MUSCULOSKELETAL SYSTEM
A&P REVIEW

STARTING POINTS

- Provide support and protection, and permits movement
- Provides points of attachment for muscles
- Important sources of vitamins and minerals
- Bone formation begins in utero and is continuously being reabsorbed and synthesized
- Bones consist of spongy and compact
- Source of mesenchymal stem cells (bone marrow)

BONE COMPONENTS

Cortical (compact) bone 80-85%

- Dense, highly organized, extremely strong
- Has haversian system
- Outer supporting structure
- Radius, skull, and long bones

Cancellous bone (spongy) 15-20%

- Less complex, irregular meshwork formation "honeycomb"
- No haversian system but trabeculae arranged a long lines of stress
- Inner supporting structure
- Found in areas of bone not subjected to stress
- Ribs, shoulder blades, flat bones of the skull

All bones have

periosteum –double-layer connective tissue
bone marrow

BONE MATRIX

○ 35% organic ○ Collagen	○ 65% inorganic ○ Calcium & phosphorus

- Other parts proteins, carbohydrates-protein complexes, ground substances
- Calcification begins as extracellular CA++ enters the matrix and forms hydroxyapatite crystals
- Contains 5-8% water

BONE MATRIX COMPONENTS

Proteoglycans	Glycoproteins
Strengthen bone by forming compression resistant networks between collagen fibrils	Bone sialoprotein Osteocalcin Osteonectin

Also control the transport and distribution of CA++ through the bone matrix	bone albumin Alk phosph Control the collagen interactions that lead to fibril formation Also play role in calcification

BONE CELLS

- Osteoprogenitor cells differentiate into Osteoblasts >>> osteocytes (do not divide)
    - Osteoblasts-bone forming cells primary function to lay down new bone
    - Osteocytes –osteoblast that has become imprisoned within matrix of mineralized bone
- Monocyte line >>> Osteoclasts
    - primary function to RESORB (remove) bone during growth and repair

OSTEOBLASTS

- Fill in bony cavity w/ bone matrix – synthesis of osteoid formation
- Produce several substances
    - Osteocalcin, TGF-b, macrophage-stimulating growth factor, RANKL, OPG
- Triggers for activity = parathyroid activity, thyroxine, and growth factors
    - Interleukins 1-6-11 & transforming growth factor B, & insulin-like growth factor
- Releases cytokines to attract Osteoclasts
- 60 – 80 % of osteoblasts die by apoptosis
- An increase in reactive oxygen species (ROS) has been implicated in the decreased bone formation associated with advancing age

RANKL and OPG

- RANKL induces osteoclast activation and bone reabsorption
- OPG (a protein) binds to a protein called OPG ligand serves as a decoy for RANKL and blocks osteoclast formation = reduced bone reabsorption
- Balance between these 2 determine bone quality

OSTEOCYTES

- Transformed osteoblasts (trapped in osteoid and hardens from minerals during ossification)
- Osteocytes secrete growth factors that regulate bone formation
- Endocrine receptors for PTH
- Mature osteocytes secrete sclerostin = inhibition of bone formation
- Respond to mechanical strain

- Send signals of bone formation or bone resorption to the bone surface
- Manage the microenvironment
- Regulate both local and systemic mineral homeostasis
    - Calcium, phosphorus, other minerals

OSTEOCLASTS

- Terminally differentiates monocytes responsible for bone resorption
- Contain lysosomes
- Release proteases
    - Dissolves bone mineral matrix
    - Dissolves collagen
- Clears away damaged bone- bind to surface of bone by integrins and use adhesive structures called podosomes
    - Ruffled border
- Releases matrix-bound growth factors
    - Chemoattractant for Osteoblasts
- Assist endocrine and renal systems
    - Maintain appropriate CA++ concentrations

OSTEOCLAST

Inhibition	Activation
Decreases bone resorption Molecules OPG Calcitonin Estrogen TGF-b IL-10	Stimulates bone resorption RANKL PTH IL-1 1,25 dihydroxy Vitamin D PGE2

COLLAGEN

- 90% type 1 collagen for strength
- Synthesized and secreted by osteoblasts
- Tensile strength and ability to bear weight
- Most abundant macromolecule within the body
- 1/3 of all protein
- Provide structural framework for all tissue
- More than 20 different types

Type of collagen	Distribution
• Type I	• Bone, ligament, vertebral disks, muscle
• Type II	• Cartilage, vertebral disks
• Type III often w/ Type1	• Skin and muscle cells
• Type IV	• Basement cell membrane, muscle
• Type IX co-distributed with Type II muscle	• Cartilage, muscle • "glue" holds together Type II articular cartilage
• Type V Co-distributed w/ Type I muscle	• Blood vessel wall, synovium, tendon, cartilage, skeletal muscle
• Type X	• Cartilage growth plate

