Osteoarthritis

• Most common joint disease
  – Slow progressive degeneration of articular cartilage of weight bearing joints
  – Subchondral bony thickening and bony overgrowths (osteophytes; “spurs”); knobby protrusions at the margins of the distal interphalangeal joints → nontender Haberden’s nodes
Osteoarthritis

• Primary: defect in cartilage, not an inflammatory disease
  – Men in midlife, somewhat later in women
  – 80% of those over 70 years; nonlinear association

• Secondary: appears at any age in a previously damaged or congenitally abnormal joint (trauma, crystal deposits, infection)

• Knees, hips, cervical and lumbar spine
Osteoarthritis

- Loss of proteoglycans and areas of decreased number of chondrocytes alternating with areas of proliferating chondrocytes with matrix basophilia
- Narrowing of joint space (loss of disk)
- Increased thickness of subchondral bone
  - Fissures, pitting and flaking of cartilage with exposure of bone (eburnated bone)
- Subchondral bone cysts
- Inflammation of the synovium
- Loose bodies in the joint
Osteoarthritis (late stage)

- Fusiform swelling of joints
- Heberden's nodes
Rheumatoid arthritis

- Systemic chronic inflammatory disease affecting the synovium (IT IS A SYNOVITIS THAT LEADS TO DESTRUCTION AND ANKYLOSIS OF AFFECTED JOINTS)
- Autoimmune disease; 1% world prevalence
- 3:1 women (3rd-4th decade)
- Diarthrodial joints bilaterally
- Remissions and exacerbations
- Heredity; EBV(?)
- HLA-Dw4 haplotype and related B-cell alloantigen
Rheumatoid arthritis

• Starts from the proximal joints of hands and feet then wrists, elbows, ankles, and knees
• Villous hypertrophy of the synovium
• Hyperplasia of the synoviocytes
• Intense lymphoplasmacytic and histiocytic infiltrates
• The synovium forms a cloak (pannus) that fills the in the joint space
• Destructive enzymes and cytokines, and the pannus, destroy the articular surfaces
• Fibrous and bony ankylosis
• Rice bodies
• Hyperplastic synovium and Pannus
• Allison-Ghormley bodies

Rheumatoid nodules

Fibroblasts
Necrosis
Non-joint manifestations

• Rheumatoid nodules in subcutaneous tissue
• Vasculitis
• Fibrosing inflammatory lesions of the lungs, pleura, pericardium, myocardium, peripheral nerves, and eyes.
Theory of Pathogenesis

- Genetically susceptible patient; HLA-DR4
- Infection? Prime suspect is EBV; mycoplasma, mycobacteria
- Inflammatory synovitis initiates and autoimmune response with formation of Abs
  - CD4+ are activated → release of IL-1 and TNFalpha → lysis of cartilage
- Autoantibodies against IgG and production of the rheumatoid factor (usually IgM, IgA, IgE and IgG); 20% of patients are RF negative
- Deposits of immune complexes in the synovium
- Activation of complement cascade
- Inflammation
- Activation of macrophages
- Homing of T cells
- Secretion of cytokines
Spondyloarthropathy

- Used to be a type of RA
- NOW comprises a group of diseases
  - Ankylosing spondylitis
    - Vertebral column & sacroileac joints, young men
  - Reactive arthritis (Reiter syndrome)
    - Polyarthritis, conjunctivitis, non-gonococcal urethritis, oral lesions
  - Psoriatic arthritis
  - Arthritis and inflammatory bowel disease (enteropathic arthritis)
    - Crohn’ dz, ulcerative colitis
Reactive arthritis
Gout

• Hyperuricemia
  – It is necessary for gout, but only a few fraction of hyperuricemic people develop gout
• Idiopathic
• Predisposing factors: alcohol, obesity
• Most cases occur in men; Almost never in women before menopause
• Attacks of acute arthritis triggered by crystallization of urates in joints
• Asymptomatic intervals
• Eventual development of chronic tophaceous gout and arthritis
Primary gout

• Hyperuricemia in the absence of other disease
  – Asymptomatic hyperuricemia can precede gout
• Impaired secretion by kidneys
Secondary gout

• Hematopoietic pathologic conditions
  – Leukemias
  – Lymphomas
• After chemotherapy
• Alcoholism
Clinical features

• Acute gouty arthritis
  – Painful
  – Involves one joint initially, then polyarticular
  – Podagra (painful, red metatarsophalangeal joint)

• Tophaceous gout
  – Development of tophi
    • Chalky, cheesy, yellow-white, pasty deposits of monosodium urate crystals
  – Helix and antihelix of ear
  – Achilles tendon
Gout

• Pathology
  – Formation of granulomas with needle-shaped crystals

• Renal failure, urate stones

• Treatment
  – Colchicine
    • Prophylactic
  – Probenecid & sulfinpyrazone
    • Interfere with urate resorption
  – Allopurinol
    • Inhibitor of enzyme that converts the xanthine and hypoxanthine to uric acid
Pseudogout

• Chodrocalcinosis
• Calcium pyrophosphate crystals deposits in joints
• Older individuals
• No gender, race predilection
• 30-60% prevalence
  – There is a hereditary form
• Can cause significant joint damage
  – Knees, wrists, elbows, shoulders, ankles
Lyme disease

