**Skeletal and Muscular Pathophysiology**

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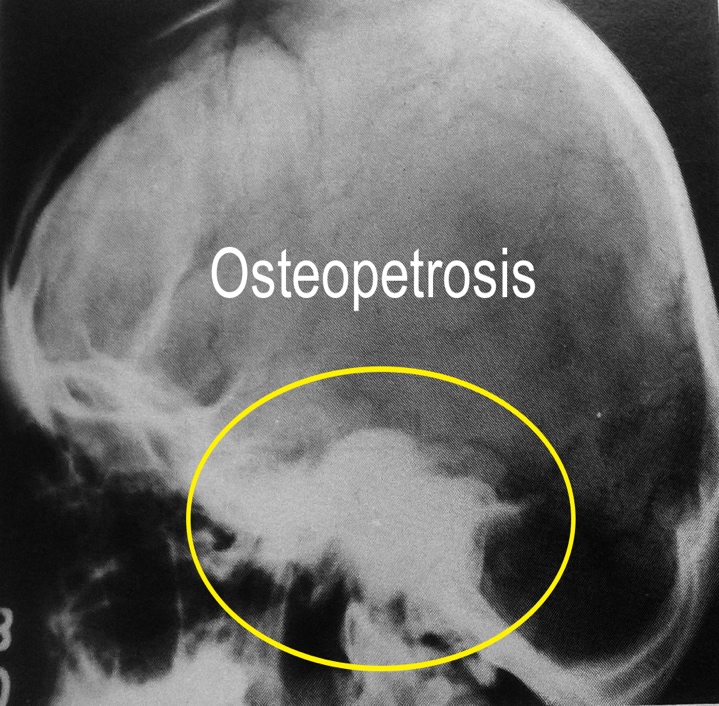
**Bone Physiology - Bone Basics:**

* Function: structure and reservoir for calcium
* Ossification - bone formation
* Osteoblasts - cells involved in bone deposition
* Osteoclasts - cells involved in bone breakdown
* Bone Metabolism:
  + **PTH** activates osteoclasts; promotes renal retention of Ca2+; promotes intestinal Ca2+ absorption indirectly with Vit. D
  + **Calcitriol** (Vit. D activated to act as a hormone) promotes active absorption of Ca2+ from intestine
  + **Calcitonin** lowers blood calcium levels by suppressing osteoclast activity

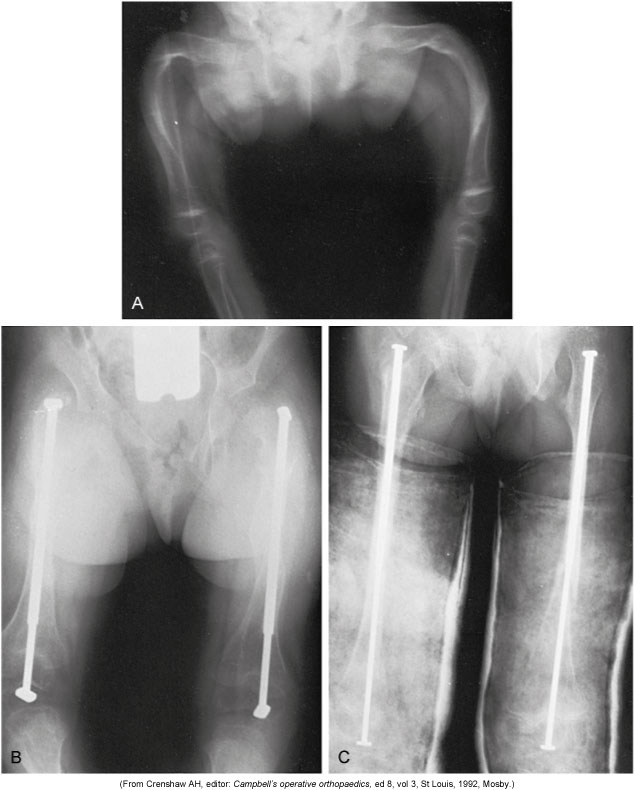
**Bone Pathophysiology**

* Bone disorders are derived from infection, tumor growth, abnormal ossification, or imbalance in bone remodeling
  + **Osteopenia -** net loss of bone
  + **Hyperostosis** - excessive, irregular, or inappropriate bone formation
  + 2 Types of Bone disorders
    - Genetic
    - Acquired