HORMONES INVOLVED IN BONE FORMATION

- Calcitonin
  - Secreted from C-cells in the thyroid gland
  - Inhibits bone resorption
  - Inhibits intestinal CA+ & PO4 absorption
  - Inhibits renal CA+ reabsorption =excretion
  - Inhibits calcitriol production in kidneys
- Calcitriol
  - Form of Vitamin D (active form)
  - Increases intestinal CA+ absorption
  - Increases intestinal PO4 absorption
  - Increases intestinal MG absorption
  - Decreases PTH secretion

- PTH
    - Released from the parathyroid gland in response to calcium levels
    - Mobilizes CA+ & PO4 from bone
    - increases calcitriol

FACTORS AFFECTING BONE FORMATION

- Glucocorticoids — Inhibition of bone formation is the major cause of glucocorticoid-induced osteoporosis and may be due to accelerated apoptosis of osteoblasts and osteocytes
- Thyroid hormones stimulate both bone resorption and formation. Thus, bone turnover is increased in hyperthyroidism, and bone loss can occur

BONE PHYSIOLOGY

- Micro-fractures occur daily via “wear and tear”- healed by remodeling
- 120-day cycles
    - >>> reabsorption of osteoclast in 20 days
    - >>> bone formation by osteoblasts in last 100 days

BONE MODELING AND REMODELING

- During development and growth, the skeleton is sculpted to achieve its shape and size by the removal of bone from one site and deposition at a different one = called modeling
- After the skeleton has reached maturity, regeneration continues in the form of a periodic replacement of old bone with new at the same location = called remodeling
- complete regeneration of the adult skeleton every 10 years

RESORPTION AND MINERALIZATION

- cycle begins with osteoclast generation and recruitment to a particular site
    - Under physiologic conditions such site may be in need for repair while under pathologic conditions it may be randomly and inappropriately targeted.
- newly formed osteoid begins to mineralize after about two weeks
- Mineralization occurs rapidly at first, then more slowly
- It takes several years for a bone structural unit to become fully mineralized.

REMODELING (MICROFRACTURES)

- Clusters of cells (called bone-modeling units -BMU) are responsible for maintaining the structure of the bone
- Existing bone is reabsorbed, and new bone laid down to replace it
- Main phases

- Quiescent
- Activation
- Resorption
- Formation
- Mineralization
- Quiescent

REPAIR (GROSS FRACTURES)

- Step 1
  - Hematoma formation where damaged BV hemorrhage
  - Fibrin and platelets within the hematoma form meshwork growth factors (PDGF & transforming GF)
- Step 2
  - Pro-callus formation occurs as fibroblasts, capillary buds, osteoblast move into the wound and produce granulation tissue enzymes and proteins aid in this step of healing
- Step 3
  - Callus formation: increased phosphate content joins with calcium as a mineral deposit to harden the callus
- Step 4
  - Replacement -Osteoblasts continue to replace
- Step 5
  - Remodeling-Synthesis of type 1 collagen predominates this step
  - Final remodeling is vital to ensure good mechanical properties for weight bearing and strength

AGING & bone function

- Loss of bone tissue
- Less stiff, more brittle
- Remodeling takes longer
- Mineralization rate decreases
- Caused by:
  - Genetics
  - hormonal factors
  - vitamin deficiency

- Female bone loss
  - increased in the post-menopausal state
  - Bone density decreases
  - Increased osteoclastic bone resorption
  - By age 70= 50% cortical bone loss

- male bone loss
    - Peak bone mass higher
    - Later age & much slower bone loss
    - Less disability than female

PEDIATRIC CONSIDERATIONS

- Infant skeleton not fully ossified
- Lower mineral content therefore more flexible and porous
- Thick stronger periosteum= greater absorption force
- growth of bones occurs at the physis growth plate region, chondrocyte synthesize cartilage
- Additional bone growth occurs at the periosteum
- Fractures very common
- Bone repair is like adults however, bones heal more quickly related to thicker periosteum and BV supply.
- Regular physical activity promotes growth & strength in muscle and bones

TESTING OF BONE FUNCTION

- Gait analysis
- Serum calcium & phosphorus
- Plain radiographs
- CT /DECT
- MRI (1* bone lesions)
- MRA (injection of joint)
- PET
- DXA

JOINT STARTING POINTS

- Site of where 2 or more bones meet
- Provide stability and mobility of the skeleton
- Joint classification based on movement provided OR the connective tissues that hold them together
    - Fibrous, synovial or cartilaginous
    - Synarthroses, amphiarthroses, diarthrosis
- Solid joints are tightly connected to provide structure (cranial sutures)
- Synovial joints have a joint space to allow for movement
- Synovium lining the joint capsule secretes fluid for lubrication (hyaluronic acid) and facilitate smooth movement
- Disorders characterized as non-inflammatory or inflammatory

JOINT TYPES

- Synarthroses, amphiarthroses, diarthrosis
    - Based on degree of movement allowed
- Also classified on type of connecting tissue-fibrous, cartilaginous, synovial
    - Articular highly organized system of collagen fibers and proteoglycans

