Musculoskeletal system pathology

Musculoskeletal system
Structure - bones and joints
Bones [Figs. 19-1, 19-2]
- bone is a specialized form of connective tissue
- composed of organic and inorganic components
  - inorganic (65%) component is hydroxyapatite [calcium and phosphate]
  - organic (35%) component consists of cells and extracellular matrix
    - ECM is 90% collagen type II
    - cells
      - osteocytes are mature bone producing cells that maintain bone
      - osteoblasts are bone forming cells that synthesize organic matrix
      - osteoclasts are bone resorbing cells function to
- types of bone
  - woven (immature) bone is newly formed bone with haphazard collagen
  - lamellar (mature) bone replaces woven bone with organized structure
- parts of a long (tubular) bone
  - diaphysis is the mid-portion of the bone
  - epiphysis is the articular portion of the bone (cortical vs. trabecular bone)
  - metaphysis is the portion of bone between the diaphysis and epiphysis
  - growth plates are located in the mid-portion of metaphysis of children

Cartilage
- cartilage is a specialized form of connective tissue
- there are three types of cartilage
  - hyaline cartilage is located on the articular surface of bones, in the trachea, bronchi etc
  - elastic cartilage is located in the eustacean tube, ear and epiglottis
  - fibrocartilage is located in synarthrotic joints and in vertebral discs

Function of musculoskeletal system
- movement/ support
- protection of vital organs
- site of hematopoiesis
- reservoir for calcium/ phosphate

Joint structure [Fig. 19-3]
- synovial joint (provides for movement)
  - ligamentous capsule
  - synovial lining
  - joint fluid
- synarthrosis (very limited movement)

Bone metabolism
- Bone is continually remodelled
  - child production > reabsorption
  - elderly reabsorption < production
- Bone is storage reservoir for calcium and phosphate
  - equilibrium with serum Ca, PO
- Hormonal control
  - Parathyroid hormone
  - Vitamin D [Fig. 19-6]
  - others
Musculoskeletal system pathology

Developmental and genetic diseases

Achondroplasia
- autosomal dominant defect of bone formation resulting in dwarfism
- defective formation of long bones which do not lengthen
- normal trunk, short limbs, relatively large heads
- 80% have normal parents (i.e., new mutation)

Osteogenesis imperfecta
- group of inherited diseases resulting from defective collagen type I
- results in production of osteopenic bone which is weak
- severe forms present with multiple fractures in fetus, usually fatal
- mild forms present with stunted growth, prone to fractures

Osteopetrosis
- group of inherited diseases resulting from defective osteoclast function
- bones grow but not remodelled resulting in thick but brittle bones

Metabolic bone diseases

Osteopenia
- radiological term for a decreased amount of bone on x-ray

Osteoporosis [Fig. 19-5]
- form of osteopenia characterized by decreased bone mass
- may be localized (e.g., immobilization of limb) or generalized
- may be primary or secondary
- primary osteoporosis
  - an age-related, accelerated bone loss, with no obvious cause
  - the most prevalent bone disease
  - multifactorial disease due to interplay of hormones, exercise, calcium
- secondary osteoporosis
  - osteoporosis is secondary to a defined cause
  - causes include hormonal imbalance, diet, immobilization, drugs, tumors

Primary osteoporosis
- risk factors
  - age (osteoporosis increases with age)
  - genetic factors (osteoporosis runs in families)
  - sex (females have accelerated bone loss after menopause)
  - hormones (deficiency of estrogen results in accelerated bone loss)
  - nutritional (inadequate Vitamin D, calcium)
  - physical activity (inactivity promotes osteoporosis)
  - environmental factors (smoking, alcohol promote osteoporosis)
- type I primary osteoporosis
  - typically occurs in post-menopausal women
  - due to increased osteoclast activity, affects bones with high percentage of cancellous bone (e.g., Vertebrae - compression fracture)
- type II primary osteoporosis (senile osteoporosis)
  - affects both men and women
  - pathogenesis not understood, affects cortical portion of long bones (e.g., Femur - femoral fracture)
- diagnosis
  - usually asymptomatic, found incidentally or after fracture
  - recognizable on x-ray only after bone loss exceeds 30-40%
  - bone density studies more effective
  - usual bone markers are normal
Musculoskeletal system pathology

