CREUTZFELDT-JAKOB DISEASE

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Kernodle Clinic
A Duke Medicine Practice

ELON UNIVERSITY

DEMENTIA, DELIRIUM

Case Study - 1

- AB is a 84 YO RH WF music teacher, lives alone after death of her husband 2 years ago.
- Very charming grandmother of 8, brought home made cookies for you at the visit.
- Her kids brought her to the appointment.
- “memory is not quite right”
- Pt says “I have no problem, my kids are over-reacting”

Conti...

- I forget something here ant there but everyone does it, don't you?
- Daughter:
  - Thanks giving dinner was terrible
  - Bounced couple of checks
  - Broke her side view mirror by hitting garage wall and did not realize it for 1 month
  - Forgets doctor's appointments
  - Can't keep track of her medicines even after putting them in a pill box.

Conti...

- Son:
  - Forgot her grandson and thought it was her son
  - Wakes up in the middle of the night to get ready for work
  - Cooks for her dead husband and kids who have moved out decades ago.
  - Can’t figure out how to use new microwave and TV remote.

PMSFS History

- Medical
  - Hypothyroidism, HTN, DM, CAD, cancer
- Surgical
  - Hysterectomy, thyroid cancer s/p resection and radiation.
- Family
  - Memory problems in mother in old age, stroke, heart attack
- Social
  - Masters in Music, loved sports, retired music teacher, never smoked, used to drink socially but “some more” after husband passed away.

ROS

- ?

Medications

- Benadryl 50 mg at night for sleep
- Amitriptyline 50 mg at night for headache
- Ranitidine 150 mg bid for “acid”
- Hydrocodone for back pain
- Warfarin for heart
- Phenobarbitol for childhood febrile seizure

Physical Exam

- Observe: clothes – stain, glasses too many spots, make up – lipstick little bit off, some smell of urine, SMILE, JOKES
- Vitals: 5’6”, 140 lb, 150/90, 82, 14, 100%
- CTAB, S1S2 regular, right carotid bruit
- Mental status exam: MMSE/SLUMS/MoCA
  - Alertness
  - Orientation
  - Apraxia
  - Memory
  - * Attention
  - * Language
  - * Mood/delusion/hallucination
  - * Other higher cortical function

Frontal Lobe Signs

- Concept: Restraint / Initiative / Order
- Plamomental reflex
- Snout / suck / root
- Palmer grasp
- Visual grasp
- Glabellar tap
- Witzelsucht (inappropriate jocularity)
- Abulia

Work up?

- Labs: CBC, CMP, Thyroid profile, Vit B12, folate, RPR
- How about genetic testing?
- CSF?
- Testing of family members
- Neuroimaging
  - MRI, CT
  - PET (FDG vs Amyvid), SPECT

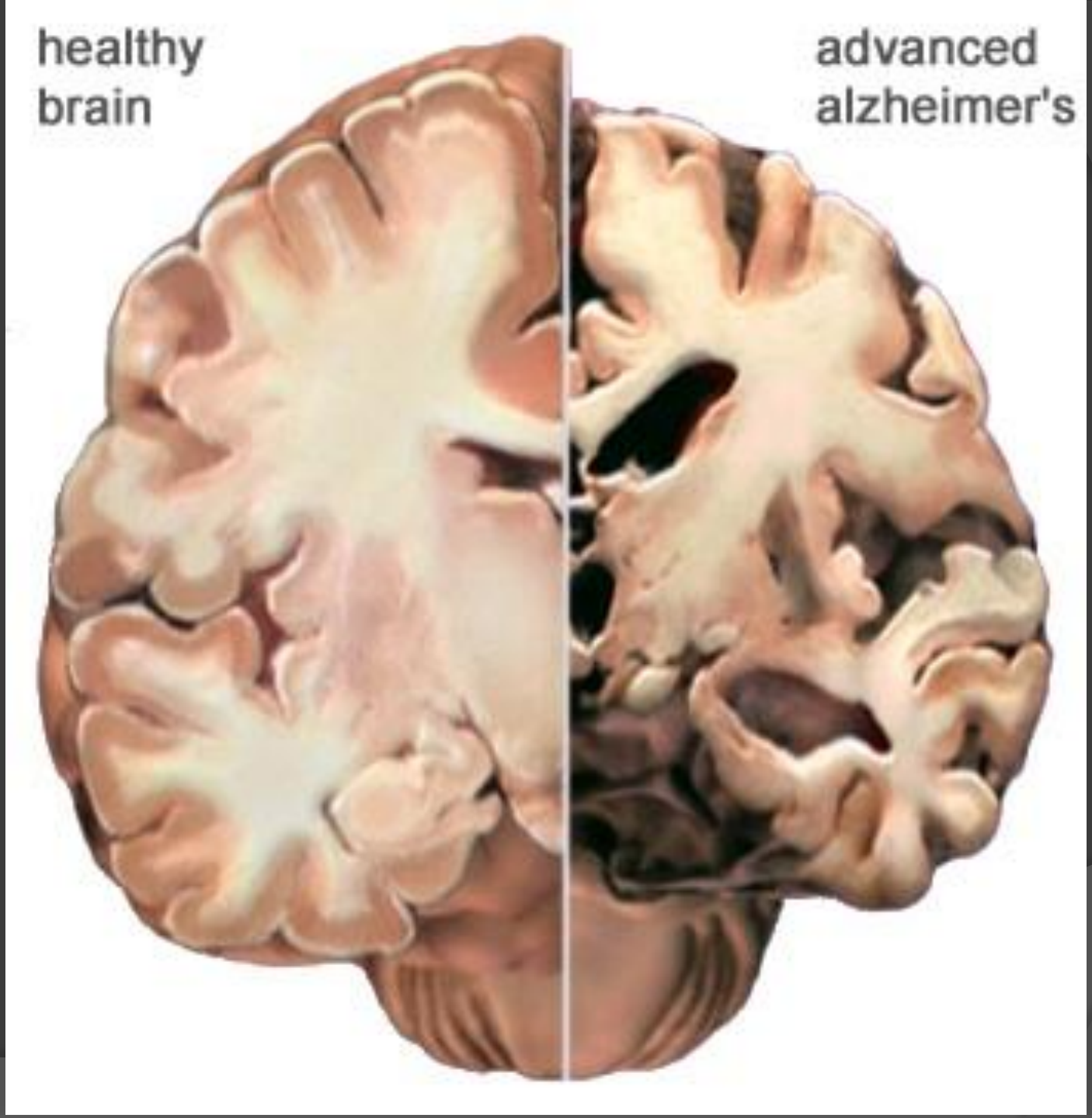
Treatment

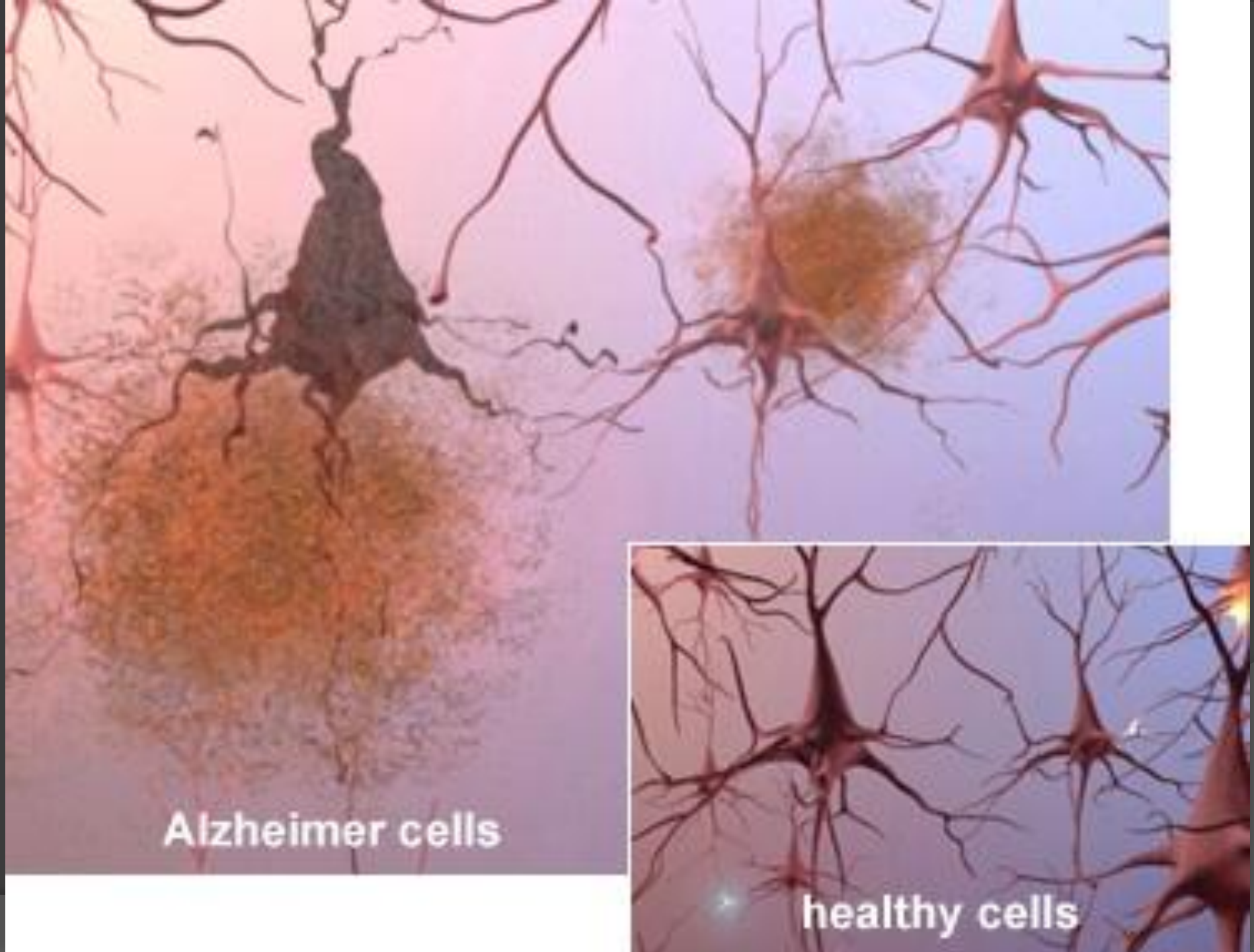
- Pharmacological
  - Donepezil 5 mg po qhs for 2 wks then 10 mg
  - Galantamine
  - Rivastigmine (patch)
  - Memantine XR titration pack to 28 mg/day.

