutz, *AnOph 13* 221

1a. J Bogousslavsky, et al (1985) Pareses of lateral gaze alternating with so-called posterior internuclear ophthalmoplegia. A partial paramedian pontine reticular formation-abducens nucleus syndrome, *N 35* 38

1b. G Komoltzell (1975) Internuclear ophthalmoplegia of unknown: Isolated impairment of phasic ocular motor activity in supranuclear lesions, *AnOph 93* 531

2. EW Willoughby, NE Anderson (1981) Lower cranial nerve motor function in unilateral vascular lesions of the cerebral hemisphere, *BMJ 289* 791

3. EW Willoughby, NE Anderson (1984) Lower cranial nerve motor function in unilateral vascular lesions of the cerebral hemisphere, *BMJ 289* 791

4. C Bogousslavsky, et al. (1979) Posterior internuclear ophthalmoplegia as isolated cranial nerve palsies, *N 29* 377

4a. S Aleksic, G Budzilovich (1973) Lateral internuclear pontine syndrome,

Clinico-pathologic study and review of literature. JNSci *18* 517

4b. ML Moster, et al (1984) Isolated sixth nerve palsies in younger adults. AmJOph *101* 1329

5. LR Caplan, JA Goodwin (1982) Lateral tegmental brainstem hemorrhages. N *32* 252

6. FR Ash, JL Kistner (1979) Neuro-ophthalmic signs in porcine leukaemia. Medicine *58* 304

7. RD Currie, et al (1962) Some comments on Wallenberg's lateral medullary syndrome. N *11* 378

7a. AB Baker (1961) IX. The medullary blood supply and the lateral medullary syndrome. N *11* 882

8. KL Bo, ER Meyer (1981) The medial medullary syndrome. ArN *38* 585

8a. T Mizuno, et al (1990) Medial medullary syndrome in a dog shown. ArN *47* 425

9. S Balagura, RG Katz (1980) Undecussated innervation in the sternocleidomastoid muscle: a reinvestigation. AnN *7* 84

9a. N Geschwind (1981) Nature of the decussated innervation of the sternocleidomastoid muscle (letter). AnN *10* 405

9b. PL Mastaglia, et al (1976) Weakness of head turning in hemiplegia: a quantitative study. BNSP *40* 195

10. RA Pedersen, HT Troost (1981) Abnormalities of gaze in cerebrovascular disease. *Stroke 12* 251

10b. T Raptan, B Cohen (1978) Brainstem mechanisms for rapid and slow eye movements. Ann Rev Physiol *40* 527

10c. RH Spector, BT Troost (1981) The ocular motor system. AnN *9* 517

11. M Reigel, et al (1984) Hypermetric saccades and low gain pursuit resulting from a thalamic hemorrhage. AnN *15* 274

11a. CJ Bruce, MP Goldberg (1985) Primate frontal eye fields. I. Single neurons discharging before saccades. *J* NPhys *53* 603

11b. E Melamed, B Lavie (1979) Cortical activation pattern during saccadic eye movements in humans. localization by focal cerebral blood flow increase. AnN *5* 79

12. MB Bender (1960) Brain control of conjugate horizontal and vertical eye movements. A survey of the structural and functional correlates. Brain *103* 23

12a. GR Lynch, et al (1981) The parietal cortico-oculomotor projections in the monkey. *J* NPhys *49* 387

13. SH Zahn, JA Sharpe (1984) Midbrain paresis of lateral gaze. AnN *16* 495

13a. RP Lesser, et al (1985) Preservation of voluntary saccades after intracarotid injection of barbiturate. N *35* 1108

13b. G House, et al (1985) The syndrome of posterior thalamic hemorrhage. *35* 995

14. TR Crone, et al (1983) Analysis of characteristic eye movement abnormalities in internuclear ophthalmoplegia. AtOph *101* 209

14a. RM Muir, D Meienberg (1985) The clinical spectrum of internuclear ophthalmoplegia in multiple sclerosis. AnN *42* 851

15. RW Baloh, et al (1975) Internuclear Ophthalmoplegia. I. Saccades and dissociated nystagmus. AnN *35* 484

15a. SB Fabian, et al (1980) Disordered inhibition in internuclear ophthalmoplegia. Analysis of eye movement recordings with computer simulations. Brain *103* 113

15b. G Kommerell (1981) Unilateral internuclear ophthalmoplegia. The lack of inhibitory innervation in medial rectus activity. Invest Oph Vis Sci *21* 592

16. J Pola, DA Robinson (1976) An explanation of eye movements seen in internuclear ophthalmoplegia. AnN *33* 647

17. LE Mays (1984) Neural control of vergence eye movements: Convergence and divergence neurons in midbrain. *J* NPhys *51* 1091

17a. SJ Judge, BG Cumming (1986) Neurons in the monkey midbrain with activity related to vergence eye movement and accommodation. *J* NPhys *55* 915

18. M Critchley (1956) Neurologic changes in the aged. *J* Chronic Dis *3* 459

19. BK Mudaliah, TJ Carlos (1977) Tonic gaze paresis in amyotrophic sclerosis (letter). N *27* 605

19a. RH Spector, et al (1976) Phenytoin-induced ophthalmoplegia. N *29* 1031

20. MA Gresty, et al (1977) Disorders of the vestibulo-ocular reflex producing oscillopsia and mechanisms compensating for loss of labyrinthine function. Brain *100* 693

20a. GL Walls (1962) The evolutionary history of eye movements. Vis Res *2* 69

20b. JA Sharpe, AW Lo (1981) Voluntary and visual control of the vestibulo-ocular reflex after contralateral hemidecortication. AnN *10* 365

21. MA Gresty, et al (1977) Disorder of the vestibulo-ocular reflex producing oscillopsia and mechanism compensating for loss of labyrinthine function. Brain *100* 693

21a. TD Clark, et al (1985) Eye rat reflexes while riding in a car. Laryngo *95* 182

21b. JR Kattah (1986) Acute vertical ocular myokymia. N *25* 56

22. F Plum, JB Posner (1980) *the Diagnosis of Stupor and Coma*, F.A. Davis, Philadelphia, pp. 56–57

22. (1974) Metabolic coma. Medical Staff Conference, University of California, San Francisco, WJM *120* 131

24. JC Kattah, et al (1983) Primary position vertical nystagmus and cerebellar ataxia. AnN *40* 310

24a. CM Halmagyi, et al (1983) Downbeating nystagmus. A review of 62 cases. AnN *40* 737

24b. JR Kattah, AD Kovacs (1982) Downbeat nystagmus with phenytoin. *J* Clin Neuph *2* 209

24c. A Fisher, et al (1983) Primary position upbeating nystagmus. A variety of central positional nystagmus. Brain *106* 949

24d. J Baumgartner, F Rayli (1985) Monocular downbeat nystagmus. JN *232* 99

24e. I Kato, et al (1985) Primary position nystagmus. Localizing value. AtN *42* 819

24f. MT. Slavin, MT. Rosenberg (1985) Unusual associations of downbeat nystagmus. Neuph *3* 265

25. RW Baloh, JW Spooner (1981) Downbeat nystagmus: A type of central vestibular nystagmus. N *31* 304

25a. RA Pedersen, et al (1980) Intermittent downbeat nystagmus and oscillopsia reversed by subsurgical cauterotomy. N *30* 1259

25b. LW Hirsh, et al (1983) Downbeat nystagmus. A case report of herpetic brain stem encephalitis. *J* Clin Neuph *3* 245

26. JR Bruce, AD Kovacs (1982) Downbeat nystagmus with phenytoin. *J* Clin Neuph *2* 209

26a. JC Kattah, et al (1983) Primary position vertical nystagmus and cerebellar nystagmus. AnN *40* 310

26b. SD Wheeler, et al (1982) Drug-induced downbeat nystagmus. AnN *12* 527

27. BT Troost, et al. (1980) Upbeat nystagmus and internuclear ophthalmoplegia with brainstem glioma. ArN *37* 633

27a. N Gillman, et al (1977) Primary position upbeat nystagmus. A clinico-pathologic study. N *27* 291

27b. T Nakada, MP Rossiter (1982) Primary position upbeat nystagmus. Another central vestibular nystagmus? *J* Clin Neuph *2* 185

28. B Katz, et al (1982) Ocular bobbing and unilateral pontine hemorrhage. *J* Clin Neuph *2* 193

28a. A Ilinca, eng al (1984) Typical and reverse bobbing. A case with localizing value. Ner N *37* 151

28b. P Lamarche, et al (1983) Ocular bobbing: Abnormal eye movements or eye movement's abnormality?. Ophthalmologica *187* 161

29. RL Knobler, et al (1981) Inverse ocular bobbing. AnN *9* 194 29a. A Roppke (1981) Ocular dipping in metastoma. AnN *38* 297

29b. SR Sharp, et al (1984) Ocular dipping. N *34* 391

30. ME Drake Jr, et al (1982) Ocular bobbing in metabolic encephalopathy. Clinical, pathologic, and electrophysiologic study. N *32* 1029

31. GM Halmagyi, et al (1979) Ocular tilt reaction with peripheral vestibular lesion. AnN *6* 80

32. LR Jones, et al (1978) Reflex vertical gaze and the medial longitudinal fasciculus. BNSP *41* 1084

32a. DE Hedges III, WB Hoyt (1982) Ocular tilt reaction due to an upper brainstem lesion: Paroxysmal skew deviation, torsion, and oscillation of the eyes with head tilt. AnN *11* 537

32b. (1957) Skew. *J* Clin Neuph *2* 115

32c. JR Kranz (1985) Alternating skew deviation: 63 patients. N *35* 725

33. RA Pedersen, JT Troost (1981) Abnormalities of gaze in autosomal-dominant disease. Stroke 12:251
34. MS Pepin, et al (1981) "Wrong-way eyes" in supratentorial hemorrhage. AnN 9:79
34a. JB Keane (1979) Contralateral gaze deviation with supratentorial hemorrhage. Three pathologically verified cases. AnN 32:110
35. C Parrot Dreuillaux, et al (1981) The "one-and-a-half" syndrome. Electro-oculographic analysis of five cases with clinico-anatomical and physiological mechanisms of lateral gaze. Brain 104:665
35c. MS Smith, et al (1989) One and a half syndrome. Occurrence after trauma with computerized tomographic correlation. AnN 37:251
35h. M Wray, SH Wray (1987) The one and a half syndrome. A unilateral disorder of the pontine tegmentum. A study of 20 cases and review of the literature. N 54:971
36. JA Buttner Ennever, et al (1982) Ventral gaze paralysis and the ventral interstitial nucleus of the medial longitudinal fasciculus. Brain 105:125
36a. V Hotz, et al (1984) Experimental gaze palsies in monkeys and their relation to human pathology. Brain 107:619
37. JJ Shyman, LB Kline (1981) Ocular oculomotor synkinesis in multiple sclerosis. N 17:196
38. AL Celis, et al (1979) Opposed sidewing excesses in convergence-retraction nystagmus. A patient with Parinaud dorsal midbrain syndrome. Brain 102:497
38a. MD Bender, et al (1990) Ventral gaze: clinical and experimental observations with particular reference to oblique movements. Neuph J 9:9
39. DH Zaken, JA Sharpe (1984) Midbrain paresis of horizontal gaze. AnN 36:491
39a. FT Fox, et al (1985) The role of cerebral cortex in the generation of voluntary saccades: a positron emission tomographic study. J Neurophys 54:348
39c. F Guitton, et al (1985) Frontal lobe lesions in man cause difficulties in suppressing reflexive glances and in generating goal-directed saccades. Exp Br Res 58:455
40. V Hotz, et al (1984) Experimental gaze palsies in monkeys and their relation to human pathology. Brain 107:619
41. LC Evinger, et al (1977) Bilateral lesions of the medial longitudinal fasciculus in monkeys: effects on the horizontal and vertical eye movements of voluntary and vestibular induced eye movements. Exp Br Res 29:1
42. Ch. Pierre-Duvillard, J Gueugneau (1984) Isolated abducens nuclear damage due to bilateralosis. I. Electro-oculographic analysis and physiologic deductions. Brain 107:1019
42a. V Hotz, et al (1982) The premotor oculomotor system. II. Premotor system. Hum Neurol 3:87
43. JA Buttner Ennever, et al (1982) Ventral gaze paralysis and the ventral interstitial nucleus of the medial longitudinal fasciculus. Brain 105:125
43a. K Fukushima, et al (1984) Interstitial-vestibular interaction in the control of head posture. Exp Br Res 57:364
43b. (1991) Interstitial nucleus of Cajal, Br Res Bull 33:613
44. GS Ford, et al (1991) Monocular elevation paresis caused by an ipsilateral lesion. N 3:588 1264
45. GS Ford, et al (1984) Monocular elevation paresis caused by an ipsilateral lesion. N 3:456 1264
45a. J Bogousslavsky, F Regli (1986) Upgaze palsy and contralateral paresis or dysesthesia from ipsilateral thalamo-mesencephalic infarction a vertical "one-and-a-half" syndrome. JN 233 43
46. C Pierre-Duvillard, et al (1986) Pontine metastasis with dissociated bilateral horizontal gaze paralysis. JNNP 47:159
46a. RW Baloh, et al (1985) Eye movements in patients with absent volitional horizontal gaze. AnN 17:381
47. CH Pierre-Duvillard, J Gueugneau (1981) Isolated abducens nuclear damage due to bilateralosis. I. Electro-oculographic analysis and physiologic deductions. Brain 104:1019
48. RW Baloh, et al (1975) Internuclear ophthalmoplegia. II. Pursuit, optokinetic nystagmus, and vestibular nystagmus. AnN 35:460
49. J Bogousslavsky, et al (1985) Internuclear ophthalmoplegia. pronuclear paresis of contralateral superior rectus and bilateral ptosis. JN 233 197
49a. LB Haines, et al (1978) Reflex vertical gaze and the medial longitudinal fasciculus. JNNP 41:1034
49b. D Mesnekoff, et al (1978) Pronuclear paresis of bilateral inferior rectus and contralateral superior oblique eye muscles. AnN 33:454
49c. LC Evinger, et al (1977) Bilateral lesions of the medial longitudinal fasciculus in monkeys: effects on the horizontal and vertical eye movements of voluntary and vestibular induced eye movements. Exp Br Res 29:1
49d. JA Buttner Ennever, et al (1982) Ventral gaze paralysis and the ventral interstitial nucleus of the medial longitudinal fasciculus. Brain 105:125
50. S Nozaki, et al (1982) Internuclear ophthalmoplegia associated with unilateral divergent nystagmus and contralateral incyclotorsion nystagmus. Ophthalmologica 185:130
51. J Bousslavsky, F Regli (1985) Nuclear and pronuclear syndromes of the oculomotor nerve. N Appl J 2:11
51a. J Biller, et al (1984) Oculomotor midbrain complex infarction. Clinical and pathological correlation. AnN 17:385
51b. VH Downey, et al (1983) Can J Opht 18:37
52. JR Kranz, et al (1967) Lesion-sparing oculomotor nerve palsy caused by a miliary malbaln case. AnN 41:240
53. DC Bienfang (1975) Crossing axons in the third nerve nucleus. Invest Opth Vis Sci 14:927
54. J Bougousslavsky, F Regli (1983) Nuclear and pronuclear syndromes of the oculomotor nerve. Neuph J 2:11
55. GS Hoyt (1979) Acquired "double elevator" palsy and polycythemia vera. J Pal Opht Strab 15:367
56. RW Burde (1983) The visceral nuclei of the oculomotor complex. Trans Am Opth Soc 81:532
57. SE Nadkarni, JD Tube (1983) Pupil sparing in oculomotor palsy: A brief review, AnN 15:143
58. JO Sanac, WF Hoyt (1977) Isolated branch palsy of the oculomotor nerve. AnN 2:339
58a. J Guy, et al (1985) Superior division paresis of the oculomotor nerve. Ophthal 92:777
58b. H Spector, MS Pandara (1986) The "classic" Tolosa-Hunt syndrome. N 36:198
59. JD Tube (1985) Isolated pupil sparing third nerve palsy. Ophthal 92:58
59c. WW Bannon 91982) Atypical clinical presentation of oculomotor (III) nerve palsy. J Clin Neuph 2:249
60. PA Sibony, et al (1984) Acquired oculomotor synkinesis. Surv Opth 28:382
61. JT Kissel, et al (1983) Pupil-sparing oculomotor palsies with internal carotid posterior communicating artery aneurysms. AnN 13:149
61a. JD Tube (1985) Isolated pupil sparing third nerve palsy. Opthal 92:58
62. PA Sibony, et al (1984) Acquired oculomotor synkinesis. Surv Opt. 28:382
63. BS Glaser (1986) Myasthenic pseudo internuclear ophthalmoplegia. Arch Opt 73:367

CHAPTER 22:

1. G Manzoni, HW Magoun (1949) Brain stem reticular formation and activation of the EEG. EEGCNP 1:425
2. RA Davis, L Davis (1982) Descemetic rigidity in animals. N/S 9:29
2a. RA Davis, L Davis (1982) Descemetic rigidity in humans. N/S 10:505
2b. N King, et al (1966) Decerebrate rigidity and vegetative signs in the acute midbrain syndrome with special regard to motor activity and intracranial pressure, Acta Neurochir 225:210
2c. J Jernigan, et al (1985) Traumatic dissociation with preserved consciousness and voluntary movement. N/S 16:71
3. JC Drummond, MM Todd (1986) Acute circulatory embolectic during surgery in the fourth ventricle. An indicator of brainstem ischemia. Anesth 69:232
4. R Schrader, et al 91985) Regional cerebral blood flow and SCP pressure during the Cushing response induced

by an intracranial expanding mass, ANS 72:273
4a. JD McGillicuddy, et al (1978) The relation of cerebral ischemia, hypoxia, and hypercarbia to the Cushing reflex, J NS 48:720
5. LH Pitts (1982) Neurological evaluation of the head injury patient, Clin NAS 29:203
6. MM Newman, et al (1984) Pulmonary hypertension, pulmonary edema, and decreased pulmonary compliance produced by increased ICP in cats, J NS 60:1207
6a. SJ Ransohoff, S Schwartzbaum (1970) Recovery from decerebration, Brain 93:331
7. W Fitch, DG McDowall (1977) Systemic vascular responses to increased intracranial pressure. 1. Effects of progressive epidural balloon expansion on intracranial pressure and systemic circulation, JNNP 40:833
7a. W Fitch, et al (1977) Systemic vascular responses to increased intracranial pressure. 2. The 'Cushing' response in the presence of intracranial space-occupying lesions: systemic and cerebral hemodynamic studies in the dog and the baboon, JNNP 40:843
7b. R Lorenz, The Cushing Response, in IWF Beks, DA Bosch, M Brock (eds) *Intracranial Pressure III*, Springer-Verlag, Berlin, 1976, pp. 270–274
8. R Lorenz, The Cushing response, in *Intracranial Pressure II* ed by IWF Beks, DA Bosch, M Brock, Springer-Verlag (1976) Berlin, p. 270–274
8a. S Hayreh, J Edwards (1971) Vascular response to acute intracranial hypertension, JNNP 34:587
9. M M Gassel (1966) Fiber localizing signs, ArN 15:226
10. MW Van Allen (1967) Transient recurring paralysis of ocular abductors, ArN 17:81
11. K Shapiro, et al (1980) Characterization of clinical CSF dynamics and neural axis compliance using the pressure-volume index. I. The normal pressure-volume index, ArN 7:908
11a. HA Wilkinson (1978) Intracranial pressure: nocrve testing, initial clinical observations, ArN 35:961
12. LR Jenkyn, et al (1978) Reflex vertical gaze and the medial longitudinal fasciculus, JNNP 41:1084
13. J Greenberg, et al (1979) Acute hydrocephalus in cerebellar infarct and hemorrhage, N 29:409
13a. MP Fitzke (1979) Cerebellar stroke, ArS 4:7
13b. RW Bucciaus, RM Berglund (1977) Acute cerebellar hemorrhage. Analysis of clinical findings and outcome in 12 cases, N 27:935
13c. N Mohamed, S Saiva-Mani (1981) Cerebellar hemorrhage. A review and reappraisal of benign cases, ArN 47:425
14. AL Harris (1982) Cytotoxic thyroid-induced vomiting is mediated via cerebellofugal pathways, Lancet 1:714
14b. PC Bajec, B. Brenn (1965) The neuroanatomy of vomiting in man: association of projectile vomiting with a solitary metastasis in the lateral segment of the pons and the middle cerebellar peduncle, JNNP 28:165
15. M Tatsuda, et al (1987) Cerebellar infarction with obstructive hydrocephalus, J NS 57:85
15a. M Khan, et al (1983) Massive cerebellar infarction: "conservative" management, Stroke 14:745
16. RA Caren, et al (1979) Upward transtentorial herniation. Seven cases and a literature review, ArN 36:618
17. DE Wilkins (1981) Acute and massive intraventricular hemorrhage of the posterior fossa, Surg Fetal Hosp Med 3:291
18. Metabolic Coma—Medical Staff Conference, University of California, San Francisco (1974), WJM 120:131
19. RP James (1968) Upward downward ocular deviation. Occurrence during oculovestibular testing in sedative drug-induced coma, ArN 17:436
19a. RH Spector, et al (1976) Phenytoin-induced ophthalmoplegia, N 29:1031
20. D Cameron (1980) Encephalopathies, in *Critical Care of Neurologic and Neurosurgical Emergencies*, ed by RA Thompson, RK Green, Raven Press, New York pp 101–115
21. LH Ciplan, D Schuster (1980) Dysconjugate gaze in hepatic coma, ArN 8:228
22. JP Cummy, M Swash (1966) Reversible encephalopathy and dysmetric posture in hepatic coma, NEJM 275:826
22a. I Tanja, A Yovic (1972) Hepatic encephalopathy, N 22:539