Metabolic bone diseases

Osteomalacia and rickets
- osteomalacia is a disease of adults due to inadequate mineralization of bone matrix in mature bones
- rickets is a disease of children due to inadequate mineralization of bone matrix in growing bones
- the major cause of inadequate mineralization is vitamin D deficiency
  - causes of vitamin D deficiency
    - inadequate intake
    - inadequate sunlight
    - malabsorption
- another cause of inadequate mineralization is hypophosphatemia
  - causes of decreased phosphate include
    - inadequate absorption
    - excess loss
- pathogenesis of disease
  - decreased absorption of Ca, PO from intestine
  - increased PTH which causes increased bone resorption
  - compensatory bone formation occurs in setting of inadequate minerals
- softening of bones with resulting deformity in children
- various manifestations in adults
  - vague skeletal pain, gradual deformity of weight-bearing bones
  - osteomalacia is reversible if supplement vitamin D, normalize calcium homeostasis

Renal osteodystrophy
- renal osteodystrophy refers to bone changes that occur in patients with chronic renal failure (CRF)
- CRF results in ↓ PO excretion, ↓ decreased activation of vitamin D
- changes include osteomalacia, osteofibrosis, and osteitis cystica

Paget’s disease [Fig. 19-7]
- chronic disease of unknown etiology characterized by irregular restructuring of bone with resulting thick and deformed bones
- three phases
  - destructive phase, mixed phase, osteosclerotic phase
- characteristic mosaic pattern on histology in osteosclerotic phase
- various clinical features
Musculoskeletal system pathology

Infection & circulatory disturbances

Osteomyelitis
- inflammation of bones, most commonly due to bacterial infection
- bacteria reach bone via hematogenous or direct spread
- bacteria
  - most common is Staphylococcal aureus
  - mixed infections in trauma
  - Mycobacterium tuberculosis infection in 1-3% of those with lung infection
  - Treponema pallidum
- treatment consists of antibiotics, +/- surgical drainage if necessary
- chronic osteomyelitis results from incompletely healed or persistent suppurative acute osteomyelitis
- complications include bone deformities, fractures, squamous carcinoma

Aseptic necrosis (avascular necrosis, osteonecrosis)
- death of part of a bone secondary to infarct
- infarct occurs as a consequence of ischemia
- if there is no obvious cause of the ischemia then called idiopathic
  - in children/adolescents, idiopathic infarcts of bone often have names
    - Legge-Calve-Perthe disease is osteonecrosis of head of femur (3-10 yo boys)
  - osteonecrosis of head of femur occurs in chronic alcoholics
- important identifiable causes of osteonecrosis include
  - trauma
  - corticosteroids
  - radiation therapy
  - systemic diseases (eg. sickle cell anemia, SLE)
  - emboli

Bone fractures
- disruption of continuity of bone, usually due to trauma

Terminology [Fig. 19-8]
- simple fracture has a single fracture line
- comminuted fracture has multiple fracture lines, fragments
- complete fracture results in bone fragments that are separated
- incomplete fracture does not cause complete discontinuity of bone
- closed (simple) fracture has intact overlying skin and soft tissue
- open (compound) fracture communicates with external environment
- pathological (“spontaneous”) fractures occur in weakened bones
  - eg. Tumor, Paget’s disease, osteoporosis
- stress fractures occur as result of repeated minor trauma

Healing
- “callus” fills in gap between the two pieces of bone
- callus undergoes various changes
  - procallus formation (granulation tissue, cartilage, osteoid)
  - fibrocartilage callus (increased collagen matrix)
  - fibrosseous callus (haphazard bone spicules and connective tissue)
Musculoskeletal system pathology

Bone tumors

Classification

• Primary bone tumors [Fig. 19-10]
  – Benign
    • osteoma, chondroma, fibroma
  – Malignant
    • osteosarcoma
    • chondrosarcoma
    • Ewing’s sarcoma