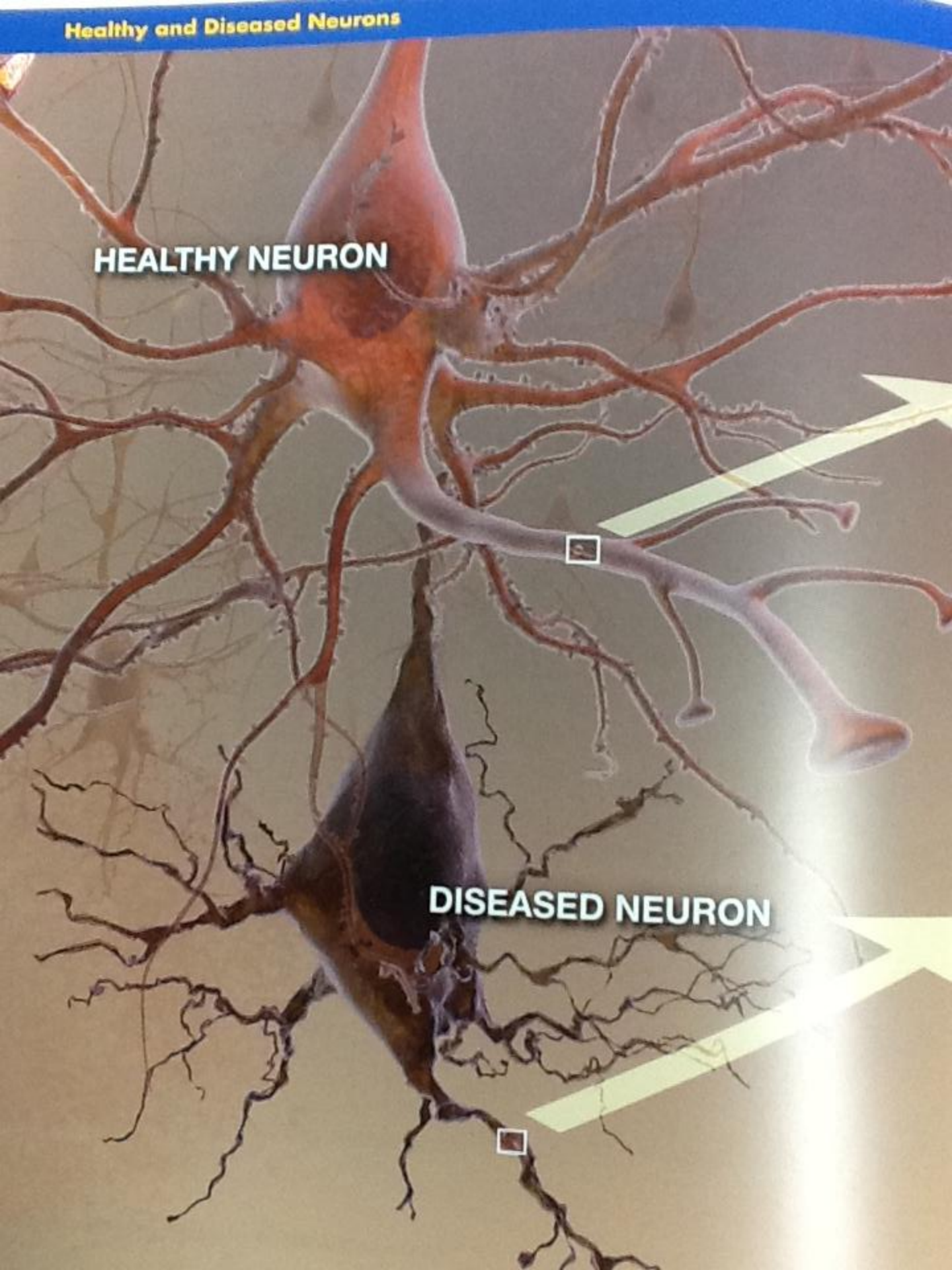
IS IT THE END OF STORY?

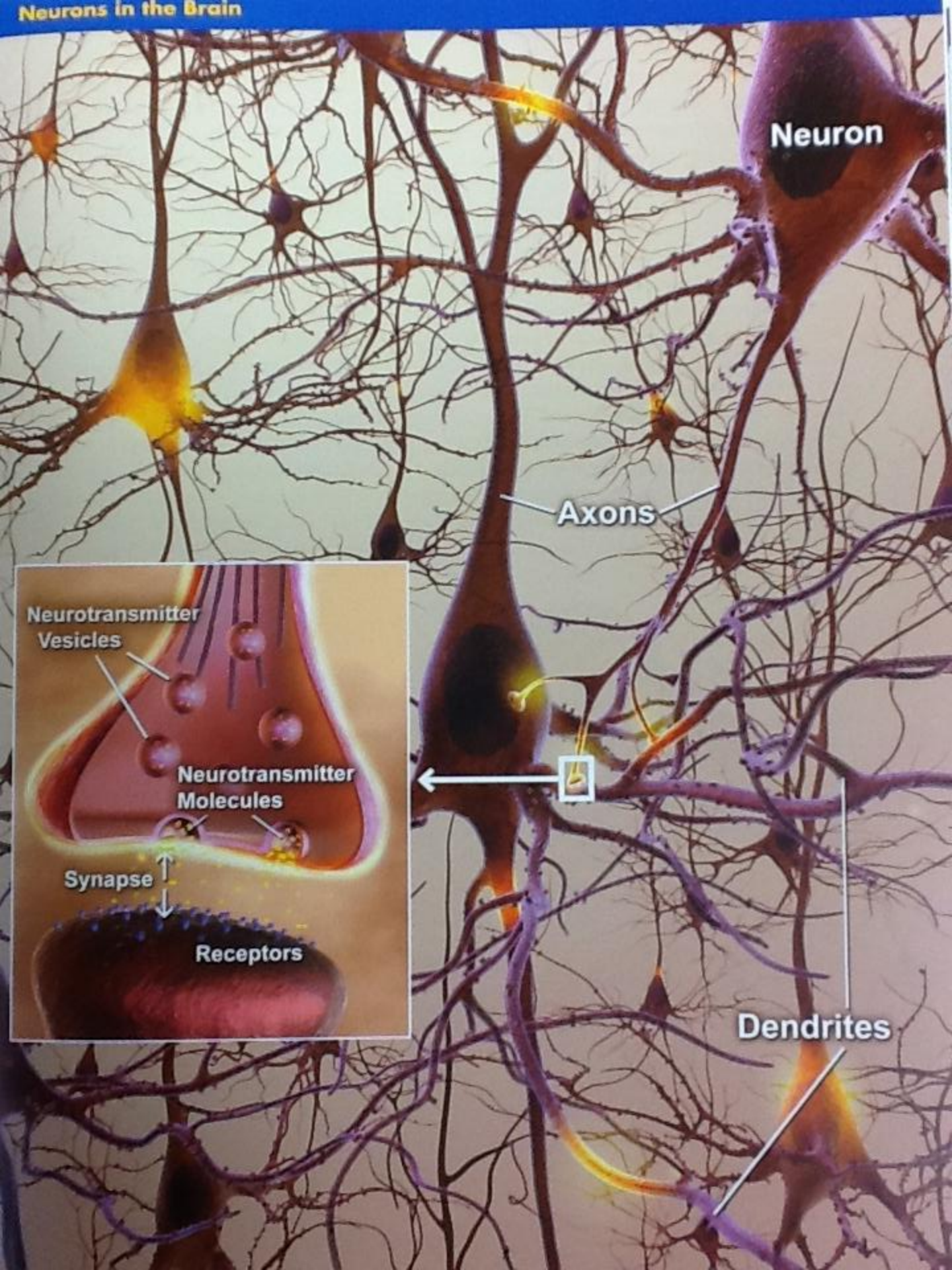

CT scan
PET scan
MRI scan

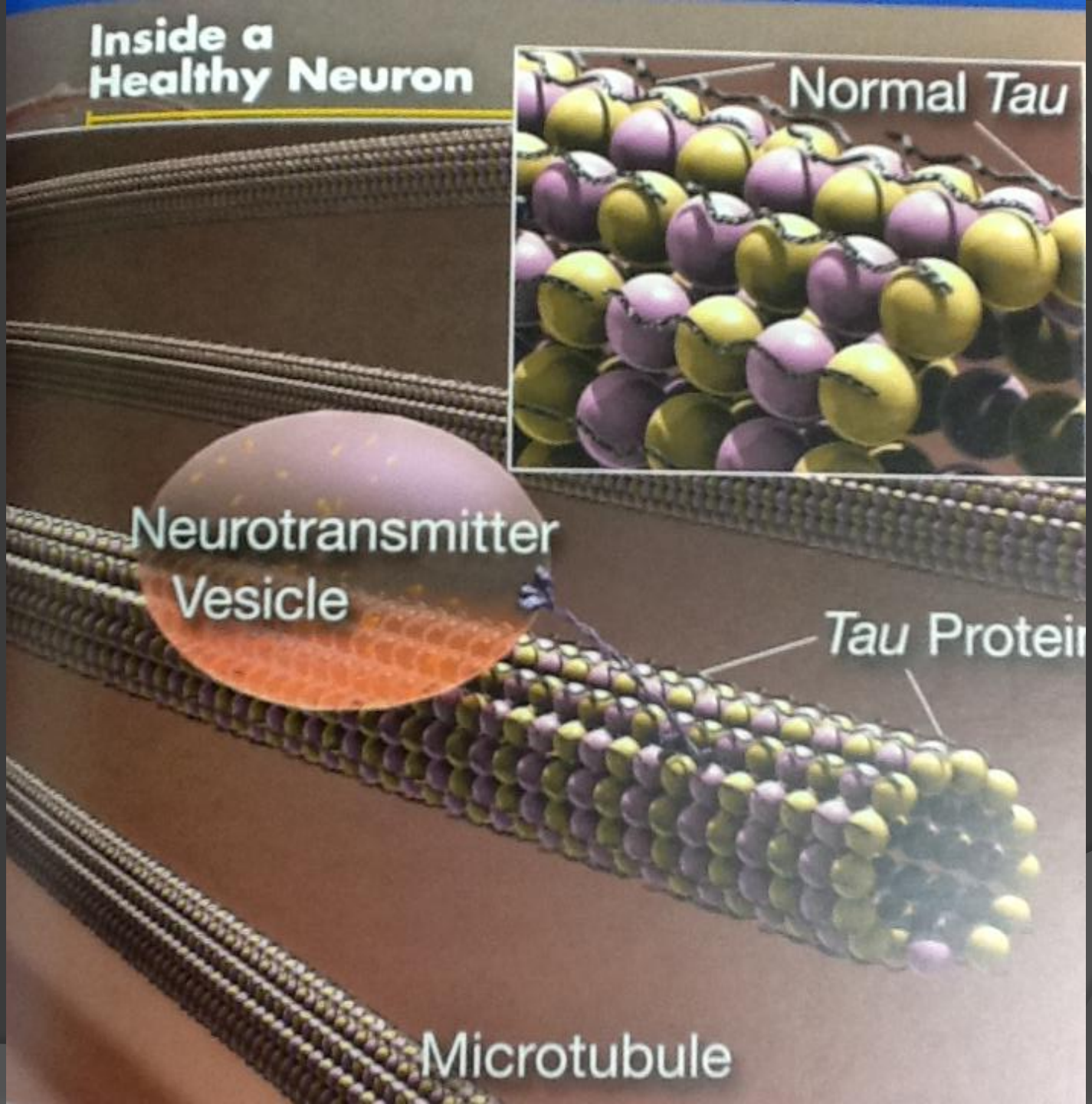
“This patient has dementia, none of the drugs work so there is little to do, so get your finances in order and plan for a painful next few years when you won't recognize your family, will need to live in a nursing home....."