**Genetic Bone Disorders**

* **Osteopetrosis** (Marble Bone disease)
  + Osteoclasts are functionally deficient resulting in defective ossification
  + Excessive deposition of bone tissue that is brittle and easily fractured
  + Therapy includes bone marrow transplants and calcitrol
  + ****Deformalities in floor of brain can lead to blindness, deafness, paralysis of facial muscles from intracranial pressure
  + Mild cases display short stature and weakened bones
  + Severe cases have little change of survival

**Genetic Bone Disorders**

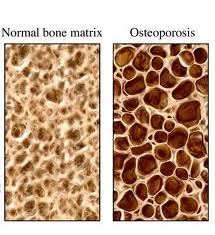
* **Osteogenesis Imperfecta**
* “Brittle bone disease”
* Defect in type I collagen production
  + Bone and vessel collagen
  + Several conditions related to defect in collagen synthesis leading to osteopenia and brittle bones
* Clinical manifestations:
  + Osteopenia
  + Increased rate of fractures
  + Bone deformity (bowing)
  + Short stature
  + Blue sclera and poor dentition
  + Aortic aneurysm
* Clinical management:
  + Surgical
    - ****Intramedullary and telescoping rod placement
  + Medical
    - Increased calcium and vitamin D
    - Biphosphates

**Achondroplasia**

* + Defect in normal cartilage development resulting in skeletal disproportion
  + Lack of cartilage development at epiphyseal plates of long bones with causes ossification to seal the plates early preventing further elongation

**Acquired Bone Disorders**

* **Paget’s Disease (Epithelial tumor)**
  + Excessive deposition of coarsely structured bone
  + **Osteolytic Phase** (initial stage)
    - Occurs during middle age
    - Bone reabsorption dominates and newly formed bone is abnormal
* **Mixed Phase** 
  + - Bone reabsorption and abnormal new bones continues
    - Pagetic bone**-** coarse structures and crude organization forming dense, focal masses
* **Osteosclerotic Phase**
  + Reabsorption declines and harder, more dense bone tissue is formed
  + In extreme cases, heavy skull can cause compression fractures
  + Hearing disorders result from thickening ossicles
  + Pain caused by microfractures of pagetic bone and nerve compression
  + Osteogenic or other sarcomas can arise in affected bones and are resistant to therapy
  + Often asymptomatic, therefore undiagnosed
* **Osteoporosis**
* Gradual and progressive loss of bone mass leading to fractures and pain
* Idiopathic
* **Primary Osteoporosis**
  + Critical point: bone is too weak to resist fracturing
  + Bone tissue rate of loss is 0.5% per year
  + Twice as common in women
* **Secondary Osteoporosis** 
  + Bone loss due to some identifiable derangement such as a nutritional deficiency, genetic abnormality, or a tumor
  + No cure🡪 Therapy aims to slow the rate of bone loss and promote new deposition of bone to prevent fracture
    - * Calcium supplements, Vitamin D, Hormone replacement



**Acquired Bone Disorders**

* **Rickets**
* Inadequate mineralization and Vitamin D deficiency in children
* Deformity of developing skeleton (ex. bowed legs)
* Bones of children are inadequately mineralized causing softened, weakened bones
* Bowed legs and deformities of the pelvis, skull, and rib cage are common
* Caused by insufficient calcium in the diet, or by vitamin D deficiency
* **Osteomalacia**
* Inadequate bone mineralization in the adult
* Pain, muscle weakness, predisposition to fractures
* **Osteomyelitis**
* Bone inflammation in response to infection by a pyogenic (pus-producing) bacterium
* Osteocytes respond to damage by forming new segments of **reactive bone** that can form walls and isolate the infection from phagocytes
* A permanent epithelium-lined tract called a **sinus** may form where pus and necrotic bone fragments drain to the surface



**Acquired Bone Disorders**

* **Bone Tumors** 
  + Disrupt organization of osseous tissue by inducing osteolysis or new bone formation
  + **Primary Bone Tumors**
* 1/3 are benign and can be surgically removed
* **Osteogenic Sarcoma -** most common malignant tumor, affects 10-20 year old and has great predisposition to blood-borne metastasis to the lungs
* Other types: Chondrosarcoma, Ewing’s tumor, Giant cell tumor
  + **Secondary Bone Tumors**
  + Most common
  + A carcinoma is usually the primary tumor and most often arises from the prostate, breast, thyroid, lung or kidney