• Ring-like rash at the site of the bite
  – Erythema chronicum migrans
• Migratory joint pain and subsequent oligoarthritis
Bursitis

- Inflammation of the bursa
  - elbow, shoulder, knee
- Fibrous thickening of the bursa wall
- Tendency to double-fault in tennis and develop a bad slide in golf
Tumors and Tumor-like Conditions

• Ganglion cyst: Wrist; connective tissue cyst; near the joint capsule or the tendon sheath
• Synovial cyst: herniation of synovium through the joint capsule (Baker cyst; popliteal fossa)
• Pigmented villonodular tenosynovitis
  – Knee, hip, ankle, pain
• Giant cell tumor of tendon sheath
  – Painless mass; wrist; Most common soft tissue tumor of the hand
Synovial Chondromatosis

- 18-75 years (median 45)
- More frequent in women in contrast with other joints
- Pain (82%), swelling (65%), combination (50%), crepitus
- X-ray: Loose irregular radiopaque bodies
- Treatment: Removal of loose bodies, some surgeons do total synovectomy
Osteochondroma

• Most frequent neoplasm of bone
• Cartilage capped bone projection
• Metaphysis
• Condylar is rare; coronoid even rarer
• Median age ~40 for condylar
• ~2F:M
Pigmented villonodular synovitis

- Uncommon
- 10-70 years
- Patients are rarely younger than 30
- Average age 43.7
- Slight female predominance
- Swelling, pain
- Bone erosion
- Diffuse or localized; diffuse can be very aggressive
- Inflammation, giant cells, hemosiderin, regular mitoses
Ganglion and synovial cyst

- Confusion with the name
- Ganglion is a pseudocyst: myxoid degeneration; does not have synovial lining
- Synovial cyst: lined by cuboidal to flattened cells
- Preauricular swelling, pain
Skeletal Muscle Pathology
Duchene muscular dystrophy

- X-linked
- Pelvic and shoulder girdles
- Deletion of gene that encodes dystrophin (DMD)
  - Dystrophin is made in the heart and skeletal muscle
  - Also in neurons in the hippocampus
- Degeneration of muscles, impaired repair, fibrosis, fibrofatty deposits
- Elevated serum creatinine kinase
- Steroid treatment
- Death from respiratory insufficiency, cardiac arrhythmia, 10-15 years of age wheel chair-bound
Myotonic dystrophy

- AD
- Most common form of adult MD
- Sustained muscular contractions and rigidity
- Progressive muscle weakness and wasting
- Chromosome 19
- Atrophy of type I and hypertrophy of type II fibers
- Anticipation
  - Earlier age of onset and increased severity in successive generations
Myotonic dystrophy

• Three clinical groups
  – Congenital
  – Adult: facial and jaw muscles, ptosis
  – Late: minimal symptoms
Frontal baldness
Cataracts
Hypothyroidism
Myotonia
Muscle wasting
Myalgia
Cancer risk
Cognitive impairment
Apathy
Hypersomnia
Conduction defect
Arrhythmia
Cardiomyopathy
Glucose intolerance
Gastrointestinal disturbance
Infertility
Testicular atrophy
Autoimmune Myopathies

• Dermatomyositis
  – Complement mediated cytotoxic Abs against microvasculature of muscle
  – Distinctive skin rash
    • Face and eyelids and on knuckles, elbows, knees, chest and back
    • The rash, which can be itchy and painful
    • It is often the first sign of dermatomyositis.
  – Muscle weakness
    • Muscles closest to the trunk, such as those in your hips, thighs, shoulders, upper arms and neck
• Inflammatory myopathy
Dermatomyositis - Complications

• Dysphagia
  – Muscles in your esophagus are affected
  – Weight loss and malnutrition
  – Aspiration pneumonia

• Shortness of breath

• Increased risk for cancer
  – Cervix, lungs, pancreas, breasts, ovaries and gastrointestinal tract
  – Raynaud’s phenomenon
    • Cold and numb toes, fingers, ears and redness of the skin

• Calcium deposits
  – Muscles and skin (tumor calcinosis)
Dermatomyositis
Gingival and periungual juvenile dermatomyositis
Autoimmune Myopathies

• Polymyositis
  – Direct damage by cytotoxic T cells
  – Inflammation of the muscles or associated tissues, such as the blood vessels that supply the muscles
Autoimmune Myopathies

- Myasthenia Gravis (serious muscle weakness)
  - Muscular fatigability caused by circulating Abs to acetylcholine receptor at the myoneural junction
  - Extraocular muscles, swelling muscles, extremities
  - Patients can develop other autoimmune diseases
  - 40% patients have thymoma
  - 75% of remaining thymic hyperplasia
  - Removal of thymus can be curative
Polyarteritis Nodosa

- Men
- Small and medium size arteries
- Vasculitis
- Decreased blood supply to organs
- Implicated
  - Hepatitis B (~30%)
  - Sulfa drugs, penicillin
Temporal Arteritis

- Inflammation of large arteries
- Temporal artery and other arteries
- Headache, visual changes
- Confirmatory biopsy
- If untreated can lead to blindness