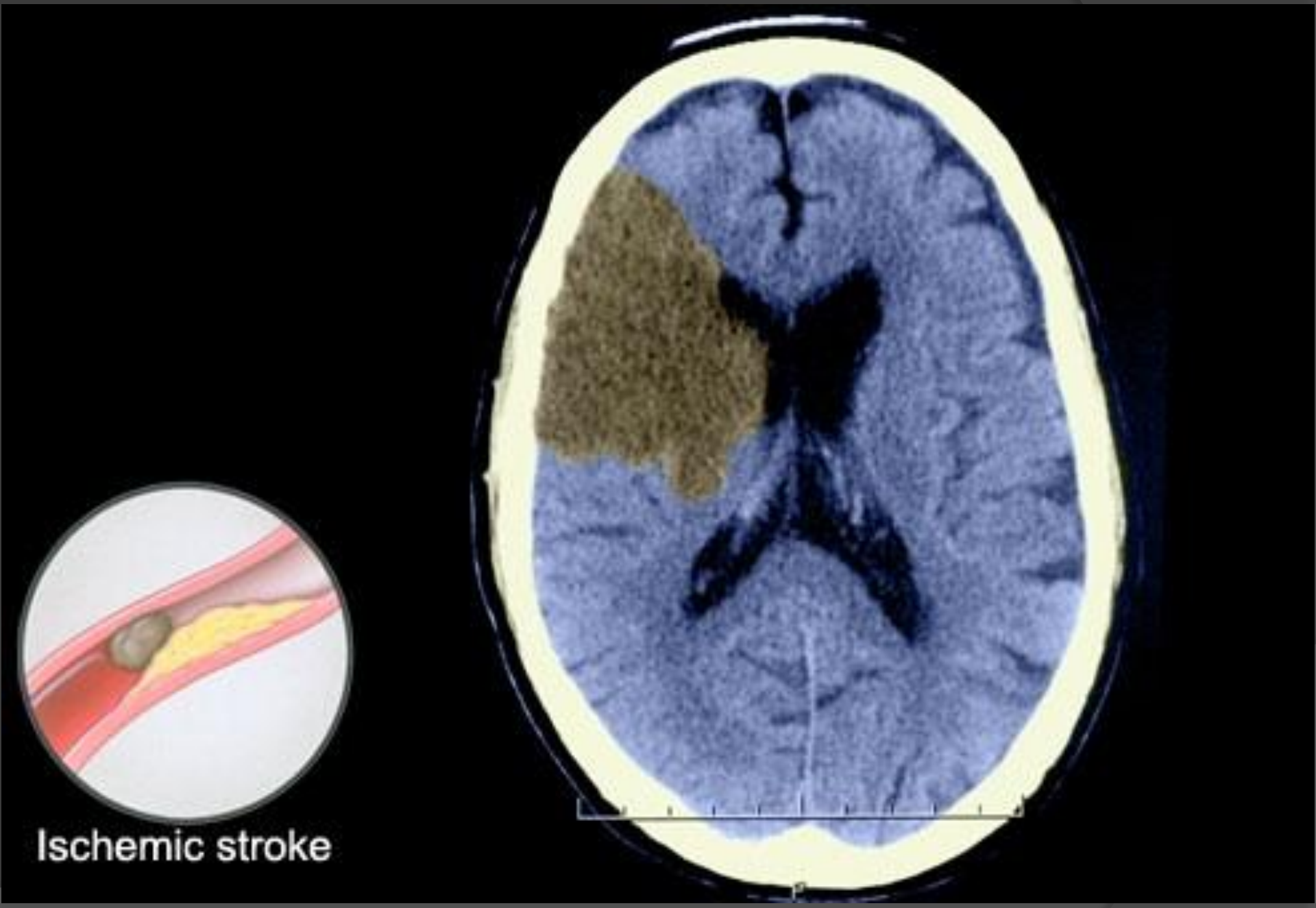

healthy
brain
advanced
alzheimer's

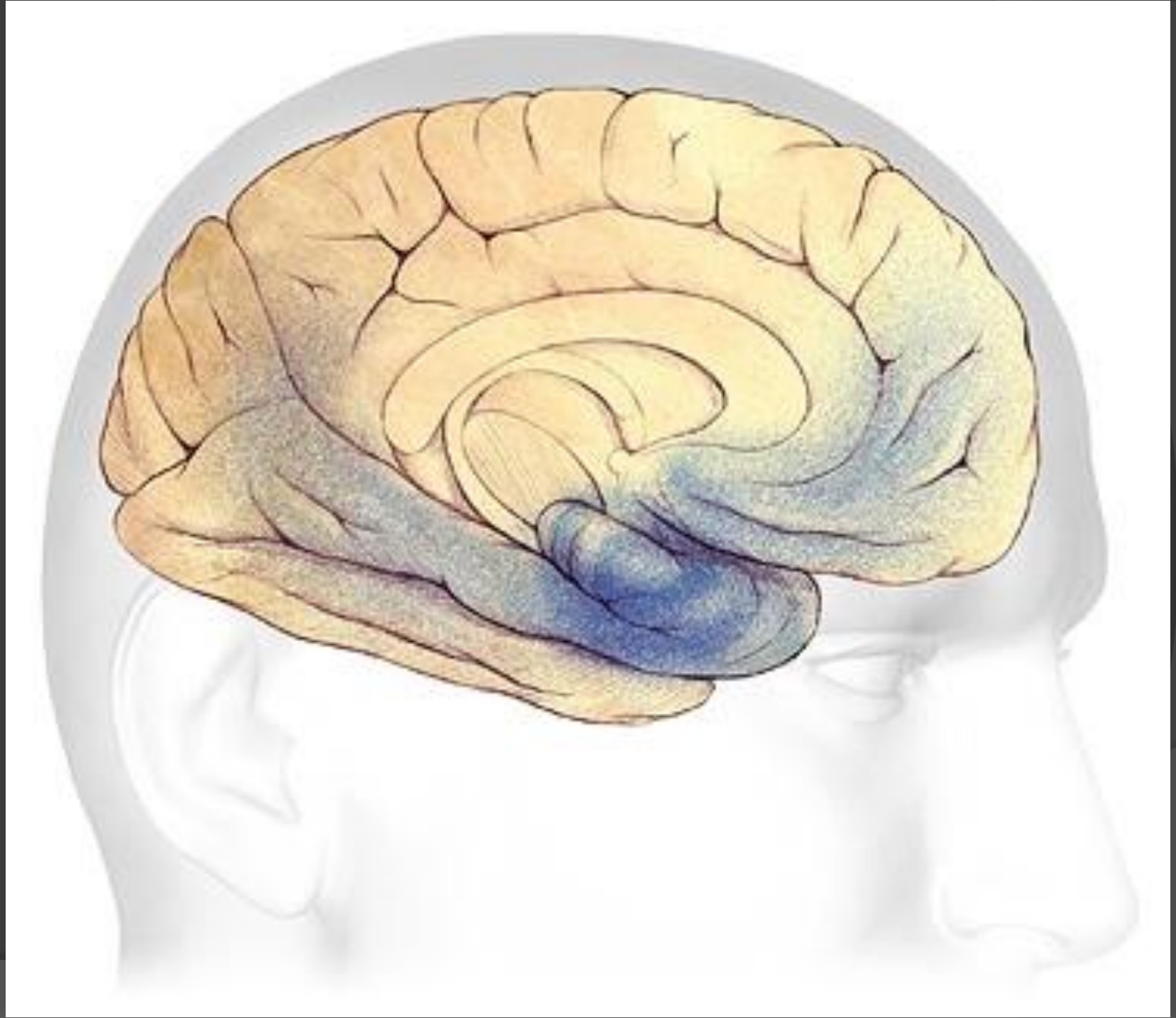

Alzheimer cells
healthy cells

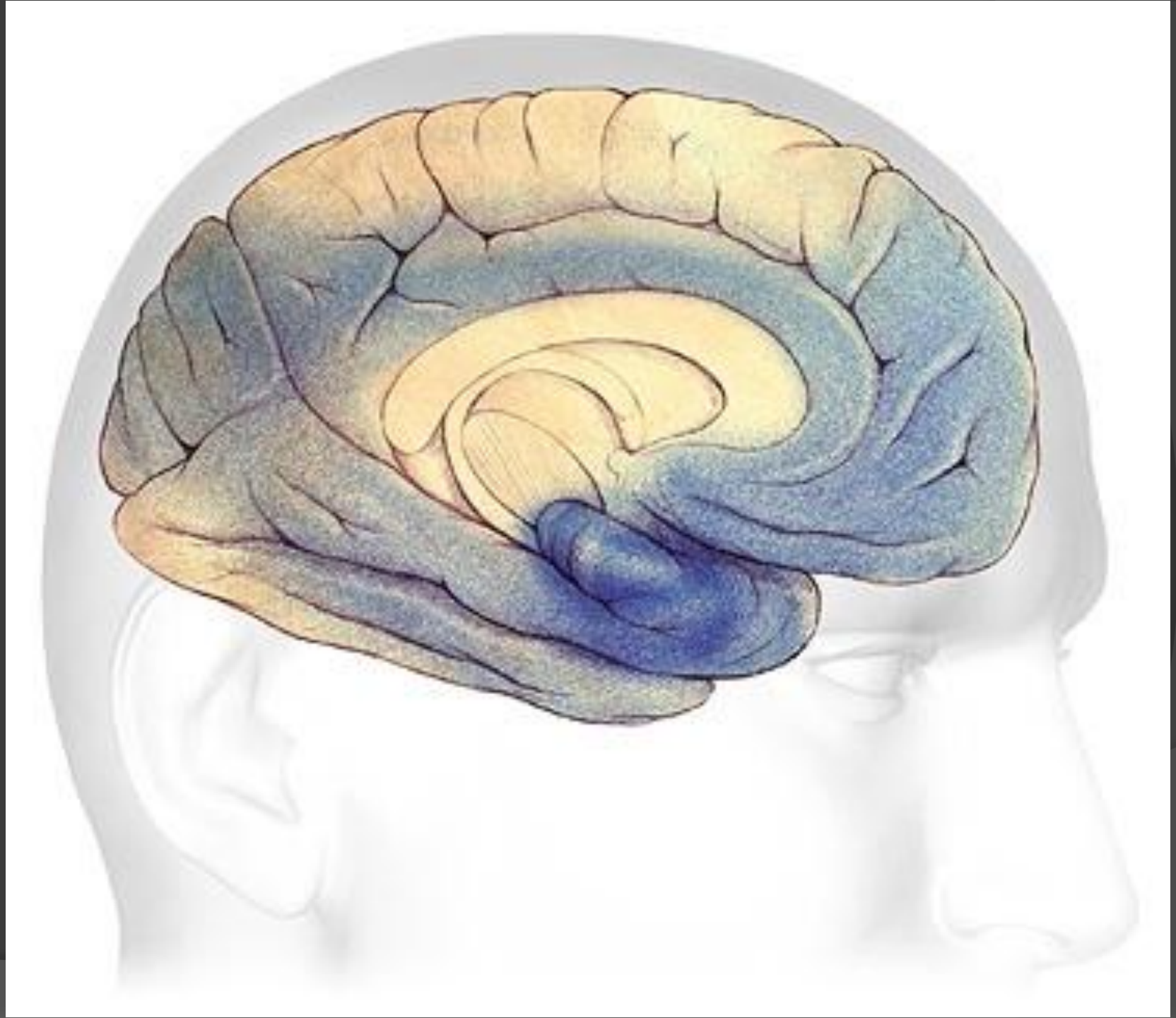

Healthy and Diseased Neurons
HEALTHY NEURON
DISEASED NEURON


Neurons in the Brain
Neuron
Axons
Neurotransmitter Vesicles
Neurotransmitter Molecules
Synapse
Receptors
Dendrites


Inside a
Healthy Neuron
Normal Tau
Neurotransmitter
Vesicle
Tau Protein
Microtubule