CHAPTER 23:

1. ED Ross, et al (1979) Prosodic and schematic emotions: functions of the dorsal somatocerebellar tracts?, ArN 5:171
1a. PD Wall, W Noordenbos (1977) Sensory functions which remain in man after complete transection of dorsal columns, Brain 100:641
1b. RJ Schwartzman, MD Bogdanoff (1969) Proprioception and vibration sensibility discrimination in the absence of the posterior columns, ArN 20:549
2. R Kuchulakanti, JG Howe (1982) Internuclear ophthalmoplegia in multiple sclerosis: a clinical survey and review of the literature, JNNP 47:308
2a. RC Chan, P Steinbok (1984) Bilateral cases of Horner's syndrome following head and/or neck injuries. Report of four cases, J Neurosurg 60:600
2b. R Sandyk, MJ Bamford (1983) "Horner's" syndrome as a presenting sign of subacute combined degeneration of the cord, ArN 17:215
3. M Hübel, et al (1987) Hand muscle atrophy in multiple sclerosis, ArN 40:811
4. A Katzenelson, et al (1982) Clinical skyline #1. S. L.: A search for an objective sign in the diagnosis of disc lesions of the lower lumbar spine, Spine 7:74
5. S Conrad, et al (1982) Pathophysiology of fasciculations in ALS as studied by electromyography of single motor units, M&N 5:202
5a. A Wettstein (1979) The origin of fasciculations in motoneuron disease, ArN 5:295
5b. G Roth (1982) The origin of fasciculations, ArN 22:542
6. SJ Oh (1978) Subacute demyelinating polyneuropathy responding to corticosteroid therapy, ArN 35:909
6a. RB Layzer (1982) Diagnostic implications of clinical fasciculations and cramps, in *Human Motor Neuron Diseases*, LP Rowland (ed) Raven Press, New York, p. 22
7. J Lamye, J Buchthal (1972) Segmental sensory innervation determined by potentials recorded from cervical spinal nerves, Brain 100:731
8. WG Bradley, et al (1975) Recurrent brachial plexus neuropathy, Brain 98:581
8a. P Tsairis, et al (1972) Natural history of brachial plexus neuropathy. Report of 99 patients, ArN 27:109
8b. GD Scholz (1985) A chronic and painless form of idiopathic brachial plexus neuropathy, JNNP 48:555
9. DM Stallworth, JB Bloch (1984) Diagnosis and management of thoracic outlet syndrome, ArS 123:1169
9a. G Chaloner, et al (1985) Dynamic approach in the diagnosis of thoracic outlet syndrome using somatosensory evoked potentials, ArPMR 66:3
10. BD Lascelles, et al (1977) The thoracic outlet syndrome, Brain 100:619
10a. DB Rosen (1976) Congenital anomalies associated with thoracic outlet syndrome. Anatomy, symptoms, diagnosis and treatment, AJS 132:771
10b. WG Jamieson, H Mowbray (1985) Representation of the thoracic outlet syndrome as a problem in extreme pain and psychiatric management, Pain 22:135
10c. M Cherington (1986) Surgery for thoracic outlet syndrome [letter], NEJM 314:332
11. RE Rice, EJ Jackman (1982) Measurement of the Achilles tendon reflex in the diagnosis of lumbosacral root compression syndromes, JNNP 45:791
12. H Grey, PM Richardson (1969) Common cervical nerve palsy: a clinical and electrophysiological review, JNNP 39:1162
12a. L Garrison, RH Rosenwasser (1985) Paralysis following secondary to lumbar disc herniation: report of two cases, NS 8:484
12b. RK Nelson (1978) The entrapment neuropathies, MRN 1:291
13. MH Crokard, JD Ross (1967) Movements induced by straight leg raising in lumbosacral roots, nerves and plexus, and in the sympathetic section of the sciatic nerve, JNNP 28:12
13a. WE Hodgins (1977) The crossed straight leg raising test [letter], NEJM 297:1129
13. JF Jabre, RW Bryan (1982) Bent-

zone pulling in the diagnosis of upper lumbar root lesions. *ArN 36* 669

16. P Dyck (1976) The femoral nerve stretch test with lumbar disc protrusions. *Surg N 6* 163

17. MN Eerbeke, et al (1962) The femoral stretching test. A valuable sign in diagnosing upper lumbar disc herniations. *J NS 57* 812

17a. LC Bertignac, et al (1966) Diagnosis and treatment of lumbosacral phlegmasias in patients with cancer. *ArN 41* 1282

18. R Wilis. (1982) Shoulder pain. *WMJ 157* 500

18a. MI Bryan (1981) Frozen shoulder: adhesive capsulitis. *BMJ 283* 1005

CHAPTER 24:

1. HR Tyler, KL Tyler (1984) Charles Edouard Brown-Séquard. Pathbreaker of physiology and pathology of the nervous system at Harvard Medical School. *N 34* 231

2. DE Selleggi, et al (1978) Spinal cord damage in surgery of the abdominal aorta. *Surgery 83* 28

3. G Di Chiro, LC Fried (1971) Blood flow currents in spinal cord arteries. *N 21* 1083

4. RD Mount (1958) Anterior spinal artery syndrome. *ANS 58* 59

4a. JR Silver, PR Buxton (1974) Spinal stroke. *Brain 97* 539

5. EB Schliesinger, et al (1981) Hydromyelia: Clinical presentation and comparison of modalities of treatment. *JNS 9* 356

6. N Shannon, et al (1981) Clinical features, investigation and treatment of post traumatic syringomyelia. *JNNP 44* 35

6a. JC Oakley, et al (1981) Postmenopausal syringomyelia. Case report. *J NS 55* 276

7. PJ Dyck, PH Lambert (1968) Dissociated sensation in amyloidosis. Compound action potential, quantitative histologic and teased fiber, and electron microscopic studies of sural nerve biopsies. *ArN 29* 400

8. M Pras, et al (1968) The characterization of soluble amyloid prepared in water. *J Clin Invest 47* 424

9. WJ Gardner, PG McMurry (1976) "Non-communicating" syringomyelia, a non-existent entity. *Surg N 6* 151

9a. WJ Gardner (1965) Hydrodynamic mechanism of syringomyelia: its relationship to myelocele. *JNNP 28* 342

9b. G Bertrand (1973) Dynamic factors in the evolution of syringomyelia and syringobulbia. *Clin N 20* 322

10. LD Celani, JR Benton (1952) Considerations in the diagnosis and treatment of syringomyelia and the Chiari malformations. *J NS 5* 224

10a. PK Nicholson, et al (1981) Some observations on the pathogenesis of syringomyelia. *JNNP 44* 964

10b. B Williams (1980) On the pathogenesis of syringomyelia: a review. *J Royal Soc Med 73* 798

11. JM Weinstein, et al (1980) Congenital Horner's syndrome. *ArOph 98* 1004

11b. TP Doyle, DM Albert (1968) Lack of adrenergic influence in the pigmentation of the iris nevus cells. *ArOph 98* 1996

12. JC Spera, et al (1983) Ocular syphilis. Acute and chronic. *J Clin Neuroph 3* 139

12a. JG Burke, et al (1953) Perspective visual loss in syphilitic optic atrophy. *J Clin Neurol 3* 5

13. CS Hoyt III (1979) Vitamin metabolism and therapy in ophthalmology. *Surv Ophth 24* 171

14. JM Scott, et al (1981) Pathogenesis of subacute combined degeneration. A result of methyl group deficiency. *Lancet 2* 334

14a. JM Scott, DG Weir (1981) The methyl folate trap. A physiological response in man to prevent methyl group deficiency in kwashiorkor megaloblastic anaemias and in vitamin B12 deficiency and in pernicious anaemia. *Lancet 2* 337

15. W Debbyser, RL Gabriel (1975) Subacute combined degeneration of the spinal cord with cystoscopic. *N 25* 994

16. RC Schneider, et al (1954) The syndrome of acute central cervical cord injury. With special reference to the mechanism involved in hyperextension injuries of cervical spine. *J NS 11* 546

16a. WI Lees, et al (1980) Central cord syndrome as a delayed postoperative complication of decompressive laminectomy. *N/S 11* 491

16b. JS Bradley, et al (1980) The syndrome of acute central cervical spinal cord injury revisited. *Surg N 14* 251

16c. R Rose, et al (1984) Resonance of central cervical cord injury: mal operation. *N/S 15* 362

17. E Carter, PK Robinson (1956) Cervical myelopathy. A complication of cervical spondylosis. *Brain 79* 483

17a. J Hall (1977) The role of ischemia in pathogenesis of cervical spondylotic myelopathy: A view and new microangiographic evidence. *Spine 2* 109

17b. MR Gooding, et al (1975) Experimental cervical myelopathy. Effects of ischemia and compression of the central cervical spinal cord. *J NS 43* 9

18. FM Wallack, et al (1926) Hemiparesis in cervical spondylosis. *JAMA 236* 2518

18a. RJ Stark, et al (1982) Spinal metastases. A retrospective survey from a general hospital. *Brain 105* 189

19. RJ Stark, et al (1981) Hand wasting in spondylotic high cord compression: An electromyographic study. *ArN 9* 58

19b. DC Gore, et al (1984) "Numb, clumsy hands" and high cervical spondylosis. *Surg N 22* 205

19c. SM Alan (1985) Denervation in wasted hand muscles in a case of primary cerebellar atrophy without symptomatology. *JNNP 48* 84

19c. JD England, et al (1986) Spondylotic high cervical spinal cord compression presenting with hand complaints. *Surg N 25* 299

20. RR Young (1976) Weekly clinicopathological exercises. Case 26-1976. *NEJM 294* 1417

21. J Lapidus, JM Bebin (1958) Diagnostic value of subcarinomesenteric reflex. *JAMA 167* 971

22. MR Pearmain, CB Adams (1978) Tumours of the cauda equina. *JNNP 41* 24

22a. NR Kee, CB Jones (1985) Tumours of the cauda equina. The problem of differential diagnosis. *BMS 6/8* 159

23. SH Subramony, AJ Wilcourt (1982) Diabetic proximal neuropathy. Clinical and electromyographic studies. *J NS/Sci 55* 295

23a. MJ Brown, AK Asbury (1984) Diabetic neuropathy. *AnN 15* 2

23b. S Chakravarty (1982) Proximal nerve dysfunction in diabetic proximal amyotrophy. Histopathology and electron microscopy. *ArN 39* 403

CHAPTER 25:

1. RK Liba, *et al* (1978) Lacertus fibrosus compression of the median nerve. Case report. *J NS* 48 [illegible]

1a. L Gessini, et al (1983) Entrapment neuropathies of the median nerve at and above the elbow. *Surg N 19* 132

1b. JB Dorwart (1981) Carpal tunnel syndrome. *Sum A&R 14* 134

1c. WW Clarkson Jr (1981) Compressive and entrapment mononeuropathies of the upper extremity. *J Hand Surg 6* 759

2. RG Miller, FF Hummel (1980) The carpal tunnel syndrome: Treatment with simple decompression. *ArN 7* 567

2a. OM Hultgren-Balmvrods, et al (1983) Carpal tunnel syndrome in rheumatoid arthritis. *ArPMR 64* 161

3. KK Nakano (1978) The carpal tunnel syndrome. *MdN 1* 761

4. HG Stack (1962) Muscle function in the fingers. *BMS 648* 899

4a. ES Kilgore Jr, WP Graham III (1977) *The Hand. Surgical and Non-Surgical Management*, Lea and Febiger, Philadelphia, pp 26-28

5. PS Spencer, et al (1979) Does a defect of energy metabolism in the nerve fiber underlie axonal degeneration in polyneuropathies? *AnN 5* 561

5a. JB Cavanagh (1981) The proximal neuropathy with long cases. *Lancet 1* 1184

6. JC Rudwell, et al (1982) Manual motor performance in a deafferented man. *Brain 105* 213

6a. GM Goodwin, et al (1972) The contribution of muscle afferents to kinesthesia shown by vibration induced illusions of movement and by the effects of paralysing joint afferents. *Brain 95* 705

7. VB Brooks (1981) Cerebellar functions in motor control. Hum Neurol 2 231

8. H Kawabe (1979) Reflex paresis initiated by the secondary sensory fiber endings of muscle spindles: A proposal. ArPMR 58 1

9. RW Gilliatt, RG Williams (1962) Peripheral nerve conduction in diabetic neuropathy. JNNP 25 11

9a. JL Ochoa, HE Torebjörk (1980) Paresthesiae from ectopic impulse formation in human sensory nerves. Brain 103 835

9b. M Nordin, et al (1984) Ectopic sensory discharges and paresthesiae in patients with disorders of peripheral nerves, dorsal roots and dorsal columns. Pain 20 231

10. MJ Murphy, et al (1981) Subacute sensory neuropathy: clinical and electrophysiological observations. JNNP 44 896

11. MS Horwich, et al (1977) Sensory neuropathy: A remote effect of carcinoma. AnN 2 4

12. AB Fleet, EW Massey (1974) Neuralgia Paresthetica. N 24 1148

12a. EW Massey, AB Fleet (1975) Herpetiform neuralgia paresthetica. N 28 1312

12b. R Warenskjold (1954) Digitalgia paresthetica and genyalgia paresthetica. N 4 306

12c. IB Santo (1983) Suprascapular nerve entrapment. Surg N 29 693

12d. HA Herrera, et al (1984) Diagnosis and management of postherpetic neuralgia. ArS 119 339

12e. W Blahak, et al (1986) Cheiralgia paresthetica (entrapment of the radial sensory nerve). IBIS 174 196

13. EW Massey (1977) Meralgia paresthetica. An unusual case. JAMA 237 1125

13a. JG Eldridge, et al (1977) Meralgia paresthetica. Clin Orthop 122 255

13b. CA Wuthrich (1990) Meralgia paresthetica: causes and cures. Hosp Pract 25 99A

14. CT Kirkpatrick (1982) External digital nerves—a predictor of neuropathy in the leg?. BMJ 284 238

15. CJ. Krebs (1984) Guillain-Barre syndrome. N Clin 2 335

16. WF Bowers, TF. Feasby (1984) Conduction block and demyelination in Guillain-Barre polyneuropathy. Brain 107 1159

17. D Clark (1983) Jules Tinel and Tinel's sign. Clin Plastic Surg 10 567

18. TR Block (1986) Pharmacology of neuralgia. Clin Neuropharm 9 481

19. C Coen, et al (1991) Neurogenic benign fasciculations, pseudomyotonia, and pseudomyotony. A disease in search of a name. AnN 30 282

19a. H Isaacs (1986) Continuous muscle fibre activity in an Indian male with idiopathic evidence of terminal motor fibre diseasemality. JNNP 30 176

20. F Miller, H Kovacs (1983) Baclofen in the treatment of stiff man syndrome. AnN 2 5 1

20a. M Dana, AJ Spiro (1981) "Stiff man syndrome" in an adolescent. Peds 67 125

21. L Fyrone, et al (1978) Schwartz-Jampel syndrome: is two daughters of first cousins. JNNP 41 161

22. PL Carlen, et al (1978) Phantom limbs and related phenomena in recent traumatic amputations. N 29 211

22a. TS Jensen, et al (1983) Phantom limb, phantom pain and stump pain in amputees during the first 6 months following limb amputation. Pain 17 243

22b. TV Sherbuch, et al (1982) A five year follow-up study of phantom limb pain in post traumatic amputees. Scand J Rehab Med 14 203

23. W Noordenbos, PD Wall (1981) Implications of the failure of nerve reunion and graft to cure chronic pain produced by nerve lesions. JNNP 44 1068

23a. M De Santo, JW Duckworth (1982) Properties of primary afferent neurons from muscles which are spontaneously active after a period of their peripheral process. Exp N 77 261

23b. WH Calvin, et al (1987) Can neuralgia arise from minor demyelination? Spontaneous firing, reactivity sensitivity and aftershocks from conducting axons. Exp N 97 355

23c. C Yiannikas, BT Shahani (1984) Special review. Painful sequelae of injuries to peripheral nerves. AJPhysMed 63 53

23d. AJ Taleisnik (1981) Causalgia, reevaluation of a chronic pain syndrome. Pain 10 157

24. Imig (1685) Causalgia and reflex sympathetic dystrophy: in which way is the sympathetic nervous system involved?. TSNS 8 471

24a. HB Steinbrocker Jr (1985) A personal overview of causalgia and other reflex dystrophies. ArS 201 236

25. SY Gloobtzer, et al (1984) Pharmacotherapeutic in the treatment of causalgia. Report of 90 cases. J NS 60 1263

25a. TJ Lepping, AF Mullan (1985) Causalgic pain relieved by profound precaine stellate sympathetic blockade: Case report. J NS 60 1095

25b. M Dewar (1981) Nerve pathophysiology and mechanism of pain in causalgia. J Anesthesia NS 7 351

25c. PW Nathan (1982) Pain and the sympathetic nervous system. J Autonom NS 5 363

26. WF Collins, et al (1960) Relation of peripheral nerve fiber size and sensation in man. AJN 3 381

26a. H Lindblom, R Verrillo (1979) Sensory functions in chronic neuralgia. JNNP 42 435

27. HB Schumacher Jr (1985) A personal overview of causalgia and other reflex dystrophies. ArS 201 238

28. T Yamada, et al (1981) Tourniquet induced ischemia and somatosensory evoked potentials. N 31 1324

28a. RG Miller (1981) Acute vs chronic compressive neuropathy. M&N 7 (7)

28b. G Lundborg, et al (1982) Median nerve compression in the carpal tunnel—functional response to experimentally induced controlled pressure. J Hand Surg 7 252

28c. HM Sterne, et al (1984) Volkmann sensory testing in acute peripheral nerve compression. J Hand Surg 9A 104

29. J Ochoa, et al (1982) Abnormal spontaneous activity in single sensory nerve fibers in humans. M&N 5 574

29a. JL Ochoa, HE Torebjörk (1980) Paresthesiae from ectopic impulse formation in human sensory nerves. Brain 103 835

29b. M Nordin, et al (1984) Ectopic sensory discharges and paresthesiae in patients with disorders of peripheral nerves, dorsal roots and dorsal columns. Pain 20 231

30. AG Archer, et al (1983) The natural history of acute painful neuropathy in diabetes mellitus. JNNP 46 491

30a. MJ Brown, AK Asbury (1984) Diabetic neuropathy. AnN 15 2

31. J Ochoa, WG Mair (1969) The normal sural nerve in man. I. Ultrastructure and numbers of fibers and cells. Acta Neuropath 13 197

31a. TL Yaksh, DL. Hammond (1982) Review Article. Peripheral and central substrates involved in the normal transmission of nociceptive information. Pain 13 1

31b. J Van Hees, J Gybels (1981) C nociceptor activity in human nerve during painful and non painful skin stimulation. JNNP 44 600

31c. B Bishop (1946) Pain: its physiology and anatomy. Its management. Part I. Neuroanatomical substrate of pain. Phys Ther 60 13

31d. DR Price, R Dubner (1977) Mechanisms of first and second pain in the peripheral and central nervous system. J Invest Derm 69 167

32. PD Wall (1978) The gate control theory of pain mechanisms. A re-examination and re-statement. Brain 101 1

32a. J Van Hees, J Gybels (1981) C nociceptor activity in human nerve during painful and non painful skin stimulation. JNNP 44 600

32b. H Beecher (1978) Pain: perspectives and mechanisms. Anesth 23 935

33. WD Willis Jr (1985) The pain system. The neural basis of nociceptive transmission in the mammalian nervous system. Pain & HA 8

33a. KI Casey (1985) Neural mechanisms of pain: an overview. Acta Anaes Scand. Suppl 81, 15

34. WD Willis Jr (1985) The pain system. The neural basis of nociceptive transmission in the mammalian nervous system. Pain & HA 8