**Joint Disorders**

* **Osteoarthritis**  or **Degenerative Joint Disease**
  + Most common joint disorder
  + Articular cartilage becomes thin, irregular, and frayed
    - Results in cracks and fissures leading to microfractures
    - Causes pain and loss of mobility associated with aging process
    - **Osteophytes** or **bone spurs** may form (bony projections)
  + **Primary OA -** **idiopathic**
  + **Secondary OA-** contributing factor to joint stress can be identified
* Degenerative arthritis - “wear and tear” arthritis
* Incidence
  + Most prevalent form of arthritis in the United States with 20-30 million cases
  + Affecting more than 70% of adults between 55 and 78
  + 90% over 45 have some OA symptoms
  + Women are affected more than men
  + Common in 20-30 year old athletes with silent symptoms
* Pathophysiology
  + With aging, the water content of the cartilage increases, and the protein makeup of cartilage degenerates.
  + Eventually, cartilage begins to degenerate by flaking or forming tiny crevasses.
  + In advanced cases, there is a total loss of cartilage cushion between the bones of the joints.
  + Repetitive use of the worn joints over the years can irritate and inflame the cartilage, causing joint pain and swelling.

**Joint Disorders**

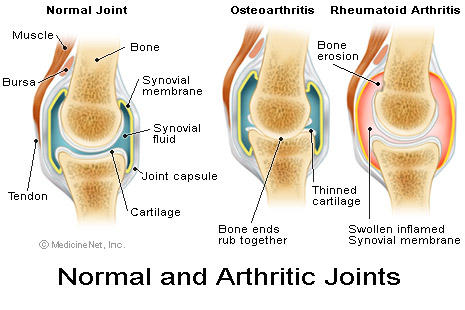
* **Osteoarthritis**  or **Degenerative Joint Disease**
  + Loss of the cartilage cushion causes friction between the bones, leading to pain and limitation of joint mobility.
  + Inflammation of the cartilage can also stimulate new bone outgrowths.
* Symptoms
  + - Develop gradually (RA is fast onset)
    - Usually starts in 1-2 joints
    - Starts with weight bearing joint pain that is better with rest
    - Eventually joint ROM decreases
* Diagnosis
  + - By history with tender joints, decreased ROM, osteophytes
    - No signs of inflammatory changes
    - Joint fluid usually WINL
    - X-rays show decreased joint spaces and osteophytes
    - Usually x-rays appear worse than the level of symptoms
* Treatment of OA
  + - Gentle exercise, pool therapy
    - PT and OT
    - Appliances (heating pads, orthotics, walkers, braces, supports, etc.)
    - Weight control
    - TENS units
    - MEDS Tylenol and NSAIDs, COX2 inhibitors

Glucosamine and chondroitin sulfate

Steroids used short term but not very helpful

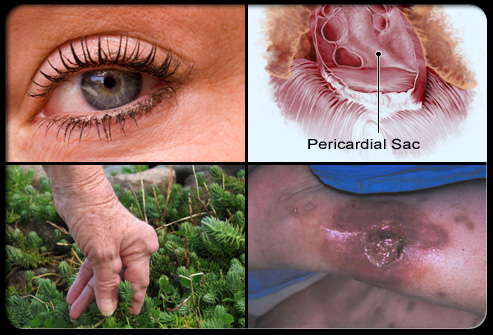
Joint injections helpful at times

OTC rubefacients helpful

* + Surgery reserved for very severe and incapicating form only

**Joint Disorders**

* **Rheumatoid Arthritis**
* Systemic disease with prominent involvement of the joints
* Inflammatory condition affecting the joints in hands, wrists, ankles, and feet; also affects heart, lungs, and skin
* Variable clinical pattern with remission and exacerbation
* **Rheumatoid Nodules -** regions of focal subcutaneous swelling found of elbow, heel, and dorsal surface of head
* **Etiology**- **idiopathic**, characterized by immune-mediated destruction of joints; genetic component
  + **Rheumatoid factor (RF)** - antibody against immunogloublin G
* **Therapy -** no cure; relieve pain and reduce swelling through anti-inflammatory drugs and stress reduction to joints
* An autoimmune disease causing chronic joint inflammation
* A progressive illness that has the potential to cause joint destruction and functional disability
* Affecting approximately 1.3 million people in USA
* Three times more common in women as in men
* It afflicts people of all races equally
* Can begin at any age, but it most often starts after age 40 and before 60
* In some families, multiple members can be affected, suggesting a genetic basis for the disorder
* **Symptoms**
  + Come and go, depending on the degree of inflammation
  + When body tissues are inflamed, the disease is active
  + The course of rheumatoid arthritis varies from patient to patient, and periods of flares and remissions are typical
  + Inflammation usually symmetrical and of the small joints
  + Pronounced morning stiffness – “morning gel”
* Rheumatoid arthritis and inflammation of organs - can affect organs and areas of the body other than the joints
  + Sjogren's syndrome is inflammation of the glands of the eyes and mouth and causes dryness of these areas
  + Rheumatoid inflammation of the pleura
  + Pericarditis
  + Can have lowered RBC (anemia) and WBC
  + Felty’s Syndrome (lowered WBC and spleenomegaly)
* Diagnosis
* Positive RF (rheumatoid factor) and RF titer, ASO titer
* WBC changes
* Joint fluid with WBC and proteins
* X-ray changes
* Treatment
* Supportive and appliance measures (Hot and cold packs, walkers, etc.)
* NSAIDs and COX2 inhibitors - Steroids are the main treatment
  + Rest and mild ROM exercises