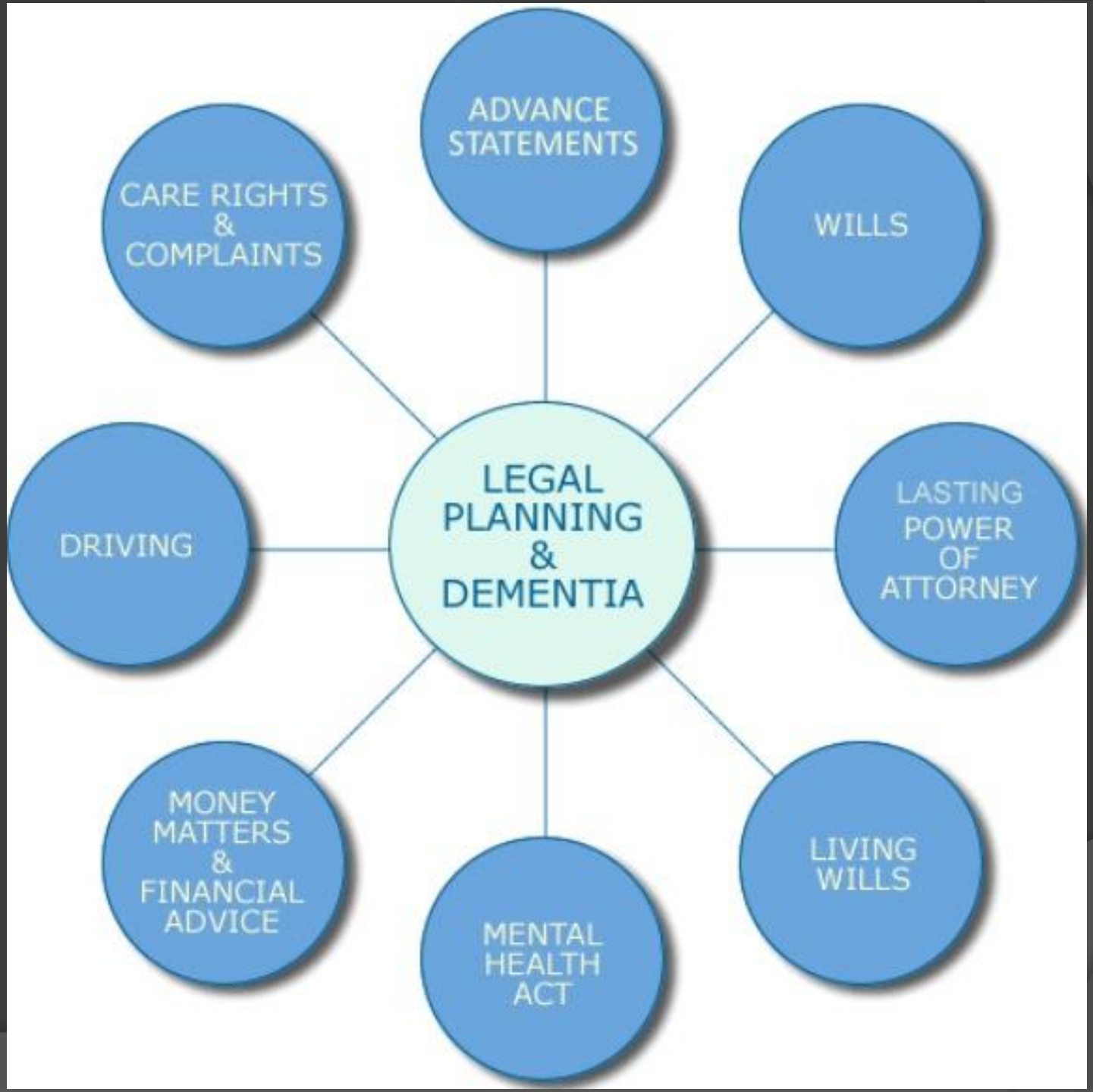

Ischemic stroke






EXIT
INTERNATIONAL
MARTIAL ARTS
ASSOCIATION


Where is my home?


LEGAL PLANNING & DEMENTIA
ADVANCE STATEMENTS
WILLS
LASTING POWER OF ATTORNEY
LIVING WILLS
MENTAL HEALTH ACT
MONEY MATTERS & FINANCIAL ADVICE
DRIVING
CARE RIGHTS & COMPLAINTS

Staging (Mild) (2-4 years)

- Problems coming up with the right word or name
- Trouble remembering names when introduced to new people
- Having greater difficulty performing tasks in social or work settings
- Forgetting material that one has just read
- Losing or misplacing a valuable object
- Increasing trouble with planning or organizing

Moderate (Middle) (2-10 years)

- Forgetfulness of events or about one's own personal history
- Feeling moody or withdrawn, especially in socially or mentally challenging situations
- Being unable to recall their own address or telephone number or the high school or college from which they graduated
- Confusion about where they are or what day it is
- The need for help choosing proper clothing for the season or the occasion
- Trouble controlling bladder and bowels in some individuals
- Changes in sleep patterns, such as sleeping during the day and becoming restless at night
- An increased risk of wandering and becoming lost
- Personality and behavioral changes, including suspiciousness and delusions or compulsive, repetitive behavior like hand-wringing or tissue shredding

Severe / Late-stage (1-3 years)

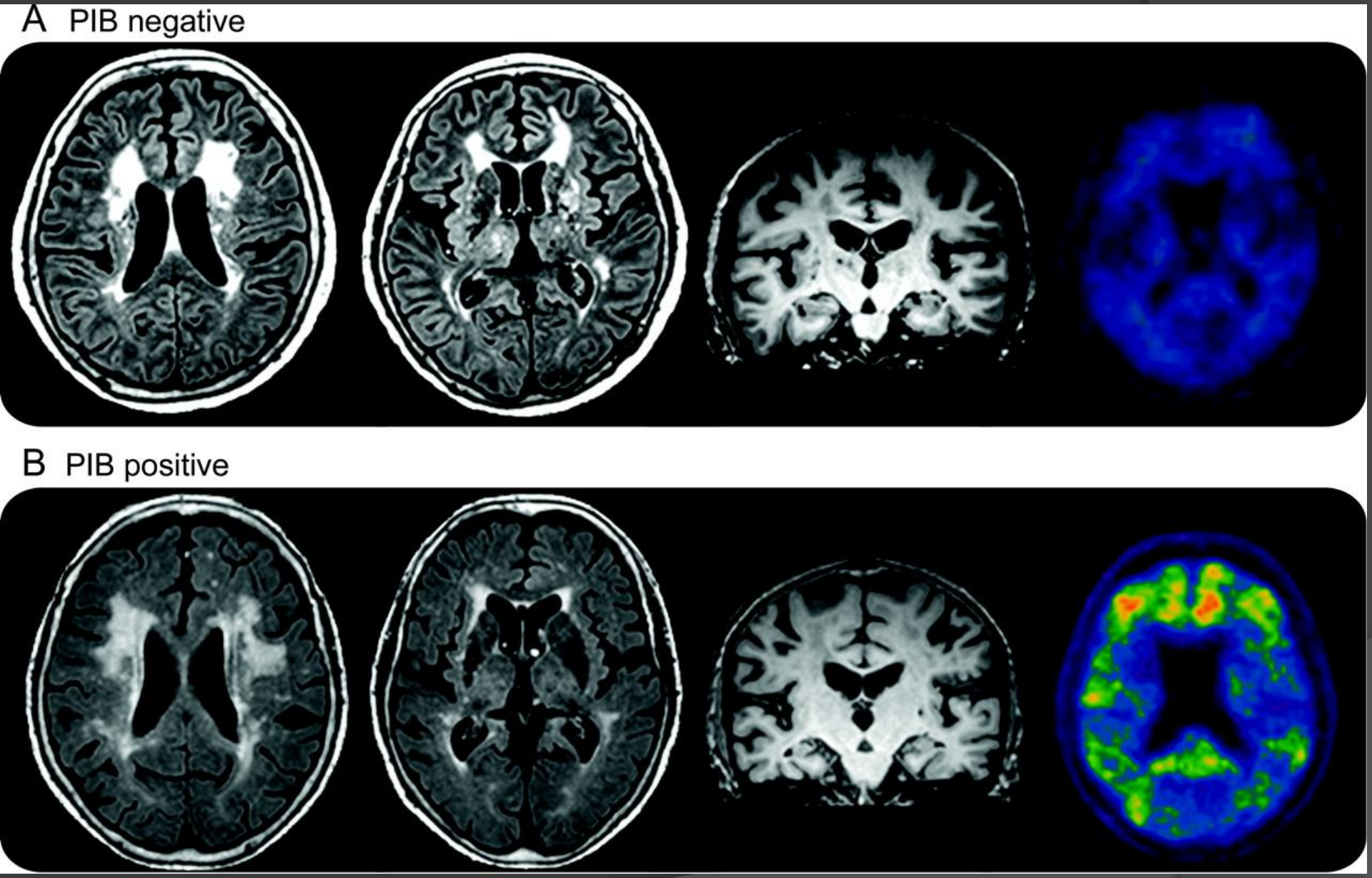
- Require full-time, around-the-clock assistance with daily personal care
- Lose awareness of recent experiences as well as of their surroundings
- Require high levels of assistance with daily activities and personal care
- Experience changes in physical abilities, including the ability to walk, sit and, eventually, swallow
- Have increasing difficulty communicating
- Become vulnerable to infections, especially pneumonia