35. T Feed, et al (1984) Transcutaneous electrical nerve stimulator: Its role in the control of chronic pain. ArPMR 65 228

35a. J Schomer, et al (1985) Substance P, enkephalins, somatostatin, cholecystokinin, caerulein, and vasopressin in human spinal cord. N 35 88

35b. T Lundeberg, et al (1984) Pain alleviation by vibratory stimulation. Pain 20 25

36. CA Cousins, L Pellegrino (1982) A clinical view on pain physiology. Acta Chir Scand 148 185

37. JJ Bonica (1978) Neurophysiologic and pathologic aspects of acute and chronic pain. Arch *172* 720
39. RH Wilkins, IA Brody (1968) The thalamic syncrome. Arch *20* 559
39a. FK Conlon (1973) Evoked response studies of the thalamic pain syndrome. ANS *49* 280
39b. BS Nashold Jr (1977) Central pain. Its origin and treatment. Clin N/S *25* 513
39. AI Basbaum, HL Fields (1978) Endogenous pain control mechanisms: review and hypothesis. Ann N *4* 451
40. AI Basbaum, HL Fields (1984) Endogenous pain control systems: brainstem spinal pathways and endorphin circuitry. Ann Rev Neuro *7* 309
40a. D Bowsher (1978) Pain pathways and mechanisms. Anaesth *33* 935
40b. RP Bruce, et al (1982) Mental and behavioral effects of brain stem and hypothalamic stimulation in man. Hum Neuro *1* 273
40c. JM Lacy, et al (1976) New concepts of chronic pain and their implications. Hosp Pract *34* (4) 111
41. UA Carlsson, L Pellettieri (1982) A clinical view on pain physiology. Acta Clin Scand *548* 305
42. Anon (1994) How does acupuncture work? BMJ *283* 746
42a. JM Chung, et al (1984) Factors influencing peripheral nerve stimulation produced inhibition of primate spinothalamic tract cells. Pain *19* 237
42b. WE Bunney Jr, et al (1979) Basic and clinical studies of endorphins. AnRM *91* 230

CHAPTER 26:

1. RH Edwards, et al (1984) Role of mechanical damage in pathogenesis of proximal myopathy in man. Lancet *1* 548
1a. SP Ringel, HN Claman (1982) Acetylcholine-mediated muscle pain-hypertrophy. AnN *36* 413
1b. I Klein, et al (1981) Hypothyroidism presenting as muscle cramps and pseudohypertrophy: Kocher-Debre syndrome. AJM *29* 881
2. KL Tyler, JC McHenry Jr (1983) Fragments of neurologic history: pseudohypertrophic muscular dystrophy and Gower's sign. N *33* 89
3. RB Layzer, LP Rowland (1971) Cramps. NEJM *285* 31
3a. RF Lazaro, et al (1981) Familial cramps and muscle pain. Arch *38* 27
4. C Cohen (1975) The protein switch of muscle contraction. Sci Am *233* 36 (Nov)
5. BV Lee, et al (1984) Management of compartmental syndrome. Diagnostic and surgical considerations. Arch *140* 585
5a. CH Rorabeck (1984) The treatment of compartment syndromes of the leg. JBJS *66B* 93
6. LP Rowland (1984) Myasthenia, 1954. Can J Neu *11* 1
61. JF Lescher (1983) Rhabdomyolysis and myoglobinuria. Ann Rev Med *34* 435
50. PA Gabow, et al (1982) The spectrum of rhabdomyolysis. Medicine *61* 141
7. ME Kidd, et al (1982) Dantrolene in human malignant hyperthermia. A multicenter study. Anesth *56* 254
7a. DJ Nelson, DH Hewelker (1982) The malignant hyperthermia syndrome. NEJM *306* 416
7b. J Wilkes, M Nakayama (1984) Commentaries in malignant hyperthermia. Can N *3* 225
8. RL Barchi (1978) Muscle membrane chloride conductance and the myotonic syndromes. Contemp Clin Neuro (EEG Suppl. No. 34) 559
8a. F Lehmann-Horn, et al (1981) Membrane defects in paramyotonia congenita with and without myotonia in a new in-vitro assay. M&N *4* 396
8b. HR Fuhner, RL Barchi (1981) 22:25 Sarcolemmal myotonia: an electrophysiological study. AnN *10* 251
8c. TL Munsat, RT Schefft (1979) Myotonia. Clin N/pharm *4* 63
9. R Mizumura, et al (1981) Miswinking phenomenon: An experimental study in rabbits. N *23* 50
10. TD Bird, et al (1983) Cognitive and personality function in myotonic muscular dystrophy. JNNP *46* 971
11. C Ruitta, F Kadi (1982) Cardiac findings in myotonic dystrophy. ArCrdh *14* 647
12. CA Stuart, et al (1983) Insulin resistance in patients with myotonic dystrophy. N *33* 679
13. JK Perloff, et al (1984) Cardiac involvement in myotonic muscular dystrophy (Steinert's disease): A prospective study of 25 patients. AJC *54* 1019
14. HM Swink, et al (1981) Pharyngoesophageal motor function in patients with myotonic dystrophy. AnN *10* 454
15. RS Young, et al (1981) Dysmaturity in infants of mothers with myotonic dystrophy. AnN *28* 726
15a. SF Sun, et al (1987) Myotonic dystrophy: obstetric and neonatal complications. SMJ *78* 823
16. A Hoare, et al (1981) Clinical study of paramyotonia congenita with and without myotonia in a warm environment. M&N *4* 388
16a. VA Nielsen, et al (1983) Electromyographic dislocation between paramyotonia congenita and myotonia congenita. Effect of cold. N *22* 927
16b. F Lehmann-Horn, et al (1983) Two cases of adynamia episodica hereditaria: in vitro investigation of muscle cell membrane and contraction parameters. M&N *6* 113
16c. K Ricker (1986) Muscle stiffness not electrical activity in paramyotonia congenita. M&N *9* 299
17. FQ Vroom, et al (1975) Acetazolamide treatment of hypokalemic periodic paralysis. Periodic mechanism of action. AnN *32* 255
17a. RC Griggs (1981) Periodic paralysis. Sem N *1* 285
18. RB Layzer (1982) Periodic paralysis and the sodium-potassium pump. AnN *11* 387
18a. JE Riggs, et al (1981) Acute effects of acetazolamide in hyperkalemic periodic paralysis. N *31* 525
18b. K Ricker, et al (1980) Adynamia episodica and paralysis periodica paramyotonica. N *30* 682
19. AH Rapper, RT Shimmi (1984) Pain in Guillain Barre syndrome. AnN *42* 51
19a. PG Nevsimal, R Langstad-Haven (1985) Pain in motor neuron disease. JNNP *48* 836
20. DA Ingram, et al (1984) Cancer-associated myasthenic (Eaton-Lambert) syndrome: distribution of thymectomy and effect of treatment. JNNP *47* 806
21. Y Dau, et al (1984) Antibody to acetylcholine receptor in myasthenia gravis: production by lymphocytes from thymus or thymoma. N *34* 182
21a. AG Engel (1984) Myasthenia gravis and myasthenic syndromes. AnN *16* 519
22. DG Cogan (1965) Myasthenia gravis. A review of the disease and a description of the lid switch as a characteristic sign. ArOph *74* 217
23. RH Osher, RC Griggs (1979) Orbicularis fatigue. The 'pick' sign of myasthenia gravis. ArOph *97* 67
24. JE Publin, et al (1976) Transient ocular paresis in myasthenia gravis. JNNP *39* 44
25. PB Gordon, et al (1981) Increased pores in myasthenia gravis. AnN *28* 33
26. EC Engel (1987) Pharmacologic enhancement of neuromuscular transmission in myasthenia gravis. Clin N/pharm *5* 277

CHAPTER 27:

1. MR Trimble (1982) Perinatal diseases. BMJ *285* 1768
2. GF Murphy (1982) The clinical management of hysteria. JAMA *247* 2539
3. P Chodoff (1982) Hysteria and women. AJPsy *139* 545
4. LM Bjerdeson, et al (1983) A neurosurgical Munchausen tale. JNNP *46* 437
4a. PG Jones, et al (1981) Probing the depths of Munchausen's syndrome. Detailed analysis of a case. AnIM *95* 120
5. G Adler (1981) The physician and the hypochondriacal patient. NEJM *304* 1943
6. A Lazare (1981) Conversion symptoms. NEJM *305* 745 6a. TE Quill (1985) Somatization disorder. One of medicine's final spoils. JAMA *254* 3075
7. DW Klass (1975) Electroencephalographic manifestations of complex partial seizures. AnN *33* 113
7a. WH Theodore, et al (1983) Complex partial seizures. Clinical characteristics and differential diagnosis. N *33* 1315
8. DW King, et al (1987) Pseudoseizures: Diagnostic evaluation. N *32* 18

8a. JS Lettich, et al (1982) Pseudoseizures: methods and video analysis to aid diagnosis. AmJM 72:458.
8b. BT Desai, et al (1982) Psychogenic seizures. A study of 32 attacks in six patients, with simultaneous monitoring. AnN 10:780.
9. WH Theodore, et al (1983) Complex partial seizures: Clinical characteristics and differential diagnosis. N 33:1115.
10a. RD Lesser, et al (1985) Postictal changes after seizures classified by EEG monitoring. N 35:31.
10b. PB Pritchard III, et al (1985) Serum prolactin and cortisol levels in evaluation of pseudoepileptic seizures. AnN 18:636.
11. RJ Cohen, C Suter (1982) Hysterical seizures: suggestion as a provocative EEG test. AnN 11:291.
12. TA Gulick, et al (1982) Pseudoseizures, total phenectomia. N 32:24.
13. AV Delgado-Escueta, et al (1982) Complex partial seizures on closed-circuit television and EEG: a study of 691 attacks in 79 patients. AnN 11:292.
13a. JR Gates, et al (1985) Ictal characteristics of pseudoseizures. AnN 42:1038.
14. BT Desai, et al. (1982) Psychogenic seizures. A study of 42 attacks in six patients, with intensive monitoring. AnN 59:208.
14a. GL Holmes (1984) Partial complex seizures in children, an analysis of 69 seizures in 24 patients using EEG, EM telemetry and videotape recording. LBGUNP 57:13.
15. R Ochs, et al (1984) Does handwriting during a seizure have lateralizing or localizing significance?, N 34:884.
15a. S Nielsbrock, JL Welch (1982) Psychometric assessment in absence status, AnN 39:536.
17. RJ Cohen, C Suter (1982) Hysterical seizures: suggestion as a provocative EEG test. AnN 11:39.
18. TL Riley, et al. (1981) The hospital experience and seizure control, N 31:912.
19. ME Rosenberg (1982) The eyes in hysterical states of unconsciousness, J Clin Neuph 2:239.
20. JR Keane (1982) Neuro-ophthalmic signs and symptoms of hysteria, N 32:757.
21. JR Keane (1982) Neuro-ophthalmic signs and symptoms of hysteria, N 32:757.
22. CC Tijssens, et al (1983) Spasm of the near reflex: functional or organic disorder?, N neph 3:59.
22a. VS Hoffenberg, SH Hemenway (1980) Spasm of the near reflex, AnOph 12:1059.
22b. JR Keane (1982) Neuro-ophthalmic signs and symptoms of hysteria, N 32:757.
23. AJ Arnett, et al (1961) The Hoover sign. An objective sign of pain and/or weakness in the back or lower extremities, AnN 5:623.
24. G Waddell, et al. (1980) Nonorganic physical signs in low-back pain, Spine 5:117.
25. AJ Barsky III (1979) Patients who amplify bodily sensations, AnIM 91:61.
26. RE Records (1980) Monocular diplopia, Surv Oph 24:300.
26a. KA Stanciel, TJ Tindall (1972) Monocular diplopia in flying personnel, AJOph 89:739.
26b. LW Hines, et al (1981) Monocular polyopia, AnN 40:756.
27. AH Ropper (1983) Illusion of tilting of the visual environment. Report of five cases. J Clin Neuph 3:1475.

CHAPTER 28:

1. RT Manning (1982) The social response test, AnVM 140:1162.
1a. A Smith (1967) The serial reverse interaction test, AnN 2:778.
2. CW Vaughan (1982) Current concepts in otolaryngology: diagnosis and treatment of organic voice disorders, NEJM 307:863.
2a. M Dedman, et al (1961) Abnormal parasympathetic vagal function in patients with spasmodic dysphonia, AnIM 109:491.
3. MH Bender, et al (1982) Agnosognosia. A disorder of directional interoceptive kinesthesia or a disconnectment in extracorporeal space, J NNS 58:55.
4. PD Wall, W Noordenbos (1977) Sensory functions which remain in man after complete transection of dorsal columns, Brain 100:641.
4a. WF Collins Jr, et al (1960) Interruption of peripheral nerve fibers and sensation in man, AnS 5:391.
5. AS Schwartz, et al (1979) The asymmetric lateralization of tactile extinction in patients with unilateral cerebral dysfunction, Brain 202:669.

CHAPTER 29:

1. WL Hurwitz (1982) Autonomic insufficiency, AnIM 142:339.
1a. S Hilz, et al. (1981) The clinical spectrum of autonomic dysfunction, AnIM 20:1091.

CHAPTER 31:

1. RN Detorg, SP Hicks (1968) Vascular malformation of the hypothalamus. Report of a case with long duration and fluctuating course, N 30:905.
1a. HH Brin, et al (1981) Occult arteriovenous malformations of the brainstem simulating multiple sclerosis, N 31:901.
2. RO Hurt, DO Sherman (1982) The diagnosis of multiple sclerosis, JAMA 247:408.
3. A Zeal, AL Rhoton Jr (1978) Microsurgical anatomy of the proximal cerebral arteries, J NNS 48:534.
4. DL McAuley, RW Ross Russell (1979) Correlation of CAT scan and visual field defects in vascular lesions of the posterior visual pathways, JNNP 42:258.
4a. LR Caplan (1980) "Top of the basilar" syndrome, N 30:72.
4b. LA Hayman, et al (1981) Correlation of CT cerebral vascular territories with function. II. Posterior cerebral artery, AJNeurol 2:219.
4c. JD Trobe, et al (1975) Isolated tuberculous hemiparesis. A review of 106 cases, ArOph 89:377.
5. GS Brindley, L Jaweta (1975) Observations on cortical blindness and on vascular lesions that cause loss of recent memory, JNNP 38:459.
5a. LR Caplan (1980) "Top of the basilar" syndrome, N 30:72.
6. GS Brindley, L Jaweta (1975) Observations on cortical blindness and on vascular lesions that cause loss of recent memory, JNNP 38:459.
7. VH Conway, et al (1953) Isolated bilateral occipital pinch, Can J Opht 18:52.
7a. J Bilbe, et al (1984) Occlusion of the middle cerebral artery. Clinical and radiological correlation, AnN 42:644.
8. JC Brust, et al (1979) The pathology of drug addiction 4. case report, N 29:746.
9. G Van Horn, A Howe (1982) Global aphasia without hemiparesis: A sign of cortical encephalopathy, N 32:403.

CHAPTER 32:

1. RS Paine, et al. (1964) Evolution of postural reflexes in normal infants and in the presence of chronic brain syndrome, N 14:1036.
2. SG Babkoff, GI Benda (1976) Growth pupils for the clinical assessment of infants of varying gestational age, J Ped 89:814.

CHAPTER 33:

1. A Kales, et al (1982) Narcolepsy-cataplexy. I. Clinical and diagnostic characteristics, AnN 39:164.
1a. HI Kupfer, CF Reynolds III (1982) Sleep disorders, Hosp Prac 20 (2):10.
2. GE Goode, HM Styer (1993) Daytime polysomnogram diagnosis of sleep disorders, JNNP 56:159.
3. C Guilleminault, WC Dement (1977) 315 cases of excessive daytime sleepiness. Diagnosis and tentative classification, J NNSci 31:13.
3a. VP Zarcone Jr (1977) Diagnosis and treatment of excessive daytime sleepiness, Clin Neurpsych 2:87.
3b. NS Chernick (1986) Breathing disorders during sleep, Hosp Prac 21:81.
4. TE Rosenthal, et al. (1984) Videoanalytic examination of the mechanism of sedation in obstructive sleep apnea, OtoHNS 92:335.
4a. WC Orr, WB Stahon (1995) Diagnosis and management of obstructive sleep apnea, AnMed 11:583, 620.
5. S Chokroverty, JT Sharp (1981) Primary sleep apnea syndrome, JNNP 44:970.
5a. MJ Thorn, et al (1983) Breathing abnormalities during sleep, AnIM 143:1223.

6. PB Sermonte, et al (1987) Snoring, and sleep obstructive sleep apnea, can be cured by oropharyngeal surgery, *AnOto 109* 503
6a. GP Kotzoronis, et al (1985) Further evaluation of uvulopalatopharyngoplasty in the treatment of obstructive sleep apnea syndrome, *OtoHNS 93* 244
7. JE Loyd (1982) Saturday confusion: Sleep apnea syndrome, *SMJ 76* 1417
7a. KP Strohl, et al (1981) Progesterone administration and paradoxical sleep apnea, *JAMA 245* 1230
8. TA Radley (1983) Differential diagnosis of episodic symptoms, *Epilepsia 24* (Suppl 1) 85
8a. CA Dreyer, et al (1975) Fever nocturnus of non-epileptic nature in epileptic children, *PSYCNP 15* 603
9. TF Anders, P Weinstein (1972) Sleep and its disorders in infants and children: A review, *Peds 50* 312

CHAPTER 34:

1. AH Ropper, LT Hedley White (1982) Parkinsonian syndrome with other neurologic manifestations, *NEJM 308* 1406
2. DB Coleman, et al (1971) Stroke in Lafora disease, *AnN 21* 396
3. ID Goldberg, et al (1982) Nervous system toxic effects of cancer therapy, *JAMA 247* 1637
3a. RS Kaplan, PH Wiernik (1982) Neurotoxicity of antineoplastic drugs, *Sem Oncol 9* 188
4. D Bassett, et al (1983) Reversible, late onset dysfunction-induced neuropathy and encephalopathy, *Ann 77* 906
5. AP Oliver, et al (1982) Neuroleptic-induced seizures. An in vitro technique for assessing relative risk, *AnGPsy 39* 206
5a. FM Bell, C Schlutes (1980) Bothersome side effects of psychotropic drugs: Practical recommendations, *JAMA 244* 1460
6. Anon (1964) Neuroleptic malignant syndrome, *Lancet 1* 545 fn, 560 illus, et al (1966) Successful treatment of neuroleptic malignant syndrome with sodium nitroprusside, *AnIM 109* 56
6b. MP Rungeman (1986) Review article: Neuroleptic malignant syndrome, *SMJ 79* 331
7. WL Nyhan, et al (1985) Lead intoxication in children, *WIM 142* 357
7a. MR Cullen, et al (1983) Adult inorganic lead intoxication: Presentation of 31 new cases and review of recent advances in the literature, *Medicine 62* 221
8. WL Schindmeister, DR Wain (1976) Arsenic poisoning, *SMJ 70* 198
8a. H Fist, et al (1982) Sources of error in the diagnosis of flaillaiform syndrome, *MRA 5* 111
8b. MJ Maglio, et al (1984) Subacute arsenic neuropathy: clinical and electrophysiological observations, *JNNP 48* 896
9. Anon (1975) Poisoning with alkylmercury compounds, *BMJ 1* 539
10. AH Greenwood (1980) Heavy metals and the nervous system,
11. BR Heinz (1985) Standardized treatment of pure methanol poisoning with ethanol and hemodialysis, *WJM 142* 357
11a. JA Sturm, et al (1987) Methanol optic neuropathy. A histopathological study, *N 11* (1)
12. H Sakoda, et al (1981) Experimental cold injury to peripheral nerve, *Brain 104* 779
13. CF Bever Jr, et al (1982) Penicillamine-induced myasthenia gravis: Effects of penicillamine on acetylcholine receptor, *N 32* 1007
13a. SR Snively, GR Hodges (1984) The neurotoxicity of antibacterial agents, *AnIM 100* 91
14. WM Houlihan, KL Bo (1982) Arachnoid response to contrast media: a comparison of iophendylate and metrizamide in experimental animals, *Radiology 142* 699
15. DK Tasker, et al (1982) Neuromuscular and related changes in malnutrition. A review, *J NtS 4* 55 207
15a. L Peters (1982) Dendritic changes in senile malnourished optic ganglion cells, *ArOph 100* 577
16. AM Nudel, PC Bunjor (1976) Wernicke encephalopathy following profound intravenous therapy, *JAMA 235* 2903
17. JT Lott, et al (1978) Vitamin B6-dependent seizures: Pathology and chemical findings in brain, *N* 28 47
17a. F Bonifacio, J Aicardi (1985) Atypical presentations of pyridoxine dependent seizures. A treatable cause of intractable epilepsy in infants, *AnN 17* 117
17b. N Ishii, Y Nishihara (1982) Peripheral encephalopathy among transcontinental patients: its relation to nutritional changes, *JNNP 48* 624
18. D Schaumburg, et al Sensory neuropathy from pyridoxine abuse, A new megavitamin syndrome, *NEJM 309* 445
18a. GI Paty, DF Bradeen (1985) Sensory neuropathy with low dose pyridoxine, *N 35* 1466
19. MJ Brust, et al (1975) Neurologic disorders responsive to folic acid therapy, *JAMA 233* 245
20. RJ Sokol, et al (1984) Vitamin E deficiency with normal serum vitamin E concentrations in children with chronic cholestasis, *NEJM 310* 1506
20a. B Wolfe, et al (1984) Neurologic disorder of vitamin E deficiency in acquired intestinal malabsorption, *N 34* 1681
20b. L Guttman, et al (1985) Vitamin E-deficient spinocerebellar syndrome due to intestinal lymphangiectasia, *N 35* 354
21. JR Duval, JP Dorse (1991) Tick paralysis with persistent weakness and electromyographic abnormalities, *AnN 38* 90
21a. TR Swift, OI Ignacio (1975) Tick paralysis: Electrophysiologic studies, *N 25* 1120
22. HV Russell, DM Pignatelli (1981) Treatment of delayed infarction necrosis of the brain: A clinical overview, *J NtS 60* 589
22a. S Sallom, et al (1985) Radiation necrosis of the brain: Time of onset and incidence related to total dose and fractionation of radiation, *N Intl 27* 61
22b. HS Reinhold, et al (1984) The latent period in clinical radiation myelopathy (abstract), In: *J Rad Oncol Biol Phy 10* 2385
23. WE Bell (1981) Treatment of bacterial infections of the central nervous system, *AnN 9* 313
23a. GD Overturf (1986) Pyogenic bacteria infections of the CNS, *Neurol Clin 4* 89
24. DL Morris, et al (1986) Hematologic characteristics of patients with hyperferremia due to occult infection and other causes, *AnIM 102* 35
24a. HR Freund, et al (1984) Regional amino acid and transmembrane derangements during abdominal sepsis and septic encephalopathy in the rat. The effect of amino acid infusions, *ArS 171* 209
25. H Morgan, et al (1973) Experience with 58 consecutive cases of brain abscess, *J NtS 38* 608
26. RH Wilkins (1964) Neurosurgical Classic—XX, *J NtS 22* 586
27. DK Henderson, et al (1956) Infectious disease emergencies. The cerebral syndromes, *WJM 129* 104
28. JM Bradley, et al (1981) Clinical features of type A and B food borne botulism, *AnIM 95* 442
29. DK Henderson, et al (1978) Infectious disease emergencies. The abdominal syndromes, *WJM 129* 101
29a. S Kapogeorgis, PB Wessels (1984) Descending paralysis resulting from occult wound botulism, *AnIM 16* 199
30. S Pollock, et al (1981) Whipple's disease confined to the nervous system, *JNNP 44* 1104
30a. JJ Halperin, et al (1982) Whipple disease of the nervous system, *N 32* 612
31. CH Binford, et al (1982) Leprosy, *JAMA 247* 2253
32. WA Clyde, Jr (1990) Neurologic syndromes and mycoplasma infections (editorial), *AnN 27* 65
32a. AS Baron, et al (1981) Neurologic disease associated with mycoplasma pneumoniae pneumonitis. Demonstration of viable mycoplasma pneumoniae in cerebrospinal fluid and blood by polymerase and immunofluorescent tissue culture techniques, *AnIM 94* 43
33. JG Frazee, et al (1980) Bacterial intracranial aneurysms, *J NtS 53* 632
33a. GL Schmidt, et al (1978) Bacterial intracranial aneurysm, *J NtS 48* 369
33b. RB Mennecke, RB Kaup (1984) Evolution and resolution of intracranial bacterial (mycotic) aneurysms, *N 3* 35-43
34. BK Marshall (1976) The dilemma of partially treated bacterial meningitis, *Scand J Infect Dis 8* 135
35. JS Salahi, et al (1981) Fungal and yeast infections of the central nervous system. A clinical review, *Medicine 60* 168

36. DL Palmer, et al (1974) Diagnostic and therapeutic considerations in nocardia asteroides infection. Medicine 53 391

36a. TJ Walsh, et al (1985) Aspergillosis of the central nervous system: clinicopathological analysis of 17 patients. AnN 18 574

37. RI Lehrer, et al (1980) Mucormycosis. AnIM 93 93

37a. R Rangel Guerra, et al (1985) Mucormycosis. Report of 11 cases. AcN 42 578

38. AS Beyer, Jr. et al (1936) Candida meningitis. Report of seven cases and review of the English literature. Medicine 15 477

38a. F Bourn, et al (1981) Coccidioidal meningitis. An analysis of thirty-two cases and review of the literature. Medicine 60 139

38b. WE Bell (1981) Treatment of fungal infections of the central nervous system. AnN 9 417

38c. T Uda, et al (1985) Cryptococcal meningitis. JNNP 48 855

39. MD Holmes, et al (1961) Clinical features of meningovascular syphilis. N 34 553

39a. MW Adler (1984) Syphilis: clinical features. BMJ 289 488 40. M Sharatha, et al (1985) Diagnosing early Lyme disease. AIM 28 235

40a. AR Pachner, AC Steere (1985) The triad of neurologic manifestations of Lyme disease: Meningitis, cranial neuritis, and radiculoneuritis. N 35 47

41. RH Lepierre (1977) Rocky Mountain spotted fever (editorial). NEJM 297 864

41a. EW Marvin, et al (1985) Neurologic complications of rocky Mountain Spotted Fever. BMJ 78 1248

42. LW Wenrick, TJ Farragana (1983) Complications of herpes zoster ophthalmicus. ArOph 101 42

43. TE Nash, FA Neva (1984) Recent advances in the diagnosis and treatment of cerebral cysticercosis. NEJM 311 1492

43a. J Sotelo, et al (1985) Neurocysticercosis. a new classification based on active and inactive forms. A study of 753 cases. AnIM 143 442

44. JJ Townsend, et al (1975) Ascaloid encephalomyelitis. A neglected cause of treatable nervous system disease. AcN 32 335

45. KS Pant, et al (1982) Arnold-Chiari malformation. Review of 71 cases. J N/S 98 183

46. KS Pant, et al (1983) Arnold-Chiari malformation. Review of 31 cases. J N/S 58 183

46a. WJ Levy, et al (1983) Chiari malformation presenting in adults: a surgical experience in 127 cases. N/S 12 377

47. GD Shah (1971) Neonatal assessment of the child with myelomeningocele. Ai Do Child 46 539

48. SB Dunatov, et al (1988) Craniovertebral anomalies. Clin N/S 27 430

49. R Shibasaki, K Nagai (1984) Motor movement: application of movement related cortical potentials. AnN 15 559

49a. R Naso (1983) Mirror movements asymmetries in congenital hemiparesis: The inhibition hypothesis revisited. N 33 1009

50. J Garcia-Uria, et al (1981) Syringomyelia: long-term results after posterior fossa decompression. J N/S 54 380

50a. V Logue, MR Edwards (1981) Syringomyelia and its surgical treatment—an analysis of 75 patients. JNNP 44 273

51. GD Perkin, et al (1978) Problems in the diagnosis of progressive supranuclear palsy (Steele–Richardson–Olszewski syndrome). Can J N/Sci 5 167

51a. AH Rajput, ET Hedley-Whyte (1980) Parkinsonism associated with other neurologic manifestations. NEJM 303 1490

52. GT Stricland, ML Lee (1975) Wilson's disease. Clinical and laboratory manifestations in 80 patients. Medicine 54 113

52a. GE Cartwright (1975) Diagnosis of treatable Wilson's disease. NEJM 290 1342

52b. GR Buchanan (1975) Acute hemolytic anemia as a presenting manifestation of Wilson's disease. J Ped 86 765

53. CD Marsden, MJ Harrison (1974) Idiopathic torsion dystonia (dystonia musculorum deformans). A review of forty-two patients. Brain 97 793

54. LE Nee, et al (1980) Gilles de la Tourette syndrome: clinical and family study of 50 cases. AnN 7 41

54a. AJ Lees, et al (1984) A clinical study of Gilles de la Tourette syndrome in the United Kingdom. JNNP 47 1

55. JE Meikes, LM Corbo (1977) Adrenoleukodystrophy. Accumulation of cholesterol esters with very long chain fatty acids. N 27 928

56. DM Bridges, S Kramer (1977) The neurological manifestations of porphyria: A review. Medicine 56 41

56a. DP Tschudy, et al (1975) Acute intermittent porphyria: clinical and selected research aspects. AnIM 83 851

57. RD Elchhorn (1982) Porphyria(s): porphyrins, porphyrins, and the porphyrias. Mayo 57 454

57a. EP Jusch, et al (1977) Effects of ketamin in porphyric neuropathy. N 27 1013

58. PM Van Erven, et al (1985) Subacute necrotizing encephalomyelopathy (Leigh syndrome) associated with disturbed oxidation of pyruvate, malate and 2-oxoglutarate in muscle and liver. ANS 72 36

58a. H Kalimo, et al (1979) Familial subacute necrotizing encephalomyelopathy of the adult form (adult Leigh syndrome). AnN 6 200

59. S Refsum (1981) Heredopathia atactica polyneuritiformis. Phytanic-acid storage disease. Refsum's disease, a biochemically well-defined disease with a specific dietary treatment. AnN 29 505

59a. TD Gibrenal, et al (1976) Heredopathia atactica polyneuritiformis (Refsum's disease) treated by diet and plasma-exchange. Lancet 1 525

60. VM Riccardi (1981) Von Recklinghausen's neurofibromatosis. NEJM 305 1617

60a. WR Kimmy, et al (1980) Central neurofibromatosis with bilateral acoustic neuromas: Generic, clinical and biochemical distinction from peripheral neurofibromatosis. N 30 851

61. HH Dotlicki, et al (1985) Successful treatment of a group of spinal cord arteriovenous malformations by interruption of dural fistula. J N/S 39 1019

61a. L Symon, et al (1984) Dural arteriovenous malformations of the spine. Clinical features and surgical

62. KL Mattingly, K Eriksen (1982) Fibromuscular dysplasia and the brain. Observations on angiographic, clinical and genetic characteristics. Stroke 13 46

62a. KL Mettinger (1982) Fibromuscular dysplasia and the brain. II. Current concepts of the disease. Stroke 13 53

62b. CA Wood, et al (1986) Fibromuscular dysplasia of the carotid arteries. AJS 151 648

63. HJ Hoffman, et al (1982) Investigation and management of supracellar arachnoid cysts. J N/S 57 597

63a. FG Van der Meche, R Braakman (1982) Arachnoid cysts in the middle cranial fossa: cause and treatment of progressive and non progressive symptoms. JNNP 45 1102

64. F Villanjo, et al (1982) Anterior sacral meningocele. Review of the literature. Surg N 14 93

64a. P Salvo, et al (1985) Anterior sacral meningocele. Current diagnosis. Surg N 27 9

65. HR Hirn, et al (1977) The manifestations and complications of intraspinal congenital dermal sinuses and dermoid cysts. N-pacd 5 231

65a. XR Powell, et al (1975) A prospective search for congenital dermal abnormalities of the craniospinal axis. J Ped 87 744

66. M Minowski, et al (1983) Surgical treatment of spinal lipomas in infancy and childhood. Child's Brain 10 317

66a. JW Walsh, WR Markesbery (1980) Histological lesions of congenital lipomas of the lower spinal canal. J N/S 52 564

67. S Poser, et al (1978) Clinical features of the spinal form of multiple sclerosis. ANS 37 151

68. SL Hauser, et al (1983) Intensive immunosuppression in multiple sclerosis. A randomized, three-arm study of high dose intravenous cyclophosphamide, plasma exchange, and ACTH. NEJM 308 173

68a. RA Hughes (1984) Immunological treatment of multiple sclerosis. JN 230 73

68b. L Durelli, et al (1986) High dose intravenous methylprednisolone in the treatment of multiple sclerosis: Clinical-immunologic correlations. N 36 238

69. RC Williams Jr (1982) Host factors in rheumatic fever and heart disease. Hosp Pract 17(8) 123

70. LP Weaver, JO Fleming (1984) Review article: Viral infections of the nervous system. J Nerv Ment Dis 172 202

71. HJ Metz (1983) Pathologic findings of neurosarcoidosis and clinicopathologic correlation. Can J Neurol Sci 10 50

72. EO Stern, et al (1985) Sarcoidosis and its neurological manifestations. Arch Int Med 145 989

72. S Mohammed, et al (1980) A clinical comparative study of multiple sclerosis and neuro Behcet's syndrome. JNNP 43 210

72a. T Shimizu, et al (1973) Behcet's disease (Behcet's syndrome). Sem A&R 3 223

73. JR Cohen, et al (1981) Vogt-Koyanagi-Harada syndrome with focal neurologic signs. AJOph 91 332

73a. DA Snyder, HH Tessler (1981) Vogt-Koyanagi-Harada syndrome. AJOph 91 89

74. JM Bicknell, JV Holland (1978) Neurologic manifestations of Cogan syndrome. N 29 276

74a. J McDonald, et al (1989) Cogan's syndrome: audiovestibular involvement and prognosis in 14 patients. Laryngo 95 650

74b. RS Vollertsen, et al (1986) Cogan's syndrome: 38 cases and a review of the literature. Mayo 61 344

75. LB Klein (1982) The Tolosa Hunt syndrome. Surv Ophth 27 79 75. EL Alexander, et al (1986) Primary Sjogren's syndrome with central nervous system disease mimicking multiple sclerosis. AnIM 104 223

77. WB Cooke, et al (1984) Computed tomography of the craniocervical junction in rheumatoid arthritis. RCNI 7 31

77a. T Komiya, et al (1985) Radiologic review: The rheumatoid spine. Sem A&R 14 187

77b. IM stevens, et al (1986) The spinal cord in rheumatoid arthritis with clinical myelopathy: a computed myelographic study. JNNP 49 140

78. SW Peters (1941) Pathology of Guillain Barre syndrome. AnN 9 (suppl) 6

79. P Lichtenfeld (1971) Autonomic dysfunction in the Guillain Barre syndrome. AJM 50 772

79a. T Ankenman, A Siden (1982) A clinical study of Guillain Barre syndrome. ANS 66 316

80. PJ Dyck, et al (1982) Prednisone improves chronic inflammatory demyelinating polyradiculoneuropathy more than no treatment. AnN 11 136

81. AH Ropper (1983) The CNS in Guillain Barre syndrome: infiltrate, AnN 40 390

81a. AH Ropper, B Shahani (1983) Proposed mechanism of ataxia in Fisher's syndrome. AnN 40 537

82. DA Fennell, FA Modrigal Jr (1982) Trigeminal neuropathy as presenting systemic sclerosis. AIM 20 57

83. J Kersey, et al (1980) Detection of thymoma in myasthenia gravis. N 30 253

83a. C Harmoun Jr, et al (1985) Myasthenia gravis: current concepts. WJM 142 1797

84. R DeVere, WG Bradley (1975) Polymyositis: its presentation, morbidity and mortality. Brain 98 637

84a. A Bohan, et al (1977) A computer assisted analysis of 153 patients with polymyositis and dermatomyositis. Medicine 56 255

84b. MC Hochberg, et al (1986) Adult onset polymyositis/dermatomyositis: an analysis of clinical and laboratory features and survival in 76 patients with a review of the literature. Sem A&R 15 168

85. ET Gansa, et al (1979) Isolation of influenza virus from muscle in myositis/rhinitis polymyositis. N 29 1123

85a. A Bohan, JE Peter (1975) Polymyositis and dermatomyositis. NEJM 292 344, 403

86. WT Agush, et al (1985) Polymyalgia rheumatica. Duration of therapy and long-term outcome. AJM 79 309

86a. SA Lauer, et al (1985) Polymyalgia rheumatica. AnIM 103 925

87. SE Ellis, MA Varley (1979) Central nervous system involvement in systemic lupus erythematosus: a review of neuropathologic findings in 57 cases, 1955-1977. Sem A&R 8 212

87a. GW Bruyn, G Padberg (1984) Chorea and systemic lupus erythematosus. A review. Eur Neurol 23 278

87b. DC Adelman, et al (1988) The neuropsychiatric manifestations of systemic lupus erythematosus: an overview. Sem A&R 15 185

88. FM Vincent, RN Van Hoewyk (1980) Trigeminal sensory neuropathy and bilateral carpal tunnel syndrome: the initial manifestation of mixed connective tissue disease. JNNP 43 458

88a. B Ashworth, GB Tait (1971) Trigeminal neuropathy in connective tissue disease. N 21 589

89. RE Kelley, et al (1984) Cerebral ischemia in the presence of lupus anticoagulant. AnN 45 521

89a. H Fei, et al (1984) Acute subdural hematomas with lupus anticoagulant (procoagulant inhibitor). N 34 519

90. ML Monticin, et al (1984) Giant cell arteritis of the posterior cerebral circulation presenting with ataxia and ophthalmoplegia. AnOph 600 602

90a. JL Kelmer (1982) Giant cell arteritis. Signs and symptoms. Opth Surg 89 1101

90b. E Gilbert, et al (1981) Progress in giant cell arteritis. BMJ 282 260

91. RI Aberhamer (1980) Takayasu's arteritis and its therapy. AnIM 103 121

91a. S Hall, et al (1985) Takayasu's arteritis. A study of 32 North American patients. Medicine 64 89

92. HW Thompson, LJ McCarthy (1983) Thrombotic thrombocytopenic purpura. Potential benefit of splenectomy after plasma exchange. AnIM 143 2117

93. SI Feaver, TP Murphy (1981) Spinal arachnoiditis. Can J N Sci 10 2

93a. FS Hoffman (1981) Spinal arachnoiditis. What is the clinical spectrum. Spine 8 559

94. TS Park, et al (1983) Medulloblastoma: clinical presentation and management. Experience at the Hospital for Sick Children, Toronto 1960-1980. J N S 58 543

94b. T Tomita, JB McLone (1981) Spontaneous seeding of medulloblastoma: results of cerebrospinal fluid cytology and arachnoid biopsy from the cisterna magna. N S 22 265

94b. MF Berry, et al (1981) Radiation treatment for medulloblastoma: A 21 year review. J

94c. JE Farwell, et al (1984) Medulloblastoma in childhood: an epidemiological study. J N S 61 653

95. F Gjerris, L Klinken (1978) Long-term prognosis in children with benign cerebellar astrocytoma. J N S 49 179

95a. K Shapiro, M Katz (1983) The acquired cerebellar astrocytoma. Child's Brain 10 168

96. RV Jeffries, et al (1982) Erythropoietin levels in posterior fossa haemangioblastoma. JNNP 45 264

97. G Krol, et al (1983) Computer tomography of axial chordomas. JCAT 7 296

98. CG Glantz, et al (1981) Pituitary tumors: clinical diagnosis with special emphasis on the significance of pituitary calcification. N S 8 656

98a. R Torres, RC Kendall (1980) Diagnosis and management of pituitary tumors. J N S 53 654

99. (1981) Clinicopathologic Conference: Headaches, inguinal mutilation, diabetes insipidus and exophthalmos in a 50 year old man. AJM 71 1027

100. RC Chan, GB Thompson (1982) Third ventricular colloid cysts presenting with acute neurological deterioration. Surg N 19 258

100a. JL Arnonic, et al (1980) Colloid cysts of the third ventricle. N S 7 450

101. G Morrison, et al (1984) Intraventricular mass lesions. Radiology 153 435

101a. R Jooma, et al (1984) Intracranial neoplasms during the first year of life: analysis of one hundred consecutive cases. N S 14 31

102. PW Carroll, et al (1982) Craniopharyngiomas in children. N S 57 382

103. MF Stevens, et al (1972) Clinical and endocrinological evaluation of 16 acromegalic patients treated by transsphenoidal surgery. J N S 37 853

104. MC Kappelman, et al (1984) Hyperplatyrrhinia, acromegaly, and palaeolithics. A retrospective assessment of twenty five cases. AnIM 100 115

105. J Turgeman, et al (1978) Neurological complications in patients with malignant tumors of the nasopharynx. Eur Neurol 17 140