- Cartilaginous joints
    - 2 types-Symphysis and synchondroses
        - is bones are united by a pad or disk of fibrocartilage
            - Symphysis pubis & intervertebral disks
        - Synchondrosis hyaline cartilage connects the 2 bones
            - Ribs and sternum
- Fibrous joints
    - Bone connected directly with bone by fibrous joint
    - Usually immovable but some may allow slight movement
    - 3 types
        - Suture >> Cranial sutures
        - Syndesmosis >> radial and ulna/ tibial and fibula
        - Gomphosis >> maxilla and mandible
- Synovial joints (diarthrosis)
    - Most moveable and most complex
    - Joint capsule (articular capsule)
    - Synovial membrane
    - Joint cavity
    - Synovial fluid
    - Articular cavity

TEST OF JOINT FUNCTION

- Arthrography
- Arthroscopy
- Synovial joint fluid analysis
- ESR
- CRP
- synovial fluid Gram stain and culture
- synovial fluid white cell count

- blood culture
- white cell count
- plain radiograph
- Ultrasound

- MRI

AGING JOINT SYSTEM

- Cartilage becomes more fragile, rigid
- Susceptible to fraying
- Decreased glycosaminoglycans
- Decreased H20 and ground substances
- Increased cross-linking
- Decreased ROM
- Intervertebral disks decrease in height

MUSCLE STRUCTURE AND FUNCTION

STARTING POINTS

- Derived from mesodermal progenitor cells myoblasts myotubules muscle fibers
- Over 600 named muscles
- 3 main types skeletal, cardiac, smooth
- Some occur in pairs shaped according to function
    - Fusiform- elongated, shaped like straps
    - Pennate-broad, flat and slightly fan shaped
- Voluntary, striated or extrafusal
    - Controlled directly by CNS
    - striped pattern when viewed under microscope and extrafusal distinguishes from other contractile fibers

MUSCLE

- Largest organ, made up of millions of fibers >> are varied in size and shape also function--> encapsulated in 3-part connective tissue framework, have a functional motor unit that is innervated by single nerve
- Type 1 and type 2 muscle fibers
- Myofibrils and myofilaments contain myosin and actin major proteins that facilitate muscle contraction and provide energy sources
- “all or nothing” theory for muscle recruitment

MOTOR UNIT

- Axon of motor nerves branches out to innervate a specific group of muscle fibers
- Comprised of lower motor neurons
- Behaves as a single entity after receiving an electrical impulse
- Innervation ratios
- higher the ratio the more endurance of the muscle/organ and prevents fatigue

- Lower ratio the more specific the action (precision of movement)

SENSORY RECEPTORS

- Spindles >> mechanoreceptors
- Lie parallel to muscle fiber and responds to muscle stretching
- Golgi tendon organs fibers dendrites that terminate
- branch to tendons near the neuromuscular junction
- Use proteoglycan neuregulin that increases the ACH (acetylcholine) receptors
- "Reports" changes in length, velocity, and tone in muscle

MUSCLE FIBERS

- Muscle membrane
- Sarcolemma
- Basement membrane
- Myofibrils
- Sarcotubular system
- Sarcoplasm
- Mitochondria

TYPE 1	TYPE 2
Red muscle Slow contraction High resistance to fatigue Oxidative metabolism Low glycogen content Low intensity contraction	White muscle Fast contraction Low resistance to fatigue Glycolysis metabolism High glycogen content High intensity of contraction

MUSCLE PROTEINS

• Sarcomeres • Actin • Myosin • Titin • Troponin • Tropomyosin • Nebulin	• Non-protein elements • Nitrogen • Creatine • Phosphocreatine • Creatinine • Purines • Uric acid • Ca++, Mag, NA++, K++

MUSCLE CONTRACTION

- 4 steps
    - Excitation
    - Coupling
    - Contraction
    - Relaxation

- Isometric
    - Static or holding contraction
    - Muscle maintains a constant length as tension is increased
- Isotonic
    - Lengthening or shortening contraction
    - Eccentric and concentric

MUSCLE METABOLISM

- ATP and phosphocreatine needed as constant source
- Protein synthesis is dependent on hormones (insulin), amino acids, substrates, and overall nutritional status
- At rest – rate of ATP by glucose or acetoacetate is sufficient
- At work- 100-fold increased need for ATP
    - Activity of more than 5 sec expends stored ATP and phosphocreatine
    - Stored glycogen and blood glucose converted to ATP (anaerobically) much less efficient the aerobic glycolysis
    - Lactic acid buildup

TESTS OF MUSCLE FUNCTION

- EMG- electromyogram
- Urinary myoglobin
- Creatine kinase –damaged muscle

AGING & THE MUSCLE SYSTEM

- Nervous, endocrine, and vascular input
- Oxidative stress results in mitochondria dysfunction
- Apoptosis of muscle cells
- Sarcopenia
- Age-related muscle loss
- Muscle strength declines 15% per year age 60-70; then jumps to 30% in 80’s
- Muscle strength decline faster than muscle mass
- Type 2 fibers decrease to greater extent than type 1