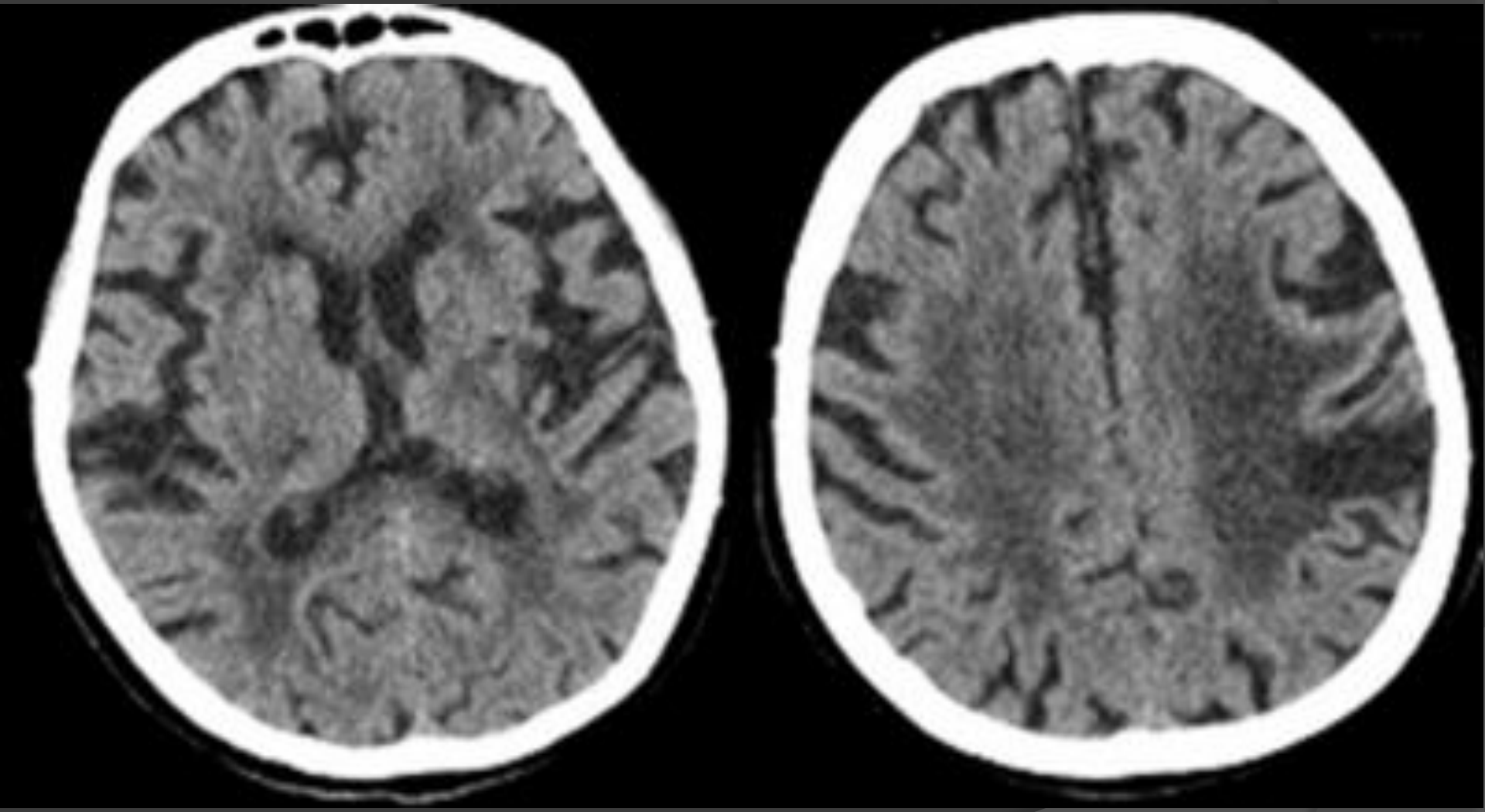
Types of Dementia

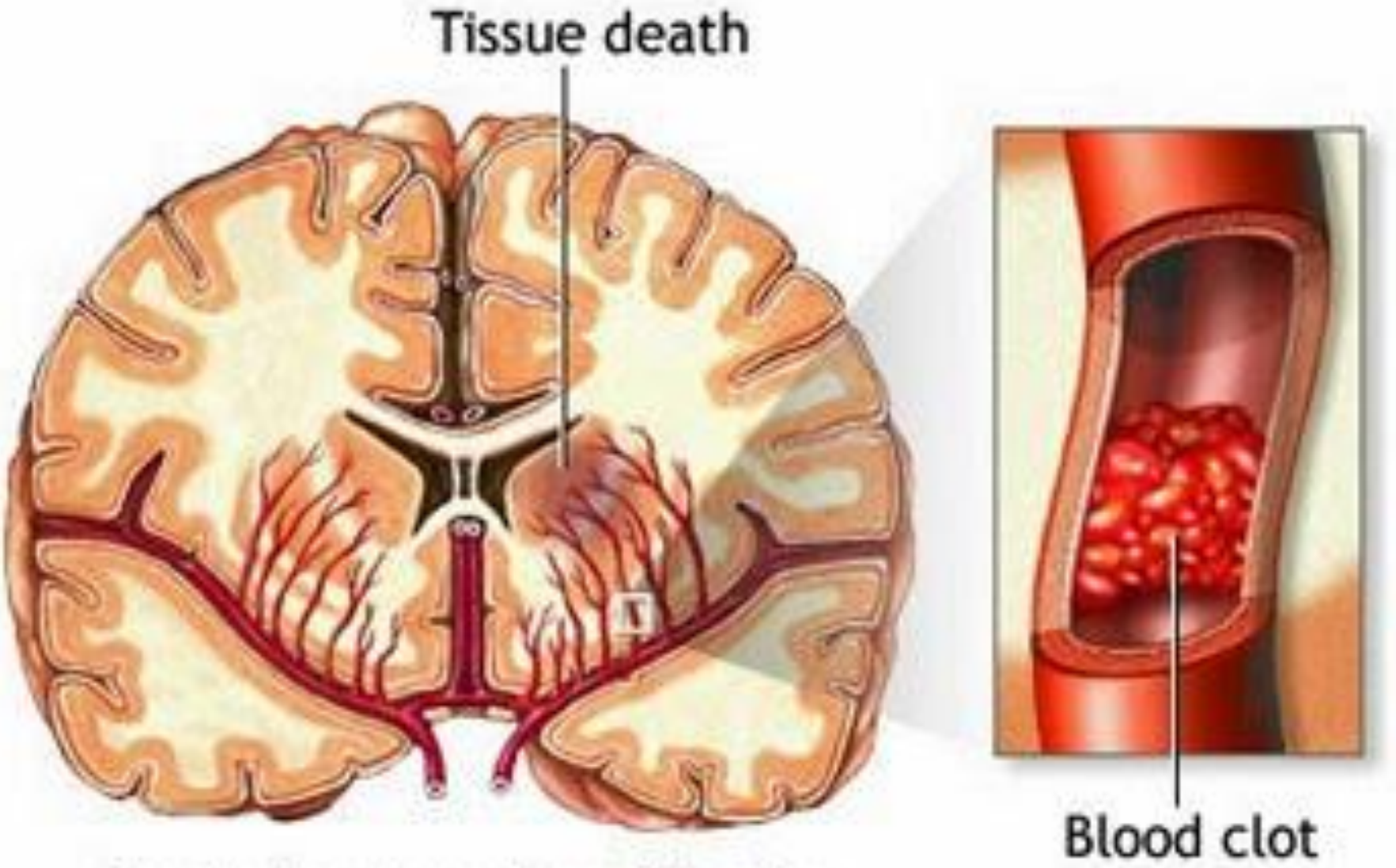
- Vascular Dementia
- Dementia With Lewy Bodies
- Mixed Dementia
- Parkinson's Disease Dementia

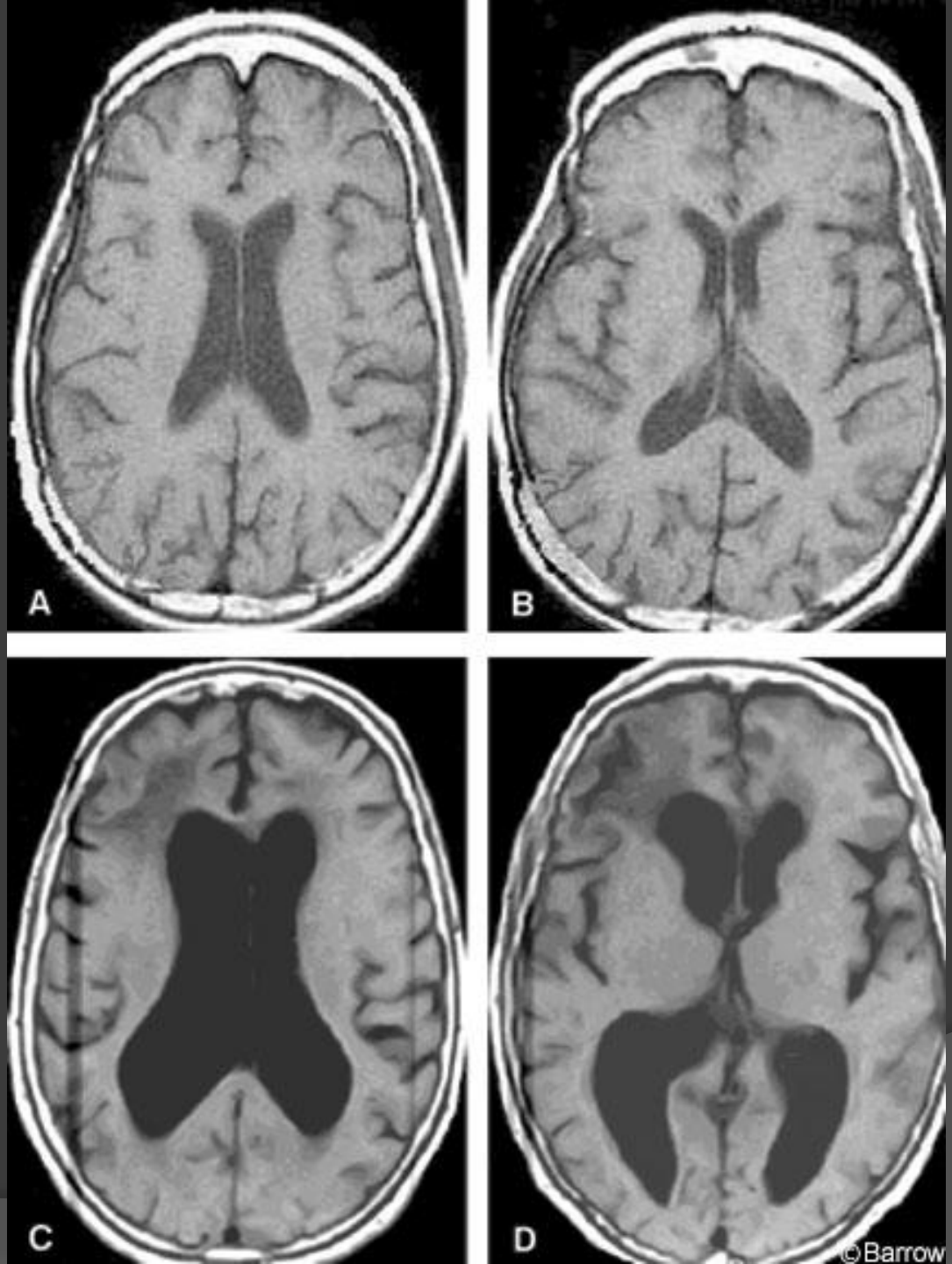
Types of Dementia

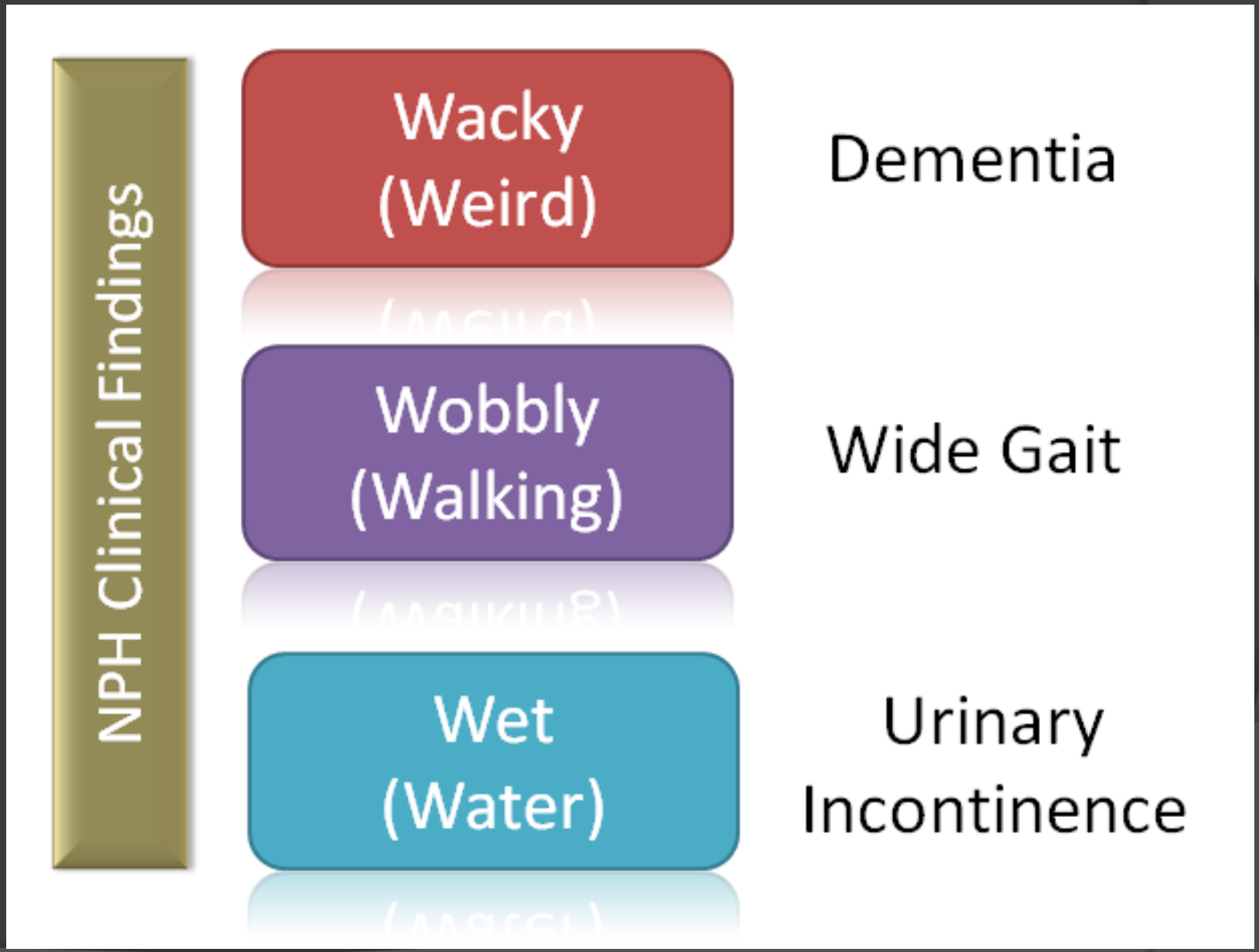
- Frontotemporal Dementia
  - Behavioral variant FTD
  - Primary progressive aphasia
  - Progressive supranuclear palsy
- Creutzfeldt-Jakob Disease
- Normal Pressure Hydrocephalus
- Wernicke-Korsakoff Syndrome