**Joint Disorders**

* **Gout**
* High levels of urate ions in the plasma produce **hyperuricemia** from nucleic acid metabolism
* Deposition of monosodium urate (MSU) crystals in joints - of foot
* Tophus- local inflammation resembling rheumatoid nodules
* Most common in adult males
* **Gouty Arthritis**
* Familial disease affects men 90% of time
* Usually starts in 30s due to uric acid crystals being laid down in certain joints
  + By product of nucleic acid metabolism
  + Body also forms uric acid from high purine foods
    - Anchovies, sardines, asparagus, mushrooms, meat gravies and broth, all organ meats
    - Alcohol increases uric acid production and decreases excretion
* Usually involve great toe, can also affect ankle, knee, wrist or elbow
* Signs and symptoms
* Episodes come on suddenly with severe excruciating pain
* Attacks are worse with emotional stress, drinking, fatigue, surgery, eating and eating high purine foods
* 25% of patients will develop nephrolithiasis
* Diagnosis with a history of typical monoarthritis with elevated uric acids on joint aspiration

**Joint Disorders**

* **Gout**
  + Treatment
    - Treated with Colchicine hourly for pain
    - NSAIDs and COX2 inhibitors
    - Codeine, demerol and morphine
    - Steroids – oral and injectables
    - Foot cradle for sleeping
* **Ankylosing Spondylitis**
* Fusion of vertebral column starting in sacroiliac joints and proceeds slowly up the spinal column
* Genetic defect that causes autoimmune attack on joint structures following infection
* Joint structures become destroyed and replaced by fibrous cartilage and bone
* Bone resorption increases reducing bone mass
  + Thinning of bone resembles bamboo, called bamboo spine
* **Systemic Lupus Erythematosus (SLE)**
* Autoimmune condition
* Widespread deposition of immune complexes in various tissues, especially joints

**Skeletal Muscle Pathophysiology**

* Skeletal muscles are remarkably resistant to disturbances - adapt to change with **hypertrophy** and **atrophy**
* Disorders develop from **inadequate contraction** stimulus caused by neurological defects
* **Myositis** - inflammation arises in response to systemic infections from viruses, bacteria, fungi, or parasites
* **Polymyositis** - condition in which signs and symptoms derive from muscle damage
* **Dermatomyositis** - occurs in about 30% of polymyositis cases
  + Skin rash present from dermal immune complex deposition
* **Polymyositis & Dermatomyositis**
* Polymyositis – disabling muscle weakness
* Dermatomyositis – hyper-pigmentation rashes
* Both occur in 40-60 year olds
* S & S
  + Affects large muscles in shoulders and hips
* Diagnosis
  + Muscle weakness of shoulders and hips in middle age is suggestive, characteristic skin rash
  + EMG, muscle biopsy
* Treatment
  + Steroids and immunosuppressive drugs

**Muscular Dystrophy**

* + Group of rare diseases characterized by genetic etiology and progressive degeneration of skeletal muscle
  + **Duchenne Muscular Dystrophy** 
    - Most common
    - X-linked recessive defect
    - Diagnosed on basis of high serum levels of creatine kinnase (CK)- enzyme released from damaged muscle fibers
    - Underlying defect condition in deficiency of muscle protein dystrophin
    - Results in muscle weakness and delayed motor development
* **Myotonic Dystrophy** 
  + - * Genetic defect produces abnormal membrane ion channels
      * Muscle atrophy, loss of strength, and myotonia
      * Muscles of face, neck, and distal limbs are most affected
      * Defects in heart can lead to serious dysrhythmias