• Metastatic bone tumors
  – breast, prostate

Osteosarcoma
  – most common primary bone tumor
  – malignant neoplasm that produces bone
  – various types based on location in relation to the bone
  – peak incidence in second decade of life
  – preferentially affects metaphysis of long bones
  – 60% occur around the knee joint
  – invades locally, metastasizes via the bloodstream (lungs)
  – aggressive tumors
    • high mortality if no therapy
    • combined chemotherapy and surgery curative in 80 %

Chondrosarcoma
  – second most common primary bone tumor
  – malignant neoplasm that produces cartilage
  – peak incidence in fifth and sixth decades of life
  – affects axial skeleton (pelvis, vertebra, shoulder, proximal femur)
  – prognosis depends on resectability, grade of tumor, metastases

Ewing’s sarcoma
  – unusual malignant neoplasm consisting of undifferentiated cells
  – diaphysis of long bones
  – metastases are common (lungs, liver, brain)
  – chemotherapy has improved prognosis
Musculoskeletal system pathology

Joint disease

Osteoarthritis [Fig. 19-14]
- chronic degenerative disease of articular joints with loss of cartilage
- very common, age related
- primary vs. secondary (previously damaged joints)
- cause unknown in most cases
  - wear and tear hypothesis, possible metabolic derangement
- loss of articular cartilage, sclerosis, eburnation, cysts, osteophytes
- variable clinical presentation, relieved with rest
- monoarticular or polyarticular distribution, asymmetric
- weight bearing joints, DIPs and PIPs
- diagnose on basis clinical/radiology

Rheumatoid arthritis [Figs. 19-15, 19-16]
- chronic systemic disease of unknown etiology characterized by inflammation of joints and variable extra-articular features
- pathogenesis unknown, genetic susceptibility in certain individuals
- may affect any joint, usually symmetric distribution, MCPs PIPs
- variable clinical course
  - swelling of joint, erosion of bone by pannus (granulation tissue)
  - immobilization of joint, ankylosis, bony deformities
- extra-articular features
  - rheumatoid nodules, lung disease, eye disease, vasculitis, anemia
- Rheumatoid factor
  - autoantibody directed against part of IgG (present in 80%)
  - not diagnostic of rheumatoid arthritis (may occur in SLE)

Infectious arthritis
- may occur due to direct or hematogenous spread
- Lyme disease
  - Borrelia burgdorferi, carried by ticks
  - skin rash + migratory arthritis several weeks after tick bite
  - second stage may involve heart, CNS, arthritis
  - in 10%, chronic arthritis develops
- bacterial
  - gonococcal arthritis following genital infection

Gout
- disease characterized by hyperuricemia and deposition of uric acid crystals in various tissues including joints
- may be primary or secondary (table 19-3)
- multifactorial trait
- males more often affected
- onset in age 20 to 40
- monoarthritis more common (big toe most commonly affected)
- excruciating pain during acute attacks, periods of remission
- tophaceous deposits are aggregates of uric acid in soft tissue
- Complications
  - bony deformities with chronic disease, renal calculi most important complication

Ankylosing spondylitis
- seronegative arthropathy preferentially affecting spine, sacrum
- males more commonly affected
- onset at 20-40 years of age
- > 90% have HLA B-27
- destruction of joints with fusion of spine
- limited chest expansion and back pain initial symptoms
- asymmetrical peripheral joint involvement
Musculoskeletal system

Skeletal Muscle – Structure [Figs. 20-1, 20-2]
- basic unit is the myocyte (a muscle cell), contains actin and myosin
- myocytes are arranged in groups (muscle fibers)
- muscle fibers are arranged in fascicles
- a muscle consists of numbers of fascicles
- connective tissue layers surround the components
- neuromuscular motor unit junction
  - individual muscle fibers innervated by branch of lower motor neuron
  - acetylcholine (Ach) is neurotransmitter
  - ACh binds to post-synaptic receptor, inactivated by cholinesterase

Function
- contraction (movement, heat, posture, breathing)
- storage (glycogen, fat)

Muscle symptom terminology
weakness
- inability to contract adequately
fatigability
- inability to sustain contraction
spasm (myotonus)
- continuous contraction
fibrillation
- uncoordinated contraction of groups of fibers
myalgia
- muscle pain