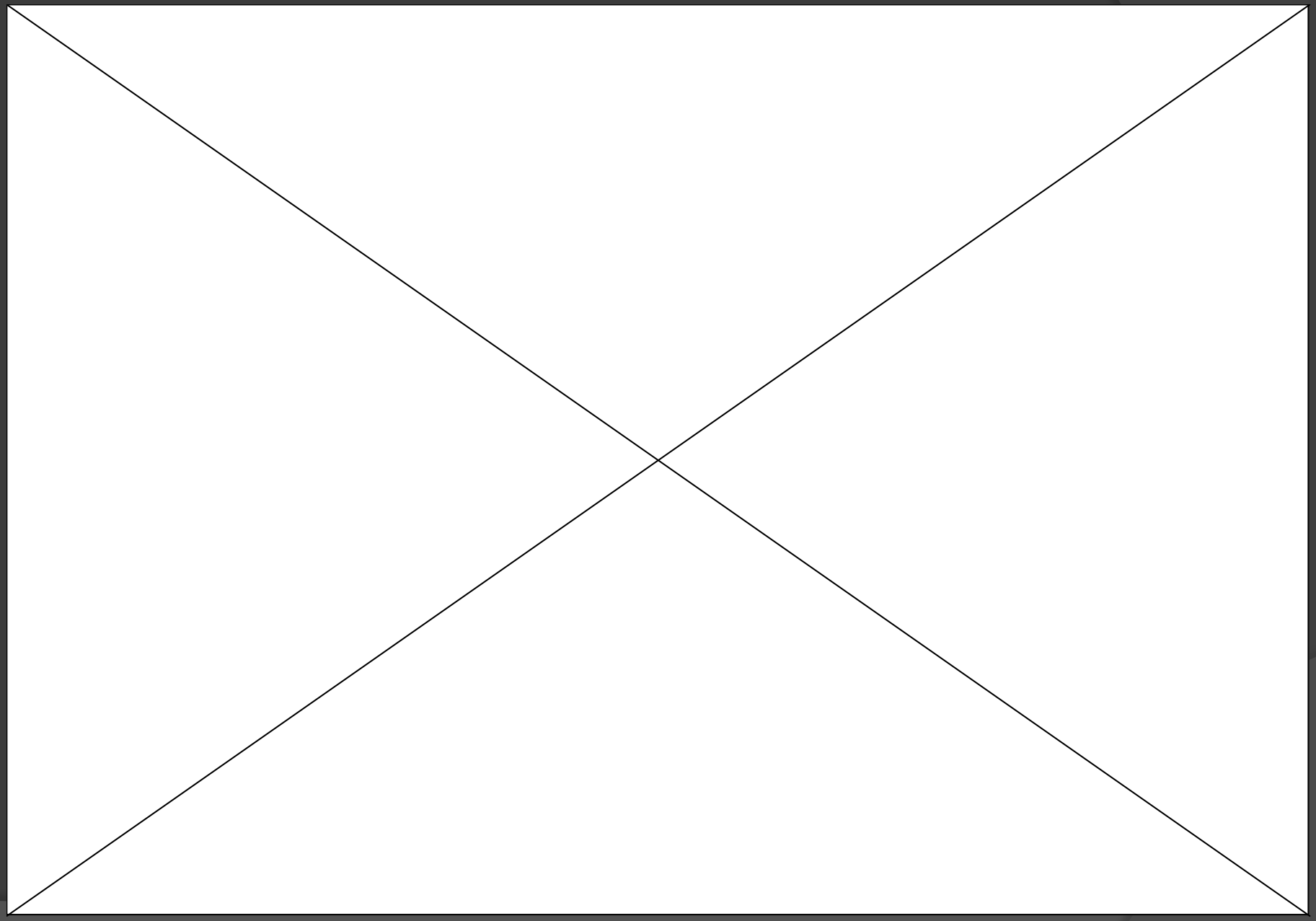

A PIB negative
B PIB positive

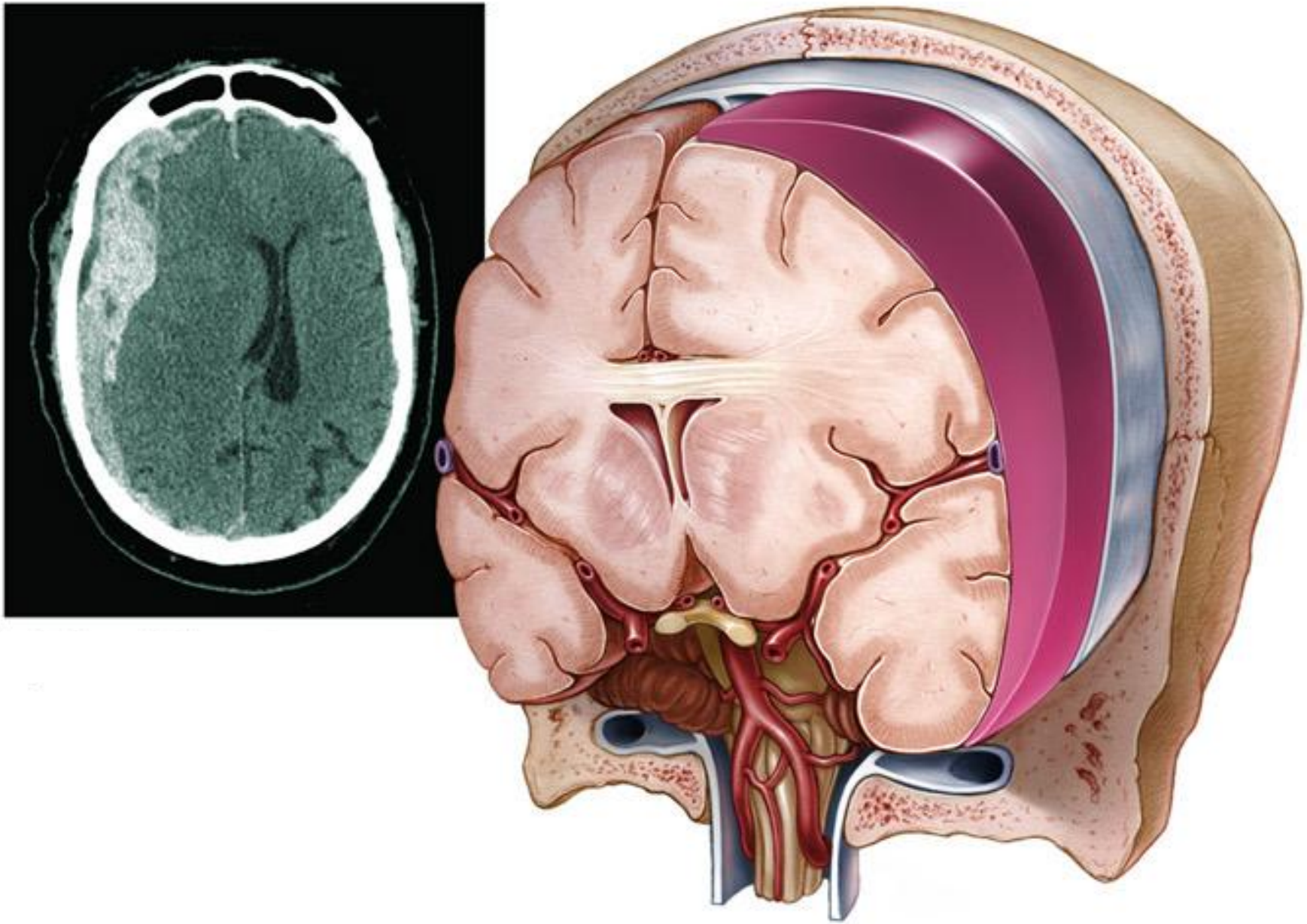



Tissue death
Blood clot
Frontal cut-section of brain
A.D.A.M.


A
B
C
D
©Barrow


NPH Clinical Findings
Wacky (Weird)
Dementia
Wobbly (Walking)
Wide Gait
Wet (Water)
Urinary Incontinence