106. LS Costa, et al (1981) Sphenoid sinus mucocele. ArS 47 897

106a. LG Close, WE O'Connor

(1983) Spheno-ethmoidal meningoceles with intracranial extension. *OtoHNS 91* 550
107. GJ Specter, *et al* (1976) Neurologic manifestations of glomus tumors in the head and neck. *AcN 33* 270
107a. CG Jackson, *et al* (1982) Glomus tumors. Diagnosis, classification, and management of large lesions. *ArOto 108* 401
108. RJ Gerlach, *et al* (1964) Meetin's cataplexia. *JRIS 66B* 586
109. GH Clamon, *et al* (1984) Myasthenic syndrome and small cell cancer of the lung: Variable response to anticholinesterase therapy. *AnIM 144* 959
109a. AG Engel (1981) Myasthenia gravis and myasthenic syndromes. *AnIN 10* 539
110. G Palma (1985) Paraneoplastic syndromes of the nervous system. *WJM 142* 787
111. JR Parisier, *et al* (1984) Clinical and cephalometric features of right atrial myxoma. *AJO 5* 345
111a. DJ Weinrich, *et al* (1984) Left ventricular mural thrombi complicating acute myocardial infarction. Long-term follow-up with serial echocardiography. *AnIM 100* 789
112. C Vanneste, *et al* (1983) Peripheral neuropathy associated with polycythemia vera. *N 33* 119
112a. JM Pearce, *et al* (1983) Lacunar infarcts in polycythemia with raised packed cell volume. *BMJ 287* 985
112b. JL Mas, *et al* (1985) Chorea and polycythemia. *JN 232* 109
113. I Raz, *et al* (1985) CNS involvement by non-Hodgkin's lymphoma. Response to a standard therapeutic protocol. *AcN 41* 1107
114. MC Dalakas, *et al* (1983) Treatment of polyneuropathy in Waldenstrom's macroglobulinemia: role of paraproteinemia and immunologic studies. *N 33* 1406
114a. SS Spector, *et al* (1980) Progressive and treatable cerebellar ataxia in macroglobulinemia. *N 30* 536
115. KS Kim, *et al* (1983) The cumulucent line: Characteristic sign of hypervitaminosis manifesting on plain. *AJRoentg 141* 1217
115a. PJ Donovan, G Guist (1979) Bone problems in meningiomas involving the base of the skull. *Clin NS 25* 455
116. S Oh (1982) Clinical and experimental morphological study of depressed skull fracture. *Acta Nchir 68* 111
117. F Vinuela, *et al* (1981) Spontaneous carotid-cavernous fistulas: clinical, radiological
117a. DL Barrow, *et al* (1985) Classification and treatment of spontaneous carotid-cavernous sinus fistulas. *J NS 62* 248
118. PA Grady (1984) Pathophysiology of extracranial cerebral arterial stenosis—a critical review. *Stroke 15* 224
118a. BK O'Connell, *et al* Dissecting aneurysms of head and neck. *N 33* 993
119. J Garcia-Uria, *et al* (1979) Empty sella and chondroma. A case report of eight treated cases. *J NS 50* 466
120. RF Spetzler, CB Wilson (1978) Management of recurrent CSF rhinorrhea of the middle and posterior fossa. *J NS 49* 393
121. D Kingsley, *et al* (1978) Growing fractures of the skull. *JNNP 41* 312
122. MS Huckman (1981) Normal pressure hydrocephalus: evaluation of diagnostic and prognostic tests. *AJNR 2* 385
122a. A Hamburn, F Alberti (1977) Differentiation of communicating hydrocephalus and procerik dementia by continuous recording of cerebrospinal fluid pressure. *JNNP 40* 630
122b. SE Borgesen, F Gjerris (1982) The predictive value of conductance to outflow of CSF in normal pressure hydrocephalus. *Brain 105* 65
122c. G Geeze, *et al* (1980) Communicating intracranial pressure recording in adult hydrocephalus. *Surg N 11* 323
123. JA Rush (1980) Pseudotumor cerebri: Clinical profile and visual outcome in 63 patients. *Mayo 55* 541
124. RA Fishman (1966) The pathophysiology of pseudotumor cerebri. An unsolved puzzle (editorial). *ArN 41* 237
125. Y Furuya, *et al* (1984) Congenital hemiplegia of cranial salvage. Part 2. Abnormalities of suture and skull deficiency in craniosynostosis. *J NS 61* 59
125a. IR White, *et al* (1984) Intracranial pressure changes in craniostenosis. *Surg N 21* 367
126. SG Kupersmith, *et al* (1984) Percutaneous transvascular treatment of giant carotid 126a. RC Heros, *et al* (1983) Large and giant paraclinoid aneurysms: surgical techniques, complications, and results. *NS 12* 153
126b. H Ammann, *et al* (1984) Neuroradiologic and neuropathologic findings with growing giant intracranial aneurysm. Review of the literature. *Surg N 21* 391
127. LN Sekhar, RC Heros (1981) Origin, growth, and rupture of saccular aneurysms: a review. *NS 8* 248
128. EM Lasoniec, *et al* (1985) Computed tomographic myelography (CTM) in adamantinomatous arteries. *Neur 27* 19
128a. JP Brasileske, *et al* (1985) Cranio-cervical pathology in Down syndrome. *ClinNNS 87* 173
129. D Goldberg, *et al* (1984) Diastematomyelia: a critical review of the natural history and treatment. *Spine 9* 367
129a. PS Pang, *et al* (1982) Diastematomyelia: Report of 31 cases surgically treated by a neurosurgical and orthopedic team. *Child's Brain 16* 337
130. S Hall, *et al* (1985) Lumbar spinal stenosis. Clinical features, diagnostic procedures, and results of surgical treatment in 68 patients. *AnIM 103* 271
130a. JI Goodman, *et al* (1979) Rational approach to the differentiation of vascular and neurogenic
131. KK Nakano (1978) The entrapment neuropathies. *M&N 1* 264
131a. C Claudcoff, *et al* (1985) Dynamic approach in the diagnosis of thoracic outlet syndrome using somatosensory evoked responses. *AnNMR 6* 3
132. DW Mulder, *et al* (1961) The neuropathy associated with diabetes mellitus. *N 11* 275
132a. RW Gilliatt, RG Willison (1963) Diabetic compressive neuropathy. *JNNP 25* 11
133. L Meyer, W Hacke (1983) Anterior interosseous nerve syndrome following supracondylar fracture of median nerve: clinical findings and electrophysiological investigations. *JN 229* 91
133a. DN Cullen, FB Wahr (1983) Anterior interosseous nerve syndrome. *SMJ 76* 1515
134. W Pryse-Phillips (1984) Validation of a diagnostic sign in carpal tunnel syndrome. *JNNP 47* 870
134a. J Wilson-MacDonald, *et al* (1984) Distal variation in nerve conduction, hand volume, and grip strength in the carpal tunnel syndrome. *JMS 206* 1042
135. SJ Oh, *et al* (1979) Tarsal tunnel syndrome: electrophysiological study. *AcN 5* 327
136. IB Sherman (1981) Abrupt changes in head position and cerebral infarction. *Stroke 12* 3
136a. JI Austman, *et al* (1985) Vertebrobasilar insufficiency: A review. *AcN 42* 810
136b. PI Yang, *et al* (1983) Bilateral vertebral artery occlusion at C1-2. *AJNR 4* 998
137. G Mancia, *et al* (1979) Control of blood pressure by carotid sinus baroreceptors in human beings. *AJC 44* 905
137a. A Almquist, *et al* (1985) Carotid sinus hypersensitivity: evaluation of the vasodepressor component. *Cir 71* 927
137b. HD Siegner, *et al* (1984) Carotid sinus hypersensitivity and syncope. *Mayo 59* 631
138. D Schatz (1984) Orthostatic hypotension. *AnIM 144* 773, 1032
139. JM Fein (1982) Hypertension and the central nervous system. *Clin NS 29* 467
140. MA Schifsky, *et al* (1978) Prolonged epileptic twilight state: Continuous recordings with nasopharyngeal electrodes and videotape analysis. *N 28* 239
140a. RS Shaley, N Amir (1982) Complex partial status epilepticus. *AcN 40* 90
141. W Arnold (1982) Pathogenetic reflections concerning Menière's disease. *Adv Otorhinolaryn 28* 138
141a. HP Krokar, *et al* (1983) Membranous rupture in Meniere's disease: Existence, location, and interaction. *OtoHNS 91* 61
142. P Kendall-Taylor, DM Turnbull (1983) Extraocular myopathies. *BMJ 287* 705
143. MC Lewis, PB Nelson (1981) Neurologic aspects of vasopressin

idiatic and the syndrome of inappropriate secretion of antidiuretic hormone, N Engl J Med 283:1037

143. AL Friedman, WE Segar (1977) Antidiuretic hormone excess, J Pediatr 90:521

144. RL Prake (1981) Recurrent spontaneous hyperthyroidism, Arch Intern Med 141:258

145. CA Garcia, RH Fleming (1977) Reversible corticospinal tract disease due to hyperthyroidism, Arch Neurol 34:664

145a. M Hatter, et al (1985) Pyramidal tract deficits and polyneuropathy in hyperthyroidism. Combination clinically mimicking amyotrophic lateral sclerosis, Arch Intern Med 145:1041

146. H Hasegawa, et al (1978) Quantitative analysis of ataxia in acute hyponatremia, J Neurol Neurosurg Psychiatry 41:570

147. ZS Agus, et al (1985) Disorders of calcium and magnesium homeostasis, Arch Intern Med 145:473

147a. MG Cogan, et al (1978) Central nervous system manifestations of hyperparathyroidism, Arch Intern Med 138:962

148. JP Knochel (1982) Neuromuscular manifestations of electrolyte disorders, Arch Intern Med 142:521

148a. BS Levine, HE Coburn (1984) Magnesium, the misunderstanded mineral, N Engl J Med 310:1253

149. RA Gabriel, PG Kennedy (1982) Hypercalcemia-induced epilepsy during lactation, Br Med J (Clin Res Ed) 285:607

149a. EF Cox (1985) Hypoparathyroidism. An unusual cause of seizures, Arch Emerg Med 2:114

150. JS Bertell (1982) Phosphate homeostasis and hypophosphatemia, Arch Intern Med 142:489

150a. SE Silvis, et al (1980) Hypophosphatemia: CNS pathologic changes secondary to oral sodium intake, Arch Intern Med 140:315

150b. JP Knochel (1985) The clinical status of hypophosphatemia. An update, N Engl J Med 313:447

151. LD Hicks (1990) Nutritional aspects of magnesium metabolism, Nutr Health 6:93

151a. R Whang (1984) Prediction of clinical hypomagnesemia: hypochlorhydria, hypocalcemia, and hypercalciuria, Arch Intern Med 144:1596

151b. C Berkelhammer, RA Bear (1985) A clinical approach to common electrolyte problems: 4. Hypomagnesemia, CMAJ 132:360

152. N Vecsei, TD Sabin (1981) Tonic focal seizures in nonketotic

152a. BM Singh, RJ Simeon (1980) Epilepsia partialis continua associated with nonketotic hyperglycemia: clinical and biochemical profile in 21 patients, Arch Neurol 37:135

152b. N Vecsei, TD Sabin (1981) Tonic focal seizures in nonketotic hyperglycemia of diabetes mellitus, Arch Intern Med 141:512

153. BM Fein, JB McConnell (1975) Cerebral oedema in diabetic ketoacidosis, Br Med J 2:208

153a. AJ Wiengard, et al. (1985) Cerebral edema in diabetic ketoacidosis, N Engl J Med 312:1301

153b. DW Foster, JD McCarry (1985) The metabolic derangements and treatment of diabetic ketoacidosis, N Engl J Med 309:159

154. SG Waxman (1978) Pathophysiology of nerve conduction: relation to diabetic neuropathy, Ann Intern Med 89:393

154a. DJ Ewing, et al (1980) The natural history of diabetic autonomic neuropathy, QJM 49:95

155. NB Ruderman, C Haudenschild (1984) Diabetes as an atherogenic factor, Prog Cardiovasc Dis 26:373

156. DG Kilburn, et al (1982) Thoracic root pain in diabetes: the spectrum of clinical and electromyographic findings, Ann Neurol 11:9

156a. LF Hirsh (1984) Diabetic polyradiculopathy simulating lumbar disc disease. Report of four cases, J Neurosurg 60:183

156b. SF Sim, EW Hirsh (1980) Diabetic thoracoabdominal neuropathy: clinical and electrodiagnostic features, Ann Neurol 9:75

157. AK Asbury (1977) Proximal diabetic neuropathy (editorial), Ann Neurol 2:179

157a. S Chokroverty, et al. (1977) The syndrome of diabetic amyotrophy, Arch Neurol 34:181

158. B Meier, et al (1984) Hypoglycemic coma, neurological sequelae, and outcome, Ann Neurol 15:425

159. WJ Kingston (1982) Endocrine neuropathies, Ann N Y Acad Sci 394

160. P Kendall-Taylor, et al (1985) Endocrine myopathies, BMJ 290:705

161. ND Ansk (1983) Pheochromocytoma. Diagnosis, localization, and treatment, Hosp Pract (Off Ed) 18:147

162. GR Gibson, et al (1981) Brain dysfunction in mild to moderate hypoxia, Am J Med 70:1247

163. Anon (1982) Hyperviscosity syndrome, Lancet 2:1439

164. TD Wunderle, et al (1984) Neurogenic pulmonary edema, Arch Neurol 39:529

165. Anon (1985) Neurogenic pulmonary edema, Lancet 1:1439

165. AW Turner, et al (1984) Factors that predict cardiac arrest ventricular tachycardia in patients, Am J Med 77:997

166. J Billes, et al (1982) Nonbacterial thrombotic endocarditis. A neurologic perspective of clinicopathologic correlates of 90 patients, Arch Neurol 39:93

166a. (1984) Cerebral infarction and death in a woman with lung cancer (CPC), Am J Med 76:129

167. BA Sandok, et al (1980) CNS aneurysm due to atrial myxoma. Clinical features and diagnosis, Arch Neurol 37:635

167a. GJ Mantle, J Billes (1984) Neurogenic cerebral mycotic aneurysm, Arch Neurol 41:1097

168. AJ Furlan, et al (1983) Cerebrovascular complications associated with idiopathic hypereosinophilic syndrome, Stroke 15:202

169. Anon (1984) Hypoxic encephalopathy rules, Lancet 1:489; 669a. CL Fraser, AJ Arieff (1985) Hypoxic encephalopathy, NEJM 313:865

170. NB Ifeadon, RA Osheroff (1976) Neurologic disorders in renal failure, NEJM 294:536

170a. CF Bolton (1980) Peripheral neuropathy in chronic renal failure, Can J Neurol Sci 7:89

171. AJ Arieff, et al (1976) Neurologic manifestations and morbidity of hyponatremia: correlation with brain water and electrolytes, Medicine 55:121

172. DG Wolfe, et al (1979) Pontine and extrapontine myelinolysis, Brain 102:361

173. R Laureno (1983) Central pontine myelinolysis following rapid correction of hyponatremia, Ann Neurol 13:232

174. JP Knochel (1982) Neuromuscular manifestations of electrolyte disorders, Am J Med 72:521

174. G Cremi, et al (1985) Potassium depletion myopathy: a clinical and morphological study of six cases, Acta Neurol Scand 71:15

175. AS Levey, et al (1985) Occult intracranial aneurysms in polycystic kidney disease: When is cerebral arteriography indicated?, N Engl J Med 312:100

176a. T Wakabayashi, et al (1985) Polycystic kidney disease and intracranial aneurysm. Early angiographic diagnosis and early operation for the aneurysmal aneurysm, J Neurosurg 62:448

176b. M Matsumoto, et al (1986) Unruptured intracranial aneurysm in polycystic kidney disease, Acta Neurochir (Wien) 79:96

176c. MJ Antonell (1978) Neurologic disorders and pregnancy, AJOG Gyn 132:325

176c. C Osborne Jr, et al (1985) CT findings in eclampsia, Neurol 27:313

176d. MH Schwartz, et al (1985) Toxemia of pregnancy: cerebral CT findings, JCAT 9:497

176e. SL Clark, et al (1985) Preeclampsia/eclampsia: hemodynamic and neurologic correlations, Obstet Gynecol 66:337

177. RJ Graham (1967) Neurological complications of pregnancy and anesthesia, Clin Obstet Gynaecol 9:553

177a. A Hopkins (1972) Neurologic disorders, Clin Obstet Gynaecol 4:435

178. B Eastan, et al (1979) Intracranial venous thrombosis in young women, Stroke 10:630

178a. MC Beal, PH Chapman (1980) Cortical blindness and hemianopsia hemorrhagia in the postpartum period, JAMA 244:2085

178. D Schmidt, et al (1982) Change in seizure frequency in pregnant epileptic women, J Neurol Neurosurg Psychiatry 45:751

179a. GD Monteiro, et al (1979) The pregnant epileptic. A review and recommendations, Arch Neurol 36:601

180. K Ishikawa, et al (1968) Chorea gravidarum. Report of a fatal case with neuropathological observations, Arch Neurol 17:429

180a. Q Gharam (1985) Recurrent chorea gravidarum in four pregnancies, Can J Neurol Sci 12:135

181. CM Lauder, et al (1977) Plasma aminoacidurias concentrations during pregnancy, N Z Med J 85:128

182a. MJ Lauder, M Kirkley (1979) Metabolism of diethylstilbestrol (placebo) during pregnancy, Br J Obstet Gynaecol 86:122

183. RH Levy, MS Yerby (1985) Effects of pregnancy on anticonvulsant

ering unknown. Epilepsia 29(Suppl 1):532

182. RB Ramsey, et al (1978) Status epilepticus in pregnancy. Effect of phenytoin malabsorption on seizure control. N 28:45

183. J Binns, LI Williams (1979) Epilepsy and pregnancy. Clin J N/Sci 6:345

183a. GD Mazzarella, et al (1979) The pregnant epileptic. A review and recommendations. ArN 36:601

184. M Lauritzen, et al (1983) Changes in regional cerebral blood flow during the course of classic migraine attacks. ArN 13:633

184a. J Edmeads (1982) Pathogenesis of unprovoked seizures of migraine. Sem N 2:61

184b. BH Spector (1984) Migraine. Surv Opth 29:392

185. PD Drummond, JW Lance (1983) Extracranial vascular changes and the source of pain in migraine headache. ArN 13:32

185a. DK Ziegler (1982) Mechanism of pain in headache. Sem N 2:32

186. LJ Dorfman, et al (1978) Cerebral infarction and migraine: Clinical and radiological correlations. N 28:911

187. JW Swanson, SA Vick (1978) Basilar artery migraine: 12 patients, with all attacks recorded electroencephalographically. N 28:782

187a. MH Stummegger, O Weinberg (1985) Basilar artery migraine: a follow-up study of 82 cases. HA 25:408

187b. S Ganji (1986) Basilar artery migraine: EEG and evoked potential patterns during acute stage. HA 26:220

188. MS Pessin, et al (1979) Mechanism of acute stroke. ArN 6:245

189. HP Adams, Jr, et al (1983) Amaurosis fugax: The results of arteriography in 59 patients. Stroke 14:742

189a. Anon (1982) Amaurosis fugax. Lancet 1:828

189b. BB Hurwitz (1985) Comparison of amaurosis fugax and transient cerebral ischemia: a prognostic clinical and arteriographic study. ArN 18:968

190. PJ Savitz, et al (1977) Retinal stroke: Is the patient at risk? ArOph 95:1185

191. MF Ehrenfeld, et al (1983) Pituitary apoplexy treated by transsphenoidal surgery. A clinicopathological and immunocytochemical study. J N/S 5:385:13

191a. ER Cushing, HW Freeman (1984) Pituitary apoplexy: a review. N/S 14:363

191b. RL Reid, et al (1985) Pituitary apoplexy: A review. ArN 42:212

192. RA Fishman (1982) Steroids in the treatment of brain edema. NEJM 306:359

193. HK Ehmahdi (1982) Hypertensive encephalopathy. Stroke 13:717

193a. RJ Weingarten, et al (1985) Computed tomographic changes of hypertensive encephalopathy. AJNRad 6:395

193b. Anon (1985) Hypertensive encephalopathy. Lancet II:555

194. EM Chester, et al (1978) Hypertensive encephalopathy. A clinicopathologic study of 20 cases. N 28:923

195. MO Tso, LM Jampol (1982) Pathophysiology of hypertensive retinopathy. Ophthal 89:1132

196. B Sigsbee, et al (1979) Nontraumatic superior sagittal sinus thrombosis complicating systemic cancer. N 29:139

196a. DM Gerstinger, E Kokmen (1977) Superior sagittal sinus thrombosis. ArN 34:2

196b. DC Dell, BB Greenberg (1985) Cerebral thrombosis in sickle cell polycythemia. AnIM 102:286

197. JP Seale, CF McGrew (1975) The anal sphincter. Ann Rev Med 26:321

197a. GL Rivellini, et al (1979) Subclavian steal syndrome. Part I: Proximal occlusive lesions of common carotid artery manipulation in three patients, and historical review. J N/S 51:623