Muscle pathophysiology
- muscle and nerves supplying it are a unit
  - severing the nerve from the muscle results in atrophy of the muscle
- chemical neurotransmitters mediate transmission of neural signal into muscle contraction
- contraction requires
  - normal muscle cells and contractile proteins
  - adequate energy generation
- hormones influence muscle function
- toxins, drugs affect muscle function
- muscle cells cannot regenerate properly
- etiology of muscle diseases
Musculoskeletal system pathology

Neurogenic atrophy [Fig. 20-4]
• Form of muscle atrophy caused by injury to nerve supplying the muscle

Upper motor neuron injury
– injury to neuron located in CNS
  • cortex lesion (stroke, amyotrophic lateral sclerosis)
  • cortical tract lesion (stroke)
  • spinal tract injury (trauma)

Lower motor neuron injury
– injury to motor neuron located in anterior horn of spinal cord
  • spinal nerve disease (poliomyelitis)
  • nerve root compression (ruptured disk, ankylosing spondylitis)
  • axonal injury (trauma, autoimmune, toxin)
  • axonal branch injury (diabetes, atherosclerosis)

Myasthenia gravis [Fig. 20-7]
– autoimmune disease due to immune-mediated injury resulting in decreased numbers of muscle ACh receptors
– antibodies directed against ACh receptor
– bind to receptor thereby preventing ACh from binding
– characterized by easy fatigability and weakness
– most patients have thymic hyperplasia or neoplasm of the thymus
– diagnosed by clinical changes
– confirmed with specific tests
  • anticholinesterase test
    – transient improvement in symptoms due to increased presence of Ach
  • identify antibodies to Ach receptor

Muscular dystrophies
– Heterogeneous group of inherited primary muscle diseases characterized by progressive muscular weakness and wasting

Duchenne muscular dystrophy [Fig. 20-8]
– most common dystrophy caused by deficiency of dystrophin an integral protein in cell plasma membrane (including skeletal muscle cells)
– gene for dystrophin protein is located on X-chromosome
– X-linked recessive inheritance, males affected
– weakness by age 5, wheelchair by age 10-12, death in early twenties
– reduced intelligence
– diagnosis
  • typical clinical findings
  • family history
  • laboratory tests

Becker’ muscular dystrophy
– same gene affected but milder disease
– less common, symptoms begin in puberty, live 40-50 yr

Myotonic dystrophy
– second most common muscular dystrophy
– mutation of myotonin protein kinase
– autosomal dominant inheritance, symptoms develop in adults
– muscle wasting, mental deterioration and diabetes
– myotonia
  • sustained involuntary contraction of a group of muscles
– facial muscle weakness (“hatchet man” faces)
Musculoskeletal system pathology

Myopathies
Congenital myopathies
– group of muscle diseases characterized by onset early in life, non-progressive or slowly progressive course, proximal or generalized muscle wasting and hypotonia (floppy baby) or severe joint contracture

Acquired myopathies
– nonspecific term for muscle weakness secondary to identifiable cause
– include muscle disease due to various metabolic and hormonal diseases
– diabetic myopathy
  • vascular, metabolic, and neuogenic components
– cancer myopathy
  • paraneoplastic syndromes

Myositis
– inflammation of muscle
Infectious myositis
– viral myositis
  • fleeting, self-limited (e.g. Influenza virus)
  • Coxsackie B associated with muscle pain, may have myocarditis
– bacterial myositis
  • localized infection
  • Tetanus and gas gangrene are serious complications of wounds infected with clostridia
– parasite
  • Trichinella spiralis-undercooked pork

Immune Myositis
– polymyositis
  • limited to muscles
– dermatomyositis
  • muscles + other organs including skin
– SLE associated myostis
– Sarcoidosis

Primary tumors of muscle and soft tissue

Benign neoplasms
– fibroma, lipoma, hemangioma

Malignant neoplasms
– rhabdomyosarcoma
  • malignant neoplasm derived from skeletal muscle cell
  • peak incidence in childhood
– malignant fibrous histiocytoma
  • malignant neoplasm of undifferentiated connective tissue cells
– liposarcoma
  • malignant neoplasm derived from adipocytes
– Prognosis depends on size, location and histologic type