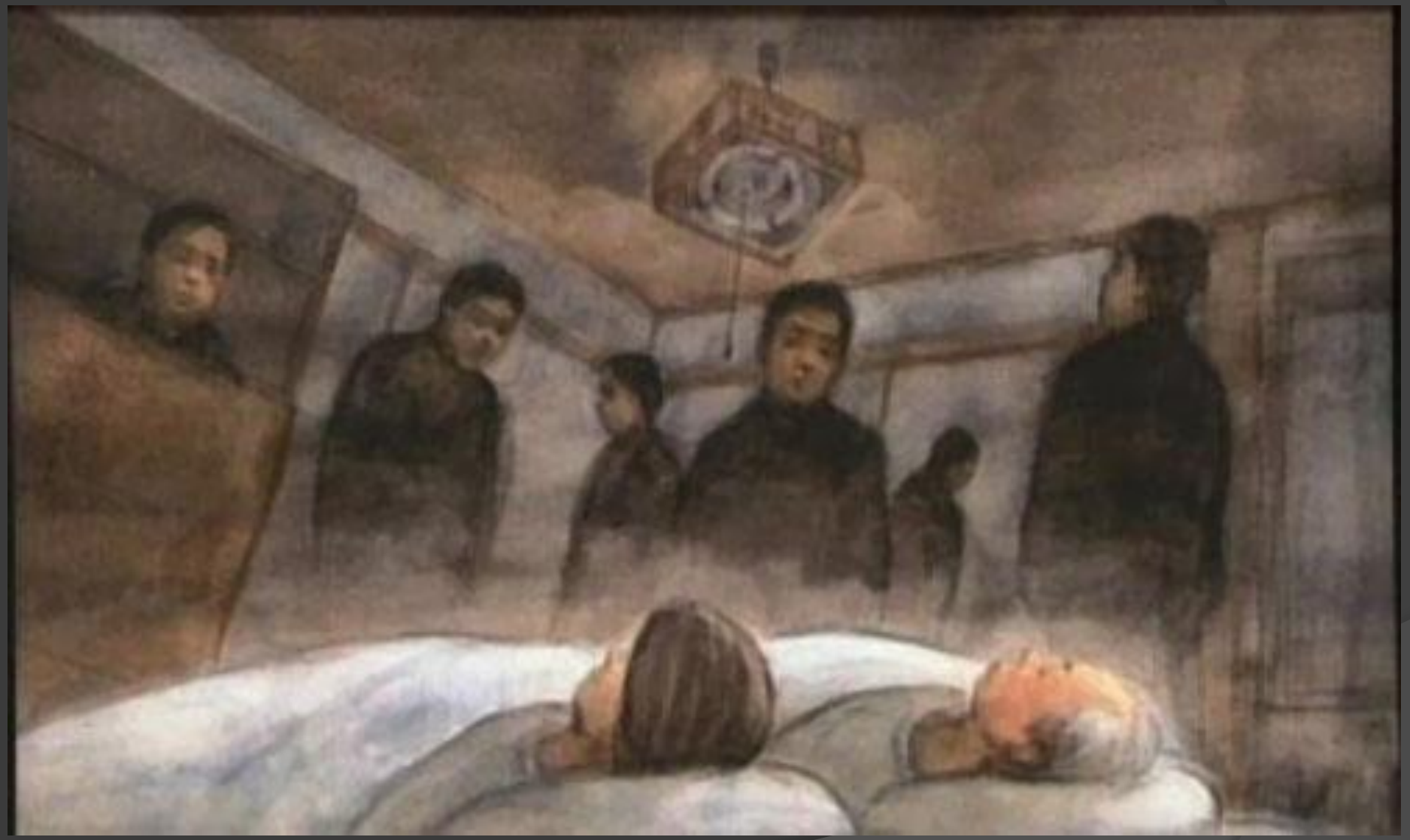
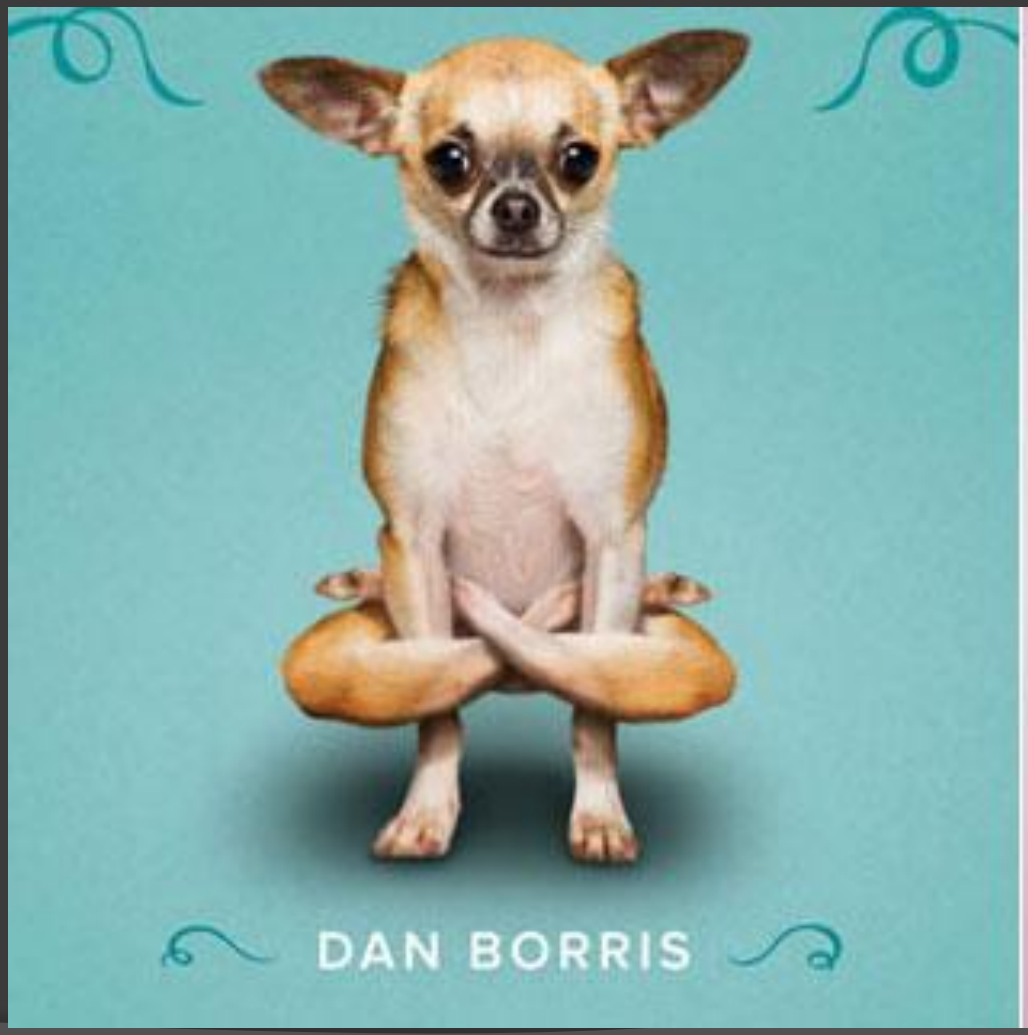
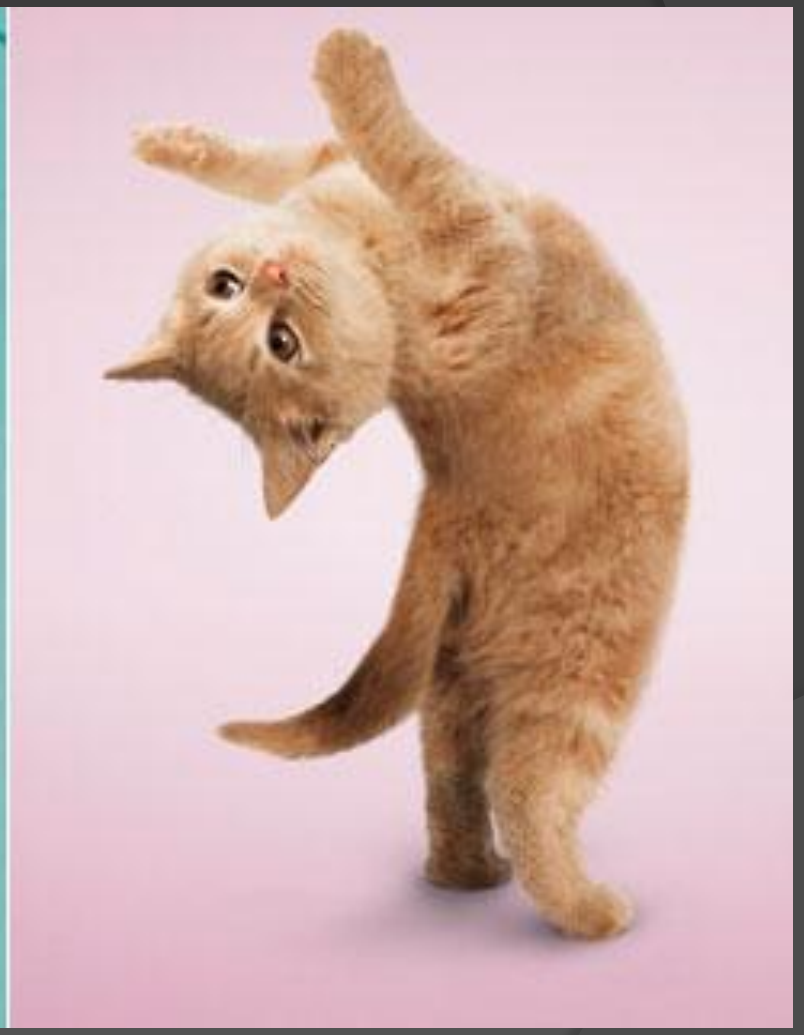


Table. **Genetic Factors Predisposing to Alzheimer Disease: Relationships to the β-Amyloid Phenotype**

Chromosome	Gene Defect	Phenotype
21	β-Amyloid precursor protein mutations	Increased production of all β-amyloid proteins or β-amyloid protein 42
19	Apolipoprotein E4 polymorphism	Increased density of β-amyloid plaques and vascular deposits
14	Presenilin 1 mutations	Increased production of β-amyloid protein 42
1	Presenilin 2 mutations	Increased production of β-amyloid protein 42

LET'S STRETCH





DEMENTIA, DELIRIUM

Video 1 & 2

Case 1

- Mr. E is a 71 yo wm with hx of asthma, BPH and HTN admitted to medicine 3 days ago for bilateral lower extremity cellulitis and asthma exacerbation. A the time of admission he was cooperative and oriented but over the past 24 hours has become occasionally confused, agitated, uncooperative and somnolent. He appears to be talking to someone in his room when no one is there.

Conti...

His current meds include: lisinopril, naproxen, cimetadine, albuterol/ipratroprium inhaler, levofloxacin, oxygen via nasal canula prn

He has no known psych history, drinks 1-2 glasses of wine/night

Family thinks he has gone “crazy” and wants to talk to somebody right away and YOU are the only one there to talk to them

Conti...

- Vitals: 99.8, 110/60, 110, 20, 83%
- When you speak to him he is difficult to rouse and falls asleep several times. He struggles to maintain focus on questions and is unable to perform the mental status exam. He believes he is in Oklahoma and that you are his cousin.
- When you are talking to family – he is grabbing things in the air.
- Jerks his arms while trying to drink water

What points to delirium?

Any Ideas?

Case 1

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What exam will you do?

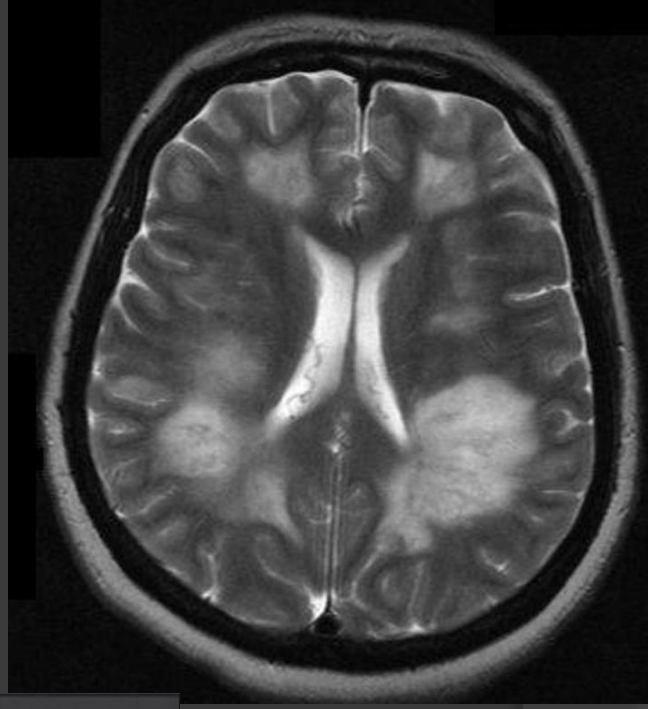
- Other than usual stuff
  - Look for source of pain
  - Bladder / bowel (story of kinked catheter)
  - Touch where it hurts
  - Look at “meds - IVs” running into pt
- Detailed neurological exam

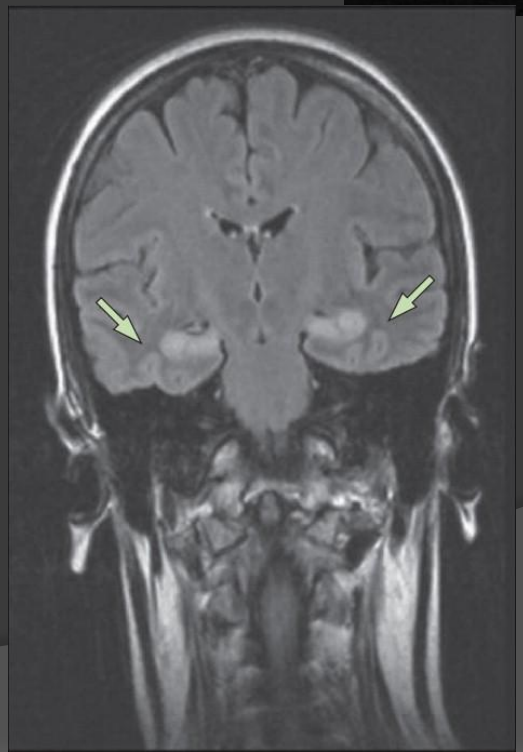
What labs will you order?

- Vitals, bed side glucose, pulse ox, orthostatics
- CBC,
- CMP (electrolytes, liver and renal function)
- Vit B12
- Thyroid function test
- Ammonia
- ABG
- Urine Analysis
- Cultures (blood, urine, etc.)
- UDS

Any thing else?

- X-ray Chest, abdomen
- CT head
- MRI Brain
- MRI Brain with/without contrast
- EEG
- Lumbar Puncture





DSM IV Criteria

1. Disturbance of consciousness with reduced ability to focus, sustain or shift attention.
2. A change in cognition or development of perceptual disturbances that is not better accounted for a preexisting, existed or evolving dementia.
3. The disturbance develops over a short period of time and tends to fluctuate during the course of the day
4. There is evidence from this hx, PE or labs that the disturbance is caused by the physiological consequence of a medical condition.

Types of delirium

- Hyperactive or hyperalert
  - the patient is hyperactive, combative and uncooperative.
  - May appear to be responding to internal stimuli
  - Frequently these patients come to our attention because they are difficult to care for.

Types of delirium...

- Hypoactive or hypoalert
  - Pt appears to be napping on and off throughout the day
  - Unable to sustain attention when awakened, quickly falling back asleep
  - Misses meals, medications, appointments
  - Does not ask for care or attention
  - This type is easy to miss because caring for these patients is not problematic to staff

Which one is common?