198. J Jabaily, et al (1983) Neurologic manifestations of essential thrombocythemia. AnIM 99:513

199. RJ Schoenstman, JB Hill (1982) Neurologic complications of disseminated intravascular coagulation. N 32:791

199a. RC Cullen, et al (1975) Neurologic manifestations of intravascular coagulation in patients with cancer. A clinicopathologic analysis of 12 cases. N 25:795

199b. JA Chiri, et al (1948) Disseminated intravascular coagulation following cranial trauma. Case report. J N/S 52:266

200. PR Weinstein, et al (1982) Spinal cord injury, spinal fracture, and spinal stenosis in ankylosing spondylitis. J N/S 57:609

CHAPTER 35:

1. *The Metabolic Basis of Inherited Disease*, ed by JB Stanbury, JB Wyngaarden, DS Fredrickson, JL Goldstein, MS Brown. 5th edition, 1983, McGraw-Hill Book Co, New York, pp. 646–669, 1843–1845

1a. A Kothschutter (1985) On the clinical presentation of aspartoacylaminopeptidase-when to investigate. *Neuropediatr* 14:91

1b. BM Watson, et al (1983) The normal lesion of the inherited methylmalonic acidemias. N/EM 308:857

1c. ER Reynolds, et al (1984) Methylobyrin and mouse. Lancet 2:196

2. JD Schulman, et al (1980) Genetic disorders of glutamine and other amino-acid metabolism. New biochemical insights and therapeutic approaches. AnIM 93:330

2a. WL Weiner (1976) Vitamin E/VE/VE in the pathogenesis and treatment of disease of the central nervous system. Clin N/Pharm 3:107

2b. S Schuh, et al (1984) Homocystinuria and megaloblastic anemia responsive to vitamin B12 therapy. An inborn error of metabolism due to a defect in cobalamin metabolism. NEJM 310:686

3. WL Nyhan (1985) Nonketotic hyperglycinemia, in JB Stanbury et al (eds) *The Metabolic Basis of Inherited Disease*, 5th edition, McGraw-Hill Book Co, New York, pp. 561–569

4. VA McKusick, EF Neufeld (1983) The mucopolysaccharide storage diseases, in JB Stanbury et al (eds) *The Metabolic Basis of Inherited Disease*, 5th edition, McGraw-Hill Book Co, New York, pp. 751–777

5. *The Metabolic Basis of Inherited Disease*, ed by JB Stanbury, JB Wyngaarden, DS Fredrickson, JL Goldstein, MS Brown. 5th edition, McGraw-Hill Book Co, New York, pp. 831–959

6. L Swenschuis, et al (1986) Infantile diffuse cerebroretinopathy with hepatosplenomegaly (pseudo-Gaucher) lipidosis. J Lipid Res 27:93

7. (1984) Clinicopathological Conference 2–1984. NEJM 310:106

7a. F GEmiliani, et al (1984) Pathological study of the optic nerve in Fabry's disease. Eur N 23:172

8. MD Wiesmann, et al (1983) Non-infantile neuronopathic Gaucher's disease: A clinicopathologic study. N 33:906

8a. DA Wenger, et al (1981) Biochemical studies in a patient with subacute neuropathic Gaucher disease without visceral glucocerebroside storage. Ped Res 17:744

8b. JJ Goto, et al (1992) Mutations in glucocerebrosidase: Discrimination of neuropathic and non-neuropathic phenotypes of Gaucher disease. Proc Natl Acad Sci USA 89:8681

8c. RH Glew, et al (1982) Enzymatic differentiation of neuropathic and non-neuropathic forms of Gaucher's disease. J N/psych Exp N 41:618

8d. LB Daniels, et al (1982) Brain glucocerebrosidase in Gaucher's disease. AnN 29:550

9. MC Rogers, et al (1966) Tuberous sclerosis: A review for the neurosurgeon. N/N 14:93

9a. JM Nyhoot, et al (1976) Retinal lesions in tuberous sclerosis. ArOph 94:1277

10. CM Conlan, et al (1976) Sturge-Weber syndrome. Sem Roent 17:25

11. VM Ricardi (1981) Von Recklinghausen neurofibromatosis. N/EM 305:1617

11a. RA Lewis, et al (1985) von Recklinghausen neurofibromatosis. II. Incidence of optic gliomata. Ophthal 92:928

11b. SM Jones, et al (1981) Familial cranial neurofibromatosis. OncHVS 9:623

12. TA Waldmann, et al (1983) Ataxia-telangiectasia: a multisystem hereditary disease with immunodeficiency, impaired organ maturation, x-ray hypersensitivity, and a high incidence of neoplasia. AnIM 99:367

12a. RL Teplitz (1978) Ataxia telangiectasia. AnN 33:553

13. WA Horton, et al (1979) Von Hippel-Lindau disease. Clinical and pathological manifestations in nine

families with 50 affected members. *AnIM 116* 709

1b. DK Subramony, et al (1982) Von Hippel Lindau disease with multiple manifestations: diagnosis and management. *N/S 8* 92

1c. F Hentsig, DM Robertson (1984) Von Hippel-Lindau disease: a familial, often lethal, multi-system phakomatosis. *Ophthal 91* 263

1d. AP Heys, et al (1981) Muscle phosphofructokinase deficiency. Abnormal polysaccharide in a case of late onset myopathy. *N 33* 1077

1e. F Cimolin, et al (1984) Clinical varieties of neuromuscular disease in debrancher deficiency. *AnN 42* 1827

1f. EL Munsat (1970) A standardized forearm subcutaneous exercise test. *N 20* 1171

1g. S Di Mauro, et al (1980) Disorders of lipid metabolism in muscle. *M&N 3* 369

1h. WR Martindale (1983) Muscle disease due to disorders of lipid metabolism. *Sem N 3* 134

CHAPTER 36:

1. GF Duffy (1987) Lumbar puncture in spontaneous subarachnoid hemorrhage. *BMJ 295* 1163

CHAPTER 37:

1. NT Zervas, J. Molloy-Wirtz (1972) Successful treatment of cerebral herniation in five patients. *NEJM 286* 1073

2. B Marmarou (1982) Clinical recording of pressure in the spinal canal and cauda equina. Part 3. Pressure in the cervical spinal canal during endotracheal intubation in patients with cervical spondylosis. *J N/S 57* 66

2c. TG Malemick, et al (1986) Cervical spine movement during endotracheal intubation. *Ann Emerg Med 15* 413

3. AM Hakim, HM Pappius (1983) Sequence of metabolic, clinical, and histologic events in experimental brain ischemia. *AnN 13* 365

3c. WD Parker Jr, et al (1984) Brain metabolism in experimental mitochondrial cytopathy. *N 34* 1447

4. WA Lishman (1981) Cerebral disorder in psychosis: Syndrome of impairment. *Brain 104* 1

4c. C Harper (1983) The incidence of Wernicke's encephalopathy in Australia—a neuropathological study of 131 cases. *JNNP 46* 593

5. HE James, et al (1977) Treatment of intracranial hypertension. Analysis of 105 consecutive, continuous recordings of intracranial pressure. *Acta Neur 36* 189

5a. JG Miller (1982) Disorders of cerebral blood flow and intracranial pressure after head injury. *Clin N/S 29* 167

6. HE James, et al (1977) Treatment of intracranial hypertension. Analysis of 105 consecutive, continuous recordings of intracranial pressure. *Acta Neur 36* 189

6a. JE Huffines, SA Saba (1983) Comment: hyperventilation in patients with intracranial hypertension, Appreciation and management. *AnIM 143* 765

7. J Guerrero, et al (1983) Quantitative CT assessment of hemorrhage and maternal induced changes in brain water content. *N 33* 198

7a. RA Ullman (1982) Steroids in the treatment of brain edema. *NEJM 306* 399

8. A Kuttner, et al. The influence of high and low dosages of mannitol 25% in the therapy of cerebral edema. Comparative study with monitoring of intracerebral pressure. in *Brain Edema Cerebrospinal Fluid Tumors* ed by K Schurmann, M Brock, HJ Reulen, D Voth, Springer Verlag, Berlin p. 81-91

8a. M Javid, et al (1954) The rebound phenomenon and hyperosmotic solutions. *J N/S 11* 1059

8b. HE James, et al (1977) Treatment of intracranial hypertension. Analysis of 105 consecutive, continuous recordings of intracranial pressure. *Acta N/Sci 36* 189

9. HE James (1980) Methodology for the control of intracranial pressure with hyperosmolar mannitol. *Acta Neurol 51* 161

9a. CP Mullan, G Bovani (1983) Effects of mannitol on increased intracranial pressure. *N/S 13* 260

9b. JD McQueen, LD James (1961) Dehydration and alleviation of the brain with hypertonic urea and mannitol. *J N/S 21* 138

10. DK Ziegler, A Zess, T Zabel (1966) Hypertensive encephalopathy. *AnN 12* 472

11. PJ Miller, JH Deck (1974) Intraocular and optic nerve sheath hemorrhage in cases of sudden intracranial hypertension. *J N/S 41* 160

12. MS Ilgaev, SS Hayreh (1972) Optic disc edema in raised intracranial pressure. I. Evolution and resolution. *ArOph 95* 1237

13. Metabolic Coma—Medical Staff Conference, University of California, San Francisco (1974), *WJM 120* 131

14. TH Kirkham, et al (1972) Divergent paralysis with raised intracranial pressure. An elusive neurological sign. *BMJ 56* 776

14c. SCW Van Allen (1967) Transient recurring paralysis of ocular origination. *AnN 17* 81

15. JJ Cocosa, RP Simon (1979) The comatose patient: a diagnostic approach and treatment. In *Acute Clin 1* 1

16. BG Benton, et al (1982) Epidural hematoma: report of seven cases with delayed evolution of symptoms. *Can J N/Sc 9* 321

16a. M Zaccarello, et al (1983) Chronic extradural hematoma. *Acta Neur 67* 57

17. JA Kenning, et al (1986) Upright patient positioning in the management of intracranial hypertension. *Surg N 15* 158

18. HA Strenio (1982) Acute epidural hematoma. *Review of 39 Cases* scanning cases with high incidence of cortical artery rupture. *J N/S 57* 251

19. T Yamashima, RL Friede (1984) Why do bridging veins rupture into the virtual subdural space?. *JNNP 47* 121

20. J Rovenstine, F Gyorfy (1978) Long term follow-up review of patients with acute and subacute subdural hematomas. *J N/S 48* 345

20a. IL Seelig, et al (1983) Subdural hematomas: I. Acute subdural hematoma: Progress in detection, current pathology, and therapy. *Surg N 13* 216

20b. B Klun, M Fatkich (1984) Factors influencing the outcome in acute subdural hematoma. *Acta N/Sci 73* (2)

21. M Silverman, The nonvascular patient, in *Neurologic Emergencies*, ed by M Salzman, Raven Press, New York, 1983, pp. 13-54

22. JM Lipton, et al (1979) Thiamine lability in Wernicke's encephalopathy. *AnN 33* 250

22a. KK Frankovich, RP Simon (1984) Neurologic manifestations of accidental hypothermia. *AnN 16* 384

22b. JH Rosier (1978) Hypothermia: Pathophysiology, clinical settings, and management. *AnIM 89* 519

23. DR Rush, SL Hutchman (1986) Intracranial metastatic emergencies. *SMJ 77* 220

24. RH Sprunt, et al (1981) Amitriptyline induced ophthalmoplegia. *N 31* 1358

24a. LR Caplan, D Schleiner (1988) Dysconjugate gaze in hepatic coma. *AnN 8* 328

24b. JR Hotson, HS Saddekni (1982) Amitriptyline: Another cause of internuclear ophthalmoplegia with coma. *AnN 12* 67

25. CH Hawkes (1974) "Locked-in" syndrome: report of seven cases. *BMJ 2* 279

25a. M Cheringron, et al (1976) Locked in syndrome caused by a tumor. *N 26* 148

26. WW Tourtellotte, et al (1964) Spontaneous subarachnoid hemorrhage. Factors affecting the rate of clearing of the cerebrospinal fluid. *N 14* 301

27. JT Carnadin, et al (1983) Quantitative CSF IgG measurements in multiple sclerosis and other neurologic diseases. An update. *AnN 40* 406

28. GD Perrin, et al (1982) IgG index and oligoclonal IgG in multiple sclerosis and other neurologic disorders. *J N/Sci 58* 325

29. WH Oldo, et al (1981) Long survival in subacute sclerosing panencephalitis. *JNNP 47* 176

30. J Kinnman, H Link (1984) Intrathecal production of oligoclonal IgM and IgG in CNS sarcoidosis. *ANS 86* 94

30a. JR Miller, et al (1985) Occurrence of oligoclonal bands in Multiple Sclerosis and other CNS diseases. *AnN 17* 55

30b. LM Gronski, et al (1985) Oligoclonal IgG bands in multiple sclerosis and subacute sclerosing panencephalitis. *N 25* 413

31. WI Powers (1981) Cerebrospinal fluid to serum glucose ratios in diabetic millions and bacterial meningitis. AJM 71 217
32a. WH Theodore, S Gendelman (1981) Meningeal carcinomatosis. ArN 38 696
32b. JJ Murray, et al (1983) Neoplastic meningitis. Marked variation of cerebrospinal fluid composition in the absence of extradural block. AJM 75 289
33. FM Vinuela (1981) Hypoglycorrhachia after intraventricular hemorrhage. N/S 8 7
34. M Barza, SG Pauker (1980) The decision to biopsy, treat, or wait in suspected herpes encephalitis. AnIM 92 641
35. JF Glaser, et al (1979) Malignant cells in cerebrospinal fluid (CSF): The meaning of a positive CSF cytology. N 29 1369
36. MT Stechenberg, CA Kauffman (1983) Comparison of cryptococcal and tuberculous meningitis. ArN 40 81
36a. M Barza, SG Pauker (1980) The decision to biopsy, treat, or wait in suspected herpes encephalitis. AnIM 92 641
36b. Clinicopathologic Exercises. Case 29-1984 (1984) NEJM 311 172
36c. D Kanamalavic, JA Shulman (1976) Recent survey of infectious meningitis in adults: review of laboratory findings in bacterial, tuberculous, and aseptic meningitis. SMJ 69 449
37. JF Spielman (1982) Post-lumbar puncture headache. Headache 22 280
37a. IM Pearce (1982) Hazards of lumbar puncture (editorial). BMJ 285 1871
38. JG McComb (1983) Recent research into the nature of cerebrospinal fluid formation and absorption. J N/S 59 369
39. D Hilton-Jones, et al (1982) Failure of postural manoeuvres to prevent lumbar puncture headache. JNNP 45 743
39a. PA Carbaat, H Van Crevel (1982) Lumbar puncture headache: controlled study of the preventive effect of 24 hours' bed rest. Lancet 2 1133
39b. J Kuvaraja, R Sirviova (1980) Duration of postural headache after lumbar puncture: effect of needle size. HCA 26 224
40. FY Tsai, et al (1982) Computed tomography in acute posterior fossa infarcts. AJNRad 3 149
40a. DW Chakeres, A Kapila (1985) Radiology of the ancient civilizations. Part I. Normal. N/Rad 27 383
40b. DL Johnson (1980) Foramen cephalic cisterna obliteration: a CT sign of hydrocephalus from failure. J N/S 64 586
40b. P Svendsen, O Dam (1981) Visibility of the temporal horn on computed tomography. N/Rad 23 139
41. LB Klatz, et al (1982) Computed tomographic evaluation of the craniopharyngioma. Ophthal 89 374
42. RD Zimmerman, et al (1982) Ultra acute intracerebral lesions on axial CT: II. Recognition and differentiation of interhemispheric subarachnoid and subdural hemorrhage. AJNRad 3 635
43. JS Ogilvy, et al (1979) Aspects of the interhemispheric subdural hematoma, including the falx syndrome. JNS 50 22
43a. JW Rozanski, J Frazee (1980) Subdural empyema—importance of early diagnosis. N/S 7 472
44. M Hadj-Djilani, L Calliauw (1982) A contribution to the rapid diagnosis of subdural empyema. Acta Neur 6 389
44a. RD Zimmerman, et al (1984) Subdural empyema: CT findings. Radiology 150 417
44b. Subdural empyema (1961) Can J Surg 27 203 (p 388)
44c. L Weinberg (1966) Subdural empyema. Clinical and computed tomographic correlations. ArN 43 491
45. MG Lucas III, MA Whelan (1980) Recent diagnostic experience with subdural empyema. J N/S 52 764
45a. DM Kaufman, et al (1983) Streptococcal subdural empyema. N 33 123

CHAPTER 38:

1. M Koskiniemi, et al (1980) Herpes simplex virus encephalitis. New diagnostic and clinical features and results of therapy. ArN 37 763
1a. RJ Whitley, et al (1982) Herpes simplex encephalitis. Clinical assessment. JAMA 247 317
1b. S Kohl, AR James (1985) Herpes simplex virus encephalitis during childhood. Importance of brain biopsy diagnosis. J Peds 107 210
2. RJ Whitley, et al (1982) Herpes simplex encephalitis. Clinical assessment. JAMA 247 317
2a. M Barza, SG Pauker (1980) The decision to biopsy, treat, or wait in suspected herpes encephalitis. AnIM 92 641
2. RJ Whitley, et al (1982) Herpes simplex encephalitis. Clinical assessment. JAMA 247 317
3a. B Skoldenberg, et al (1984) Acyclovir versus vidarabine in herpes simplex encephalitis. Randomised multicentre study in consecutive Swedish patients. Lancet 2 707
4. CC Ballenger III, et al (1982) Partial complex status epilepticus. N 13 1515
4a. ON Markand, et al (1976) Complex partial status epilepticus (psychomotor status). N 26 159
4b. RS Shaw, M Aminoff (1982) Complex partial status epilepticus. ArN 40 40
4c. J Engel Jr, et al (1978) Prolonged partial complex status epilepticus: EEG and behavioral observations. N 28 863
5. MA Bolshko, et al (1978) Prolonged epileptic seizure stress: Correlations recordings with nasopharyngeal electrodes and videotape analysis. N 28 239
5a. E Niedermeyer, et al (1974) Absence status (petit mal status) with focal characteristics. ArN 36 417
5b. RW Finetsm, et al (1979) Electroencephalographic absence status with minimal behavior change. ArN 36 176
6. EB Larson, et al (1981) Computed tomography in patients with psychiatric illnesses. Advantages of a "rule in" approach. AnIM 95 360

CHAPTER 39:

1. RT Ross (1983) Transient tumor attacks. AdN 40 653
2. ML Mosier, et al (1983) Chronic subdural hematoma with transient neurological deficits. A review of 15 cases. ArN 14 539
3. BH Dobkin (1978) Syncope in the adult Chiari anomaly. N 28 715
3a. F Hampton, et al (1982) Syncope as a presenting feature of tracheitis herniation with syringomyelia. JNNP 45 919
4. AA DeMaria Jr, et al (1984) EEG in orthostatic syncope. N 34 571
5. EM Critchley, JS Wright (1983) Evaluation of syncope. BMJ 286 s80
6. DN Donlan, et al (1972) Micturition syncope. BHeartJ 34 536
WN Kapoor, et al (1985) Micturition syncope: a reappraisal. JAMA 253 786
7. ML Lapkin, et al (1977) The electroencephalogram in childhood basilar artery migraine. N 27 580
7a. JW Swanson, NA Vick II Basilar artery migraine. 12 patients with an attack recorded electroencephalographically. N 28 782
8. RJ Simpson Jr, et al (1983) Vagal syncope during treatment pulmonary aneurysm. JAMA 249 980
9. BT Desai, et al (1982) Psychogenic seizures. A study of 42 attacks in six patients, with intensive monitoring. ArN 39 202
9a. AV Delgado-Escueta, et al (1979) Videotaping epileptic attacks during stereoelectroencephalography. N 29 455
9b. PD Williamson, et al (1985) Complex partial seizures of frontal lobe origin. AdN 18 497
10. RJ Cohen, C Suter (1982) Hysterical seizures: Suggestion as a provocative EEG ice. AdN 11 39
10a. BT Desai, et al (1982) Psychogenic seizures. A study of 42 attacks in six persons, with intensive monitoring. AdN 39 202
11. WV Kapoor, et al (1983) A prospective evaluation and follow-up of patients with syncope. NEJM 309 197
11a. SL Tilkian, et al (1985) The value of electrophysiologic studies in syncope of undetermined origin: report of 110 cases. AHJ 110 468
11b. JA Reiffel (1982) Electrophysiological testing in patients with recurrent syncope: are results predictive for prior ambulatory monitoring?, AHJ 103 1046
12. AV Delgado-Escueta (1979) Epilepsy paroxysms: Modern approaches and clinical correlations. N 29 1034