Hypo OR Hyper Active

Etiology: Drugs

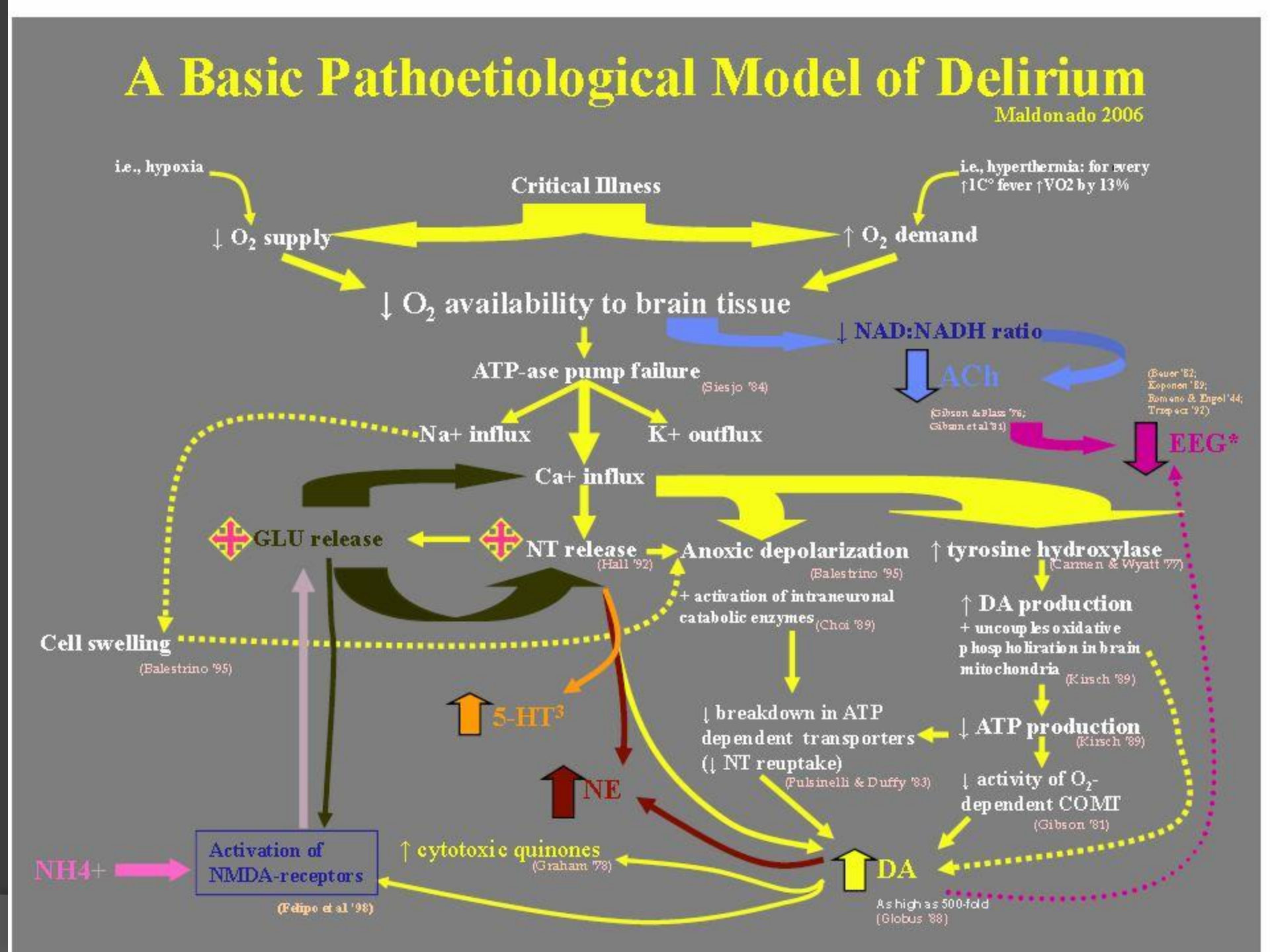
- Anticholinergics (furosemide, digoxin, theophylline, cimetidine, prednisolone, TCA's, captopril)
- Analgesics (morphine, codeine..)
- Steroids
- Antiparkinson (anticholinergic and dopaminergic)
- Sedatives (benzodiazepines, barbiturates)
- Anticonvulsants

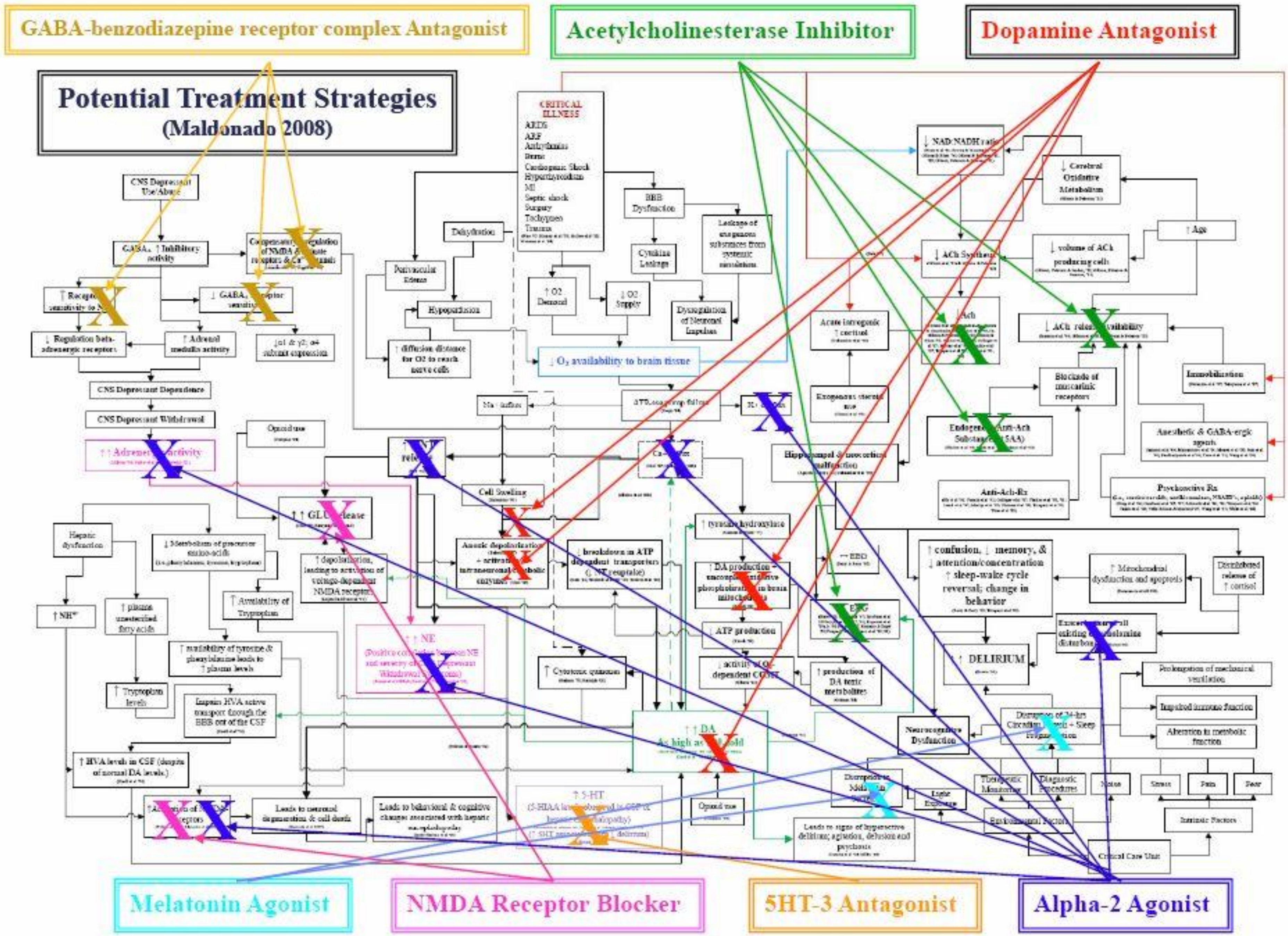
Etiology: Drugs continued

- Antihistamines
- Antiarrhythmics (digoxin)
- Antihypertensives
- Antidepressants
- Antimicrobials
- Sympathomimetics
- Antidiarrheal
- Antispasmodic

A Basic Pathoetiological Model of Delirium

Maldonado 2006





GABA-benzodiazepine receptor complex Antagonist
Acetylcholinesterase Inhibitor
Dopamine Antagonist
Potential Treatment Strategies
(Maldonado 2008)
CRITICAL ILLNESS
ARDS
ARF
Cardiogenic Shock
MI
Septic shock
Surgery
BBB Dysfunction
Dehydration
Perivascular Edema
Hypoperfusion
↑ diffusion distance for O2 to reach nerve cells
↑ O2 Demand
↓ O2 Supply
Dysregulation of Neuronal Impulses
↓ O₂ availability to brain tissue
CNS Depressant Use/Abuse
CNS Depressant Dependence
CNS Depressant Withdrawal
Opioid use
↓ Regulation beta-adrenergic receptors
↑ Adrenal medulla activity
↓ NAD:NADH ratio
↓ Cerebral Oxidative Metabolism
↑ Age
↓ ACh Synthesis
↓ volume of ACh producing cells
Acute iatrogenic ↑ cortisol
↓ ACh release/availability
Blockade of muscarinic receptors
Immobilization
Exogenous steroid use
Anesthetic & GABA-ergic agents
Anti-Ach-Rx
Psychoactive Rx
Hippocampal & neocortical malfunction
Cell Swelling
Hepatic dysfunction
↑ NH⁺
↑ plasma unesterified fatty acids
↑ Availability of Tryptophan
↑ Tryptophan levels
Impairs HVA active transport through the BBB out of the CSF
↑ HVA levels in CSF (despite of normal DA levels)
↑ tyrosine hydroxylase
↓ breakdown in ATP dependent transporters
↓ ATP production
↑ production of DA toxic metabolites
↑ Cytotoxic quinones
↑ confusion, ↓ memory, & ↓ attention/concentration ↑ sleep-wake cycle reversal; change in behavior
↑ Mitochondrial dysfunction and apoptosis
Diminished release of ↑ cortisol
↑ DELIRIUM
Neurocognitive Dysfunction
Prolongation of mechanical ventilation
Impaired immune function
Alteration in metabolic function
Leads to neuronal degeneration & cell death
Leads to behavioral & cognitive changes associated with hepatic encephalopathy
Leads to signs of hyperactive delirium; agitation, delusion and psychosis
Opioid use
Light Exposure
Therapeutic Monitoring
Diagnostic Procedures
Noise
Stress
Pain
Fear
Environmental Factors
Intrinsic Factors
Critical Care Unit
Melatonin Agonist
NMDA Receptor Blocker
5HT-3 Antagonist
Alpha-2 Agonist

Treatment

- Treat the cause
- Take away meds
- Non-pharmacological
- Rarely antipsychotics

My Note: AMS1

- This patient's encephalopathy, seem to have multifactorial etiology.
- Toxic-metabolic derangement are common cause of acute encephalopathy in vulnerable population. Common derangements are hypo/hyperglycemia, dehydration, electrolyte imbalance, acute renal insufficiency, liver failure, endocrinopathies.
- - Please check CBC, CMP, calcium, finger stick glucose, ammonia, TSH, UDS (if not already checked)
- Patient doesn't seem to have sensory aphasia (Wernicke's aphasia), neglect syndrome, cortical blindness. Lesion in silent areas of brain can be difficult to appreciate on neurological exam.
- - Consider MRI brain to look for lesion.
- Post ictal confusion (may be seizure was not witnessed) or sub-clinical status epilepticus, should be considered.- Consider EEG

AMS2

- - Poor pain control can cause confusional state in patients with poor cognitive reserve.
- Psychotropic medication overdose, withdrawal and improper use can lead to acute encephalopathy.
- - Please avoid anticholinergics, older generation anti-psychotics, anti-histaminics etc.
- Hypoxia and hypercarbia can also cause acute encephalopathy.
- - Please consider ABG
- Acute bladder distension
- - Please consider in and out cath to check for residual bladder volume.
- Bowel impacted by stool
- - Please consider x-ray abdomen
- - Consider placing nicotine patch in smokers.
- Please give multivitamin, minerals, THIAMINE 100 mg, if suspect use of alcoholism or malnutrition from any cause.
- Sleep deprivation and circadian rhythm abnormalities in vulnerable population can cause confusional state.

AMS3

- Non phamacological measures/instructions for nursing staff:
- Provide frequent orientation/reorientation (date, day, month on notice board)
- Room should be well lit during day time and turn off lights at night time.
- Avoid unnecessary interruption to patient's sleep.
- Turn off TV, if patient is not watching and specially at night time.
- Avoid noisy environment to facilitate sleep/rest.
- Remove Foley catheter/NG tube as soon as possible.


Work
Let's go Racing