12a. AV Delgado-Escueta, FE Rael, DM Treiman (1981) Complex partial seizures on closed-circuit television and EEG: a study of 691 attacks in 79 patients. AnN *11* 292
13b. P Perrigin, et al (1985) Deep attacks. An anatomic change in the evolution of partial epilepsy. N *35* 1725
13. H Gastaut, M Fischer-Williams (1957) Electroencephalographic study of syncope: its differentiation from epilepsy. Lancet *2* 1018
14. HG Wieser (1980) Temporal lobe or psychomotor status epilepticus. A case report. EEGCN/P *48* 558
15. AV Delgado-Escueta, et al (1982) Complex partial seizures on closed-circuit television and EEG: a study of 691 attacks in 79 patients. AnN *11* 292
16. BT Desai, et al (1982) Psychogenic seizures. A study of 52 attacks in six patients, with intensive monitoring. AnN *39* 780
16a. JP Lieb, et al (1976) A comparison of EEG seizure patterns recorded with surface and depth electrodes in patients with temporal lobe epilepsy. Epilepsia *17* 127
17. ZD Nahmias, et al (1977) Cardiac arrhythmias that masquerade as epilepsy. BMJ *1* 1434
18. A Aguirre, AJ Gabor (1980) Movement-related seizures in nonketotic hyperglycemia. N *30* 600
18a. JE Thomas, et al (1977) Epilepsia partialis continua: A review of 32 cases. AnN *34* 296
18b. BM Singh, RI Sinclair (1980) Epilepsia partialis continua associated with nonketotic hyperglycemia: Clinical and biochemical profile of 21 patients. AnN *8* 155
19. G Siesjo, et al (1978) Epileptic brain damage: Do role of systemic factors that modify cerebral energy metabolism. Brain *101* 687
19a. G Fernandez, et al (1985) Status epilepticus in willowy-normal rats causes neuronal necrosis. AnN *19* 281
20. RJ Porter, C Simon (1985) Management of status epilepticus. Ortho. NEJM *307* 1146
21. RE Cranford, et al (1978) Intravenous phenytoin in acute treatment of seizures. N *29* 1474
21a. AV Delgado-Escueta, et al (1982) Management of status epilepticus, NEJM *306* 1337
21b. BJ Wasdell, et al (1979) Efficacy of intravenous phenytoin in the treatment of status epilepticus: Kinetics of central nervous system penetration. AnN *7* 511
21c. JC Cloyd, et al (1980) Status epilepticus: the role of intravenous phenytoin. JAMA *244* 1479
22. R Kobayashi, et al (1968) Neurological sequellae following Dilantin overdosage in a patient and in experimental animals. N *15* 823
22a. M Ikeda (1970) The number of Purkinje cells after diphenylhydantoin intoxication in monkeys. Epilepsia *11* 191
22b. WK Bleck, et al (1981) Cerebellar atrophy following diphenylhydantoin intoxication. N/pol *15* 76
22c. G Lindvall, B Nilsson (1964) Cerebellar atrophy following phenytoin intoxication. AnN *16* 258
23. AV Delgado Escueta, JG Bajorek (1982) Status epilepticus: Mechanisms of brain damage and rational management. Epilepsia *23* (Suppl. 1) 529
23a. J Engel Jr, et al (1982) Recent developments in the diagnosis and therapy of epilepsy. AnIM *97* 584
24. MP Lechat, et al (1993) Comparisons of intravenous phenytoin for acute treatment of seizures. Recommendations for usage. JAMA *249* 762
25. HJ Probst, C Simon (1980) Maintenance of status epilepticus factory. NEJM *307* 1146
26. PC Singhal, et al (1978) Myoglobinuria and renal failure after status epilepticus. N *28* 202
27. AJ Chesser, et al (1983) Postictal elevation of serum creatinine kinase level. AnN *49* 515
27a. GP Sechi, et al (1986) Myocardial infarction complicating status epilepticus, Epilepsia *26* 532
28. CF Tomasulo, et al (1981) Neurogenic pulmonary edema in intracranial, unexplained death of epileptic patients. AnN *9* 158
29. AV Delgado-Escueta, et al (1982) Management of status epilepticus, NEJM *306* 1337
29a. JW Lampert, et al (1977) Ventricular hazards of prolonged anoxia, N *27* 540
29b. AV Delgado Escueta, JG Bajorek (1982) Status epilepticus: mechanisms of brain damage and rational management. Epilepsia *23* (Suppl. 1) 529
30. JF Leppik, et al (1983) Double-blind study of lorazepam and diazepam in status epilepticus, JAMA *249* 1452
30b. PJ Daudick, et al (1984) Hemodynamic response to diazepam: Dependence on acute left ventricular end-diastolic pressure. Anesth *60* 469
31. RE Ramsay, et al (1979) Brain uptake of phenytoin, phenobarbital, and diazepam, AnN *36* 535
31a. AV Delgado-Escueta, JG Bajorek (1982) Status epilepticus: Mechanisms of brain damage and rational management, Epilepsia *23* (Suppl. 1) 529
32. JF Leppick, et al (1983) Double-blind study of lorazepam and diazepam in status epilepticus, JAMA *249* 1452
32a. RJ Levy, RL Kraft (1984) Treatment of status epilepticus with lorazepam, AnN *45* 865
33. M Pacifico, J Kawasaki (1981) Status epilepticus treated by barbiturate anesthesia with continuous monitoring of cerebral function, BMJ *282* 520
33a. GE Young, et al (1990) Acute thiamine bioavailability in refractory status epilepticus. Can J N Sci *17* 251
33b. JF Dreyfuss, et al (1984) Hypothermia and barbiturate coma for refractory status epilepticus, Crit Care Med *12* 567
34. RC Cervos, et al (1980) Post-Salkeld therapy in childhood status epilepticus, AnN *40* 137
34a. G Kuroda, et al (1986) Intravenous paraldehyde for seizure control in neonates infants, N *36* 138
35. AV Delgado-Escueta, et al (1982) Management of status epilepticus, NEJM *306* 1337
35a. AV Delgado-Escueta, et al (1982) Management of status epilepticus (letter), NEJM *307* 1143
36. AV Delgado-Escueta, et al (1982) Management of status epilepticus, NEJM *306* 1337
36a. CG Bernhard, et al (1955) A new treatment of status epilepticus. Intravenous injections of a local anesthetic (lidocaine). AMA ArN Psych *74* 709
37. MJ Aminoff, RP Simon (1980) Status epilepticus. Causes, clinical features, and consequences in 98 patients, AJM *69* 657
38. CG Bowen (1983) The alcohol withdrawal syndrome, WJM *138* 539
39. JR Feussner, et al (1981) Computed tomography brain scanning in alcohol withdrawal seizures. Value of the neurologic exam. AnIM *94* 519

CHAPTER 40:

1. W Tennyson, et al (1979) Ocular findings in botulism type B. JAMA *241* 475
1a. IM Hughes, et al (1986) Clinical features of types A and B food borne botulism. AnIM *95* 442
2. CD Tacket, et al (1984) Equine antitoxin use and other factors that predict outcome in type A foodborne botulism. AJM *76* 794
3. S Fuchs, et al (1984) Antibody to acetylcholine receptor in myasthenia gravis: production by lymphocytes for thymus cell clones. N *34* 11
3a. C Hermanns Jr, et al (1985) Myasthenia gravis—current concepts, WJM *142* 297
4. IT Fitzsimons, et al (1982) Vanillin toxicity in myasthenia gravis, JNNP *45* 217
5. JB Roslan, et al (1985) Wernicke's encephalopathy. NEJM *312* 1035
5a. DG Cogan, et al (1983) Ocular signs in thiamine deficient monkeys and in Wernicke's disease in humans, Arch Oph *101* 1272
5b. CG Harper, et al (1986) Clinical signs in the Wernicke-Korsakoff complex: a retrospective analysis of 131 cases diagnosed at necropsy. JNNP *49* 341
6. HS Layrer (1975) Remediable neuromuscular diseases, Primary Care *2* 559
7. Clinical picture GBS
8. Spinal of GBS
9. JD Eaton, DG Sherman (1983) Carotid endarterectomy (editorial), Mayo *58* 205
9a. DE Ziegler (1985) Carotid lesions: to operate or not to operate, Stroke *16* 639
9b. S Dion, et al (1982) Natural history of neurologic, symptomatic ulcerative lesions of the carotid artery, Ann *12* 1491

18. GD Roderick, et al (1984) The natural history of carotid arterial disease in asymptomatic patients with cervical bruits, Stroke *15* 805

18a. WJ Quinones-Baldrich, WS Moore (1983) Asymptomatic carotid stenosis. Rationale for management, AJS *42* 378

18b. FM Yatsu, WS Fields (1985) Asymptomatic carotid bruit. Stenosis or ulceration, a conservative approach, AJS *42* 383

11. Castaigne, et al (1978) Internal carotid artery occlusion. A study of 61 instances in 50 patients with post mortem data, Brain *97* 179

11a. TS Riles, et al (1984) Common carotid occlusive. Assessment of collateral vessels, AJS *39* 363

12. JF Whisnant, et al (1983) Carotid endarterectomy for unilateral carotid system transient cerebral ischemia, Mayo *58* 171

12a. MC Dalcell, et al (1985) Carotid endarterectomy in the stroke patient: computed axial tomography to determine timing, J Vasc Surg *2* 231

12b. R. McCullough, et al (1985) Carotid endarterectomy after a competed stroke: Reduction in long-term neurologic deterioration, J Vasc Surg *2* ?

12c. (1988) Benefit of CEA Stroke *17* 308 12d. (1984) Does CEA work?, Stroke 1068

12e. CJ Poole, RW Ross Russell (1985) Mortality and stroke after anastomosis fistula, BMJP *46* 902

13. J Hindfelt, WS Moore (1978) A new look at emergency carotid artery operations for the treatment of cerebrovascular insufficiency, Stroke *9* 999

13a. RM Mentzer Jr, et al (1981) Emergency carotid endarterectomy for thrombosis, Surgery *89* 68

13b. L. Caplan, et al (1986) Intracranial clot of the carotid artery detected radiographically, N *34* 125

14. RM Wilkins (1964) Neurosurgery Classic—XXVI, J NS *21* 1108

14. RM Wilkins (1964?) Neurosurgery Classic—XXI, J NS *21* 140

15. S Ventrup, et al (1984) Hemodynamically significant stenosis of the internal carotid artery treated with endarterectomy, Case report, J NS *60* 1099

16. JS Meyer, HO Portnoy (Peter) Post epileptic paralysis. A clinical and experimental study, Brain *82* 167

16a. M Saleh, et al (1993) Postictal blindness in adults, JNNP *46* 366

17. PR Vernell (1929) Todd's paralysis. A cardiovascular phenomenon, Stroke *6* 301

18. PA Hansen, R Cholka (1971) Hemiparetic seizures, N *18* 630

18a. ML Mastri, et al (1983) Carotid subdural hematoma with transient neurologic deficits: a review of 25 cases, AnN *14* 519

19. NA Lassen, S Ventrup (1984) Ischemic penumbra exists in recent cerebral infarction: a flat sleeping beauty dead? Letters, Stroke *15* 795

19a. M Britton, A Rodes (1985) Prognosis of stroke after arrival at hospital, Stroke *16* 620

19b. L Caplan, et al (1985) Occlusive disease of the middle cerebral artery, N *35* 979

19c. J Lauder, EL Cornwell (1985) Progressive stroke caused by CT-verified small deep infarcts: relation with the size of the infarct and clinical outcome, ANS *71* 153

20. JP Wade (1953) Transport of oxygen to the brain in patients with elevated haematocrit values before and after venesection, Brain *76* 113

20a. DB Koe Jr, JH Wood (1964) Rheology of the cerebral circulation, Neurosurgery *15* 125

20b. EH Thomas (1965) Hemodilution in acute stroke (editorial), Stroke *16* 763

21. J Levitt, PD Swanson (1968) Minipalic thrombocytosis. A possible cause of transient ischemic attacks, N *18* 711

22. RG Ojemann, RC Heros (1982) Spontaneous brain hemorrhage, Stroke *14* 168

23. M von Arbin, et al (1981) Accuracy of bedside diagnosis in stroke, Stroke *12* 239

24. S Strandgaard, UH Paulson (1984) Cerebral autoregulation, Stroke *15* 413

24a. FM Yatsu (1985) Hypertension in acute ischemic stroke, AnN *42* 969

25. M Romner-Lassegard, et al (1986) Treatment of acute ischemic stroke: Open trial with continuous intravenous heparinization, AnN *42* 186

25a. M Romner-Lassegard, MH Quinones (1985) Heparin therapy in stroke: hemorrhagic complications and risk factors for intracerebral hemorrhage, N *34* 114

26. HJ Gelmers (1984) The effects of nimodipine on the clinical course of patients with acute stroke, ANS *99* 232

26a. HJ Gelmers (1985) Calcium-channel blockers: effects on cerebral blood flow and potential uses for acute stroke, AJC *55* 1468

26b. J van Reempts, M Borgers (1985) Ischemic brain injury and calcium: recent biologic and therapeutic aspects, AnPM *14* 336

27. Stroke August 1984 28. El Tantawi, et al (1986) Acute middle cerebral artery occlusion: Experience with volume expansion therapy, NS *18* 987

28a. The multicenter trial of hemodilution in ischemic stroke—background and study protocol, Stroke *16* 885

29. J Hantovsky, et al (1985) Double blind controlled trial of the therapeutic effects of pentoxyfilin in patients with competed ischemic stroke, Stroke *16* 810

29a. VF Miller, et al (1984) Pentoxyfilin infusion in acute cerebral infarction, N *34* (4)

29b. RJ Grzalewski, et al (1985) Treatment of ischemic stroke with pentoxyfilin, Stroke *54* 197

30. PR Humphrey, J Marshall (1984) Transient ischemic attacks and strokes with recovery prognosis and investigation, Stroke *15* 965

30a. JA Barnett, et al (1982) Is carotid endarterectomy beneficial in prevention of recurrent stroke?, AJS *117* 1401

30b. SC Lumsden, Jr, FA Elliott (1981) Prevention of recurrent stroke, Stroke *12* 731

30c. DO Wirtzen, et al (1987) Reversible ischemic neurologic deficit (RIND) in a community: Rochester Minnesota, 1955-1974, N *37* 439

30d. C Sacquegna, et al (1981?) Long term prognosis after occlusion of middle cerebral artery, BMJ *284* 1490

31. JN Cinker, et al (1984) Stroke after carotid endarterectomy: risk as predicted by preoperative computerized tomography, AJS *117* 497

31a. Radiology *153* 651 1984

31b. AD Weinberger, et al (1984) Early carotid endarterectomy in patients with small fixed neurologic deficits, J Vas Surg *1* 795

31c. SM Dorsch, et al (1985) Carotid endarterectomy in the stroke patient: Computerized axial tomography to determine timing, J Vasc Surg *2* 231

32. JG Gallenich, RB Monsowitz (1987) Some clinical aspects of superficial temporal-middle cerebral artery bypass surgery, Clin Neu *34* 13

33. CA Read, JF Toole (1981) Clinical technique for demonstration of internal carotid lesions, N *31* 764

33a. KJ Korte (1994) Dynamic vascular auscultation, AJM *75* 1006

CHAPTER 41:

1. D Rankin (1982) A psychiatrist's view of chronic pain, Int Anesth Clin *21* 177

1a. RK Beals (1984) compensation recovery from injury, WJM *140* 235

2. J Reich, et al (1983) Psychiatric diagnosis of chronic pain patients, AJPsy *140* 1495

3. RL Fields (1981) Pain II. New approaches to management, AnN *9* 101

3a. JJ Bonica (1990) I'm in that head: the ethics of living practice, AnPM *97* 112

3b. J. Thompson, et al (1983) Morton's diseases: A 5-year follow-up of patients in a double blind placebo controlled study, Adv Orthotherapy *30* 358

4. JB Reuler, et al (1980) The chronic pain syndrome: misconceptions and management, AnIM *93* 588

5. TH Welsh (1984) Opiate receptors in chronic cancer pain, Pain *5* 14

5a. MT Nyswander, VP Case (1967) The treatment of chronic pain, Intern NYAM *169* 909

5b. MT McGivnes, GM Crooks (1984) The care of patients with severe chronic pain at terminal illness, JAMA *252* (16)

6. M Angell (1982) The quality of mercy (editorial), NEJM *306* 98

6a. PE Newberger, SE Sallan (1981) Chronic pain: Principles of management, J Ped *99* 30

6b. TD Wolfe (1984) Severe stroke

final metaphor in chronic cluster pain. Pain 18:1
7. SH Ameriso, et al (1991) Headache in cerebral embolic disease. Stroke 22:382
7a. AB Gerdelat, JF Toole (1974) Headache and transient ischemic attacks. Stroke 5:669
7b. JE Edmeads (1979) The headache of ischemic cerebrovascular disease. HA 19:345
7c. RK Portenoy, et al (1986) Headache in cerebrovascular disease. Stroke 17:1009
8. J Bille, et al (1982) Temporal arteritis associated with severe subarachnoid hemorrhage. JAMA 247:486
9a. T Kerry, et al (1971) Giant cell arteritis with normal sedimentation rate. ArN 24:63
9. N Raskin (1978) Headache associated with organic disease of the nervous system. MCNA 62:459
10. MM Palmer (1936) Headaches and head pains associated with diseases of the eye. Res Pub Stud Headache 9:15
11. GR Bedford, JE Scarlett (1987) Pseudotumor cerebri: papilledema and hypertensive headaches. HA 22:65
12. SE Lauritzen, et al (1982) Changes in regional cerebral blood flow during the course of classic migraine attacks. ArN 37:851
12a. IN Blau (1981) Migraine pathogenesis: the round hypothesis reexamined. JNNP 47:437
12b. M Lauritzen, J Olesen (1984) Regional cerebral blood flow during migraine attacks by xenon-133 inhalation and emission tomography. Brain 107:447
13. LJ Hoffman, et al (1949) Cerebral induction and migraine. Clinical and radiological correlations. N 29:317
14. JM Pearce (1984) Migraine: a cerebral disorder. Lancet 2:96
14a. I Fibromalo (1984) Migraine: new views on an old theory. Can J Neu Sci 11:363
14b. PD Drummond, JW Lance (1983) Extracranial vascular changes and the source of pain in migraine headache. AnN 13:32
14c. MA Mastaglia (1981) The neurological complications of vascular head pain. AnN 10:537
14d. E Shields (1977) Hemodynamic studies within the brain during migraine. ArN 25:95
15. JL Merlis, S Diamond (1981) Cyclical migraine. ArN 38:503
15a. O Sjaastad (1979) Pathogenesis of the cluster headache syndrome. Res Clin Stu Headache 6:35
15b. JM Pearce (1989) Chronic migrainous neuralgia. A variant of cluster headache. Brain 112:1549
15c. JL Merlis, S Diamond (1972) The clinical line between migraine and cluster headaches. ArN 54:420
15d. S Solomon, et al (1982) Migraine-cluster headache syndrome. HA 23:236
16. X Vignon, C Warren (1982) Evaluation of oculocephalic sympathetic function in vascular headache syndromes. Part II: Oculocephalic sympathetic function in classic headache. HA 23:200
16a. HC Lumbye (1967) Time in the temporal cluster headache. HA 22:158
16b. O Appenzeller, et al (1981) Cluster headache: Ultrastructural aspects and pathogenetic mechanisms. ArN 38:307
16c. S Solomon (1986) Classic headache and the nervous intermediate. HA 25:3
17. D Blumer, M Heilbronn (1982) Chronic muscle contraction headache and the pain-pattern disorder. HA 23:159
17a. S Diamond (1985) Depression and migraine. HA 23:122
17b. CM Silverstein (1983) Chronic pain and depression: Universal or personal helplessness? Pain 15:309
17c. KU Kretzinger, et al (1990) Are patients with chronic pain depressed? AJPsy 147:917
17d. Aaron (1984) Headache and depression. Lancet 1:596
17e. NG Ward, et al (1977) The effectiveness of tricyclic antidepressants in the treatment of chronic pain and depression. Pain 3:133
18. JR Couch, RS Hassanein (1979) Amitriptyline in migraine prophylaxis. ArN 36:695
18a. HL Fields (1981) Pain II: New approaches to management. AnN 9:101
18b. D Sherwin (1979) A new method for treating "headaches". AJPsy 135:1161
18c. NT Mathew (1981) Pseudodisease or migraine and minor headache. A randomized controlled study. HA 21:105
18d. DP Moore (1980) Treatment of chronic pain with tricyclic antidepressants. SSE 21:1505
19. JN Blau (1992) Resolution of migraine attacks: sleep and the recovery phase. JNNP 45:223
20. JL Merlis, et al (1990) Urinary catecholamine changes for classic headache: Changes in number of platelets and serotonin and histamine levels. ArN 47:596
21. JL Merlis, S Diamond (1984) Cluster headache variant. Spectrum of a new headache syndrome. ArN 38:703
21a. RW Price, JD Pearce (1978) Chronic paroxysmal hemicrania. A disabling headache syndrome responding to indomethacin. AnN 3:183
21b. DP Graney (1953) Indomethacin-responsive episodic cluster headache. JNNP 49:360
22. L Kudrow (1981) Response of cluster headache attacks to oxygen inhalation. HA 22:1
22a. L Fanan (1985) Treatment of cluster headache. A randomized comparison of oxygen v. air inhalation. ArN 42:967
23. F Bartl (1982) Clonidine as an effective agent in cluster headache. HA 22:69
23a. J Nimmo (1985) Pain relief for classic cluster headaches lidocaine. HA 23:199
23b. JP Kittrelle, et al (1982) Cluster headache. Local anesthetic nerve ablation. ArN 42:496
23c. S Diamond, et al (1986) Treatment of intractable cluster. HA 29:42
24. JN Blau (1980) Towards a definition of migraine headache. Lancet 1:434
24a. JR Saper (1982) The cranial headache syndrome: A new perspective. HA 22:284
24b. CD Anderson, JCD Franks (1981) Migraine and tension headache: Is there a physiological difference? HA 22:63
24c. H Wolff (1984) Is the muscular model of headache still viable? A review of conflicting data. HA 24:185
24d. H Ramirez (1980) A critical analysis of the traditional tension headache model. HA 23:332
24e. HJ Featherston: Migraine and muscle contraction headaches: a continuum. HA 23:75
24f. DK Ziegler (1985) The headache symptom. How many sources?. ArN 42:223
25. NT Mathew, et al (1982) Transformation of episodic migraine into daily headache: Analysis of factors. HA 22:96
26. RH Martin (1979) Psychogenic factors in headache. MCNA 62:559
26a. HI Featherston, RD Beamish (1982) "Daily" common migraine: psychosocial predictors of outcome of medical therapy. HA 22:118
26b. JM Pearce (1977) Migraine: a psychosomatic disorder. HA 47:125
27. NT Mathew, et al (1982) Transformation of episodic migraine into daily headache: Analysis of factors. HA 22:86
27a. M Feuerstein, et al (1983) Stress, symptom activity, and pain in migraine headache: a prospective analysis. HA 23:296
28. LJ Budzynski (1985) Facial musculature and EMG biofeedback in treatment of muscle contraction headache. HA 23:86
29. M Bakal, et al (1982) Action of some paracranial muscles during spontaneous attacks of common migraine. Pain 14:121
29a. HC Philips, MS Hunter (1982) A psychotherapeutical investigation of tension headache. HA 22:173
29b. SN Haynes, et al (1982) The psychophysiological clinique of muscle contraction headache. HA 22:172
29c. EP Sainsbury, CD Bebbington (1982) Tension headache patients versus controls: A study of EMG parameters. HA 22:175
29d. P Tfelt-Hansen, et al (1981) Prevalence and significance of muscle tenderness during common migraine attacks. HA 21:49
30. EP Sainsbury, CD Bebbington (1982) Tension headache patients versus controls: A study of EMG parameters. HA 22:175
30a. A van Knorring, et al (1983) Abso-

lize and postprocessual rating (MG) levels in muscle contraction and migraine headache patients, H/A 23 213
30f. WSS Chan (1985) An approach to the nature of tension ?? headache, H/A 25 198
31. LH Raff, et al (1982) 5-hydroxytryptamine in platelets of patients with muscle contraction headache, H/A 21 19
32. NT Mathew (1981) Prophylaxis of migraine and mixed headache: A randomized controlled study, H/A 21 105
32a. D Blumer, M Heilbronn (1982) Chronic muscle contraction headache and the pain-prone disorder, H/A 22 180
32b. D Sherwin (1979) A new method for treating "headaches", AJPsy 136 1181
32c. DP Moore (1998) Treatment of chronic pain with tricyclic antidepressants, SMJ 73 1583
33. K Spiegel, et al (1983) Analgesic activity of tricyclic antidepressants, AnN 23 462
33a. C Feinmann (1985) Pain relief by antidepressants: possible modes of action, Pain 23 1
34. JW Richardson III, E Richardson (1964) Amitriptyline: a clinical update for medical practitioners, Mayo 59 139
35. M Bonney, HL Fields (1983) Amitriptyline potentiates morphine analgesia by a direct action on the central nervous system, AnN 13 168
35a. RT Malseed, FI Goldstein (1979) Enhancement of morphine analgesia by tricyclic antidepressants, Neuharm 18 827
36. L von Knorring, et al (1983) Pain as a symptom in depressive disorders, I. Relationship to diagnostic subgroup and depressive symptomatology, Pain 15 19
36a. NG Wade, et al (1979) The role of tricyclic antidepressants in the treatment of coexisting pain and depression, Pain 7 351
36b. JA Ghia, et al (1981) Serotonergic activity in man as a function of pain, pain mechanisms, and depression, Anesth Analges 60 854
37. NH Rieker, RK Schwartz (1980) Interval therapy of migraine: Long term results, H/A 20 336
38. BP O'Neill, JD Mann (1978) Aspirin prophylaxis in migraine, Lancet 2 1179
39. GD Solomon, et al (1984) Verapamil prophylaxis of migraine: A double-blind, placebo-controlled
39a. SJ Peroutka, GS Allen (1984) The calcium antagonist properties of cyproheptadine: Implications for antimigraine action, N 24 364
39b. HG Markley, et al (1984) Verapamil in prophylactic therapy of migraine, N 24 925
39c. GD Solomon (1985) Comparative efficacy of calcium antagonist drugs in the prophylaxis of migraine, H/A 25 368
40. JM Lacomis, et al (1983) Biofeedback and relaxation in the treatment of migraine headache: comparative effectiveness and physiological correlates, JNNP 46 525
41. P Budzynski, et al (1973) Controlled trial of EMG feedback in muscle contraction headache, AnN 6 54
41a. NW Bell, et al (1980) Biofeedback, brief psychotherapy and tension headache, H/A 27 162
42. CE Rosenberg, et al (1982) Computed tomography and EEG in patients without focal neurologic findings, AnN 39 291
42a. GJ Cannon, et al (1972) Computed tomography of the brain in patients with headache or temporal lobe epilepsy: Findings and cost-effectiveness, JCAT 1 330
42b. EB Larson, et al (1980) Diagnostic evaluation of headache: Impact of computerized tomography and cost effectiveness, JAMA 243 339
43. N Raskin (1978) Headaches associated with organic disease of the nervous system, MCNA 62 459
44. JW Lance (1951) Headache, AnN 26 1
44a. Anon (1982) Treatment of Migraine (editorial), Lancet 1 1358
45. PL Lutz, R Rose (1985) Intravenous chlorpromazine: preliminary results in acute migraine, H/A 25 302
45a. MC Gilhotra, N Raskin (1986) A controlled study of clonidine in the treatment of acute migraine headache, H/A 26 168
46. M Lauprasert, J Orbon (1984) Drug abuse in migraine patients, Pain 19 81
47. JA Lloyd, JBM Leyt (1983) Adhesive capsulitis of the shoulder: Arthrographic diagnosis and treatment, SMJ 76 879
48. ST Lee, D Fairbanks (1985) Intradural rupture of lumbar intervertebral disc, Clin J N Sci 10 192
48a. CJ Herger, et al (1978) Intradural hematoma of lumbar intervertebral disc, Spine 3 346

CHAPTER 42:

1. BT Tusa (1983) Dizziness and vertigo in cerebrovascular disease. Part I. Peripheral and systemic causes of dizziness, Stroke 11 301
2. BT Tusa (1983) Dizziness and vertigo in cerebrovascular disease. Part II. Central causes and vertebrobasilar disease, Stroke 11 413
2a. RA Basta (1972) Basilar-vertebral artery insufficiency as a cause of vertigo, OtoCNA 6 287
3. CW Dieter, et al (1979) Acute cerebellar infarction in the PICA territories, AnN 32 364
3a. C Huang, Y Yu (1985) Small cerebellar strokes may mimic labyrinthine lesions, JNNP 48 263
3b. DE Tranowski, MJ Reeves (1983) Cerebellar infarction: analysis of twenty-one cases, Surg N 24 223
4. J Kregenow, DF Swift, M Swash (1981) Epileptic dizziness, BMJ 282 687
5. T Brandt, RB Daroff (1980) The multisensory physiological and pathological vertigo syndromes, AnN 7 195
5a. PR Ash, JL Kelmer (1979) Neuro-ophthalmic signs in psychiatric lesions, Medicine 58 301
5b. WP Gibson (1984) The diagnosis of Meniere's disease: individual, Clin Oto 8 223
5c. WJ Gottesfeld (1980) Meniere's disease, signs and symptoms, J Laryngol Oto 94 885

CHAPTER 43:

1. CPC Case 46-1979 (1979) NEJM 301 1104
1a. HP Brech, et al (1985) Somatosensory evoked potentials in motor neuron disease, MRN 8 556
2. AK Afifi (1968) Steroid myopathy. Clinical, histologic and cytologic observations, Johns Hopkins Med J 123 158
2a. A Amato (1946) Steroid myopathy in connective tissue disease, AJM 56 685
2b. AA Khaledi, et al (1983) Corticosteroid myopathy: a clinical and pathological study, Clin Endocrinol 18 133
3. FL Mastaglia, VJ Ojeda (1985) Inflammatory myopathies, AnN 17 215, 317
4. DH Lennhoff, CA Clemens (1984) Endocrine opthalmopathy: current ideas concerning etiology, pathogenesis, and treatment, Endo Review 5 303
5. R Cravioto, et al (1961) Wernicke's encephalopathy: A clinical and pathological study of 28 accepted cases, AnN 4 510
6. DK Henderson, et al (1978) Infectious disease emergencies: The statistical spectrum, West J Med 129 18
7. JM Hughes, et al (1981) Clinical features of Type A and B food-borne botulism, AnIM 95 442
8. DM Kaufman, et al (1980) Infectious agents in spinal epidural abscesses, N 30 844
9. D Leys, et al (1985) Decreased antibody from acute bacterial epidural abscesses using computed tomography and aspirational treatment in severe patients, AnN 17 353
9b. EF Vecsei, DM Mealey (1985) Spinal epidural abscess, MCNA 69 775
9. BC Haas (1982) Cerebellar hemorrhage and infarction, Stroke 13 [8]
9a. GA Rosenberg, DM Kaufman (1979) Cerebellar hemorrhage: Reliability of clinical evaluation, Stroke 7 [3]
10. JM Scelfo, et al (1981) Ventriculostomy for hydrocephalus in cerebellar hemorrhage, N 31 1337
11. JP Krehbiel, et al (1980) Cauda equina syndrome and lumbar disc herniation, JAOS 564 389

CHAPTER 44:

1. DH Hubel (1964) Learning disturbance without blindness, NEJM 270 581
2. SG Waxman (1980) Determinants

of conduction velocity in motor and sensory nerves. MSS 3:141
3. H Barry, PM Richardson (1976) Common peroneal nerve palsy: a clinical and electrophysiological review. JNNP 39:1162
3a. RF Townes, et al (1981) Usefulness of electrophysiological studies in the diagnosis of lumbosacral root disease. AnN 9:305
3b. A Eeles (1985) Electrodiagnosis of mononeuropathies. Neurol Clin 3:595
4. JB Pickett (1984) Localizing peroneal nerve lesions to the knee by motor conduction studies. AnN 47:192
5. J Kimura (1979) The carpal tunnel syndrome. Localization of conduction abnormalities within the distal segments of the median nerve. Brain 102:619
6. J Warren, et al (1969) Electrocyclographic changes of brachial plexus root avulsions. J Neurosurg 31:137
7. RW Fincham, DA Capp (1968) Sensory nerve conduction in syringomyelia. N 18:280
8. PJ Dyck, et al (1971) Segmental demyelination secondary to axonal degeneration in uremic neuropathy. Mayo 46:409
8a. SC Wiesner (1980) Determinants of conduction velocity in myelinated nerve fibers. MSS 7:141
9. F Buchthal, F Rosenfalck (1978) Polyneuropathy. Facts and fancies. Contrib Clin Neurol (EEG Suppl No 34):375
10. E Stalberg (1980) Clinical electrophysiology in myasthenia gravis. JNNP 43:622
10a. J Daube (1983) Disorders of neuromuscular transmission. A review. ArPMR 64:195
11. J Daube (1983) Disorders of neuromuscular transmission. A review. ArPMR 64:195
12. E Stalberg (1980) Clinical electrophysiology in myasthenia gravis. JNNP 43:622
13. SI Ito, et al (1985) Neurophysiological and clinical correlation in myasthenia gravis. AnN 17:348
13. SG Cull-Candy, et al (1980) On the release of transmitter at normal, myasthenia gravis and myasthenic syndrome affected human end-plates. J Physiol 299:621
14. SI Ito, et al (1982) Electrophysiological and clinical correlation in myasthenia gravis. AnN 12:348
15. TA Udell, et al (1953) Wound botulism associated with a positive tendon test. WJM 159:218
16. E Kugelberg, L Edström (1968) Differential histochemical effects of muscle contractions on phosphorylase and glycogen in various types of fibers: relation to fatigue. JNNP 31:415
16a. L Edström, E Kugelberg (1968) Histochemical composition, distribution of fibers and fatiguability of single motor units. Anterior tibial muscle of the cat. JNNP 31:424
17. A Blumcke, et al (1981) Human myoglobin gene: an unusually large gene. Nature 401:712
18. L Gulli (1983) An overview of motor unit structure and function. ArPMR 64:468
19. G Karpati, WK Engel (1968) "Type grouping" in skeletal muscles after experimental reinnervation. N 18:447
20. L Zivin, CA Marsan (1968) Incidence and prognostic significance of "epileptiform" activity in the EEG of non-epileptic subjects. Brain 91:751
20a. JC Watts, et al (1977) Benign epileptiform transients of sleep. Characteristics of the small sharp spike configuration. N 27:1061
20b. J Reiher, DW Klass (1968) Two unusual EEG patterns of doubtful clinical significance. MUNA 32:933
20c. ES Goldensohn (1976) Paroxysmal and other features of the electroencephalogram in migraine. Res Clin Stud Headache 4:138
20d. KA Kooi, et al (1964) Electroencephalographic patterns of the temporal region in normal adults. N 14:1029
21. OC Snead III (1982) On the neural theories for neurochemistry of epilepsy. Int Rev Neurobiol 24:95
21a. DS Gazzaniga, MJ Aminoff (1984) Does the interictal EEG have a role in the diagnosis of epilepsy? Lancet 1:837
21b. DW Klass, BF Westmoreland (1985) Nonepileptogenic epileptiform electroencephalographic activity. AnN 18:627
22. WT Blume, et al (1984) EEG morphology of partial epileptic seizures. EEGCNP 57:295
22a. WT Blume, N Pillay (1986) Electrographic and clinical correlates of secondary bilateral synchrony. Epilepsy 26:636
22b. CT Lombroso, G Erba (1970) Primary and secondary bilateral synchrony in epilepsy. A clinical and electroencephalographic study. AnN 22:821
23. SS Spencer, et al (1985) Effects of corpus callosum section on secondary bilaterally synchronous interictal EEG discharges. N 35:1649
23. WT Blume, et al (1984) EEG morphology of partial epileptic seizures. EEGCNP 57:295
23. R Orrechia, et al (1979) Value of EEG in acute confusional states. JNNP 42:28
24. Alzheimer's dementia and death in a 50-year-old woman (clinicopathologic conference). AJM 76:1087
25. TT Chi-en, et al (1977) Characteristic early electroencephalographic changes in herpes simplex encephalitis. AnN 31:304
25a. JR Smith, et al (1979) A distinctive clinical EEG profile in herpes simplex encephalitis. Mayo 59:469
25b. WA Cobb (1979) Evidence for the periodic mechanism in herpes simplex encephalitis. EEGCNP 46:315
26. WJ Au, et al (1980) Periodic lateralized epileptiform complexes (PLEDs) in Creutzfeldt-Jakob disease. N 30:611
26a. B Westmoreland, et al (1986) Chronic periodic lateralized epileptiform discharges. AnN 47:499
26b. N-S Chu (1980) Periodic lateralized epileptiform discharges with pre-existing focal brain lesions. Role of alcohol withdrawal and atypical encephalopathy. AnN 17:551
26c. Y Kuroiwa, GG Celesia (1980) Clinical significance of periodic EEG patterns. AnN 17:15
27. DS Kernan, RG Bickford (1964) Triphasic waves: a reassessment of their significance. EEGCNP 17:191
28. DS Kernan, et al (1982) EEG monitoring of clinical coma. The compressed spectral array. N 32:709
29. AB Grindal, et al (1977) Alpha-pattern coma: 34 cases with 9 survivors. AnN 1:371
29a. K Sorensen, et al (1978) Prognostic significance of alpha frequency EEG rhythm in coma after cardiac arrest. JNNP 41:840
29b. VJ Ingvar, CB McCutchen (1983) Physiologic and prognostic significance of "alpha coma." JNNP 46:632
30. I Hashimoto, et al (1981) Brain stem auditory-evoked potentials recorded directly from human brain stem and thalamus. Brain 104:841
30a. AR Møller, et al (1981) Intracranially recorded responses from the human auditory nerve: new insights into the origin of brain stem evoked potentials (BSEP). EEGCNP 52:18
31. WB Wilson, BB Kessler (1980) Comparison of the pattern and diffuse light visual evoked responses in diffuse multiple sclerosis. AnN 7:30
32. LJ Sidtis, et al (1981) Visual evoked potentials in occipital lobe lesions. AnN 10:80
32a. Y Kuroiwa, GG Celesia (1981) Visual evoked potentials with hemifield pattern stimulation. Their use in the diagnosis of retrochiasmatic lesions. AnN 10:89 (also see correction p 390)
32b. CG Maitland, et al (1982) Evoked potentials in the evaluation of visual field defects due to chiasmal or retrochiasmal lesions. N 32:956
33. U Nilsonstierner, B Jakobi (1982) Do visual evoked potentials give relevant information on the neuro-ophthalmological conclusion in optic nerve lesions? ANS 66:52
33a. A Pinkus, et al (1985) Comparison of visual cortical potentials and color vision in presumed demyelinating disease. N Opt 3:161
34. C Yiannikas, JC Walsh (1985) Somatosensory evoked responses in the diagnosis of thoracic outlet syndrome. JNNP 46:234
34a. AJ Wilbourn, RJ Lederman (1984) Evidence for conduction delay in thoracic outlet syndrome is challenged (letter). NEJM 310:1687
34b. SA Jones, et al (1984) Thoracic outlet syndrome. Electrophysiologic reappraisal. AnN 47:960
35. A Iragui (1982) Subject Review: The somatosensory evoked potential. Can J N Sci 9:65

35a. SK Powers, et al (1982) Spinal cord pathways mediating somatosensory evoked potentials. J NS 57:472
36. FJ Massry (1982) An overview of hydrogen ion regulation. AnIM 242 1019
36a. TD Du Bose Jr (1981) Clinical approach to patients with acid-base disorders. MCNA 67:399
36b. DM Schreck, et al (1986) Diagnosis of complex acid-base disorders: Physician performance versus the microcomputer. AnIM 15:164

CHAPTER 45:

1. SH Wanzer, et al (1984) The physician's responsibility toward hopelessly ill patients. NEJM 310:955
2. N Cousins (1982) Denial: Are sharper definitions needed? (commentary). JAMA 248:210
3. JE Wilberger Jr, D Pang (1982) Syndrome of the incidental herniated lumbar disc. J NS 56:127
4. AA Mohs (1982) A new medical oath (letter). NEJM 307:764
4a. EJ Cassel (1982) The nature of suffering and the goals of medicine. NEJM 306:639
4b. SM Del Guidice (1982) The nature of suffering and the goals of medicine (letter) NEJM 307:759
4c. S Braithwaite, DC Thomasma (1988) New guidelines on foregoing life-sustaining treatment in incompetent patients: An axiomatic policy. AnIM 109:731
5. JA Beall (1983) Mercy—for the terminally ill suicide patient. JAMA 249:2881

The following drugs can be obtained commercially.

Thorazine	Smith Kline & French
Tensilon	Roche
Mestinon	Roche
Cafergot	Sandoz
Indocin	Merck Sharpe & Dohme
Periactin	Merck Sharpe & Dohme
DHE 45	Sandoz
Antabuse	Ayerst
Valium	Roche
Dilantin	Parke-Davis
Metrizamide	Winthrop-Breon

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