Osteoarthritis

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

• 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

• 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
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

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 & sacroiliac joints, young men
  - Reactive arthritis (Reiter syndrome)
    - Polyarthitis, conjunctivitis, non-gonococcal urethritis, oral lesions
  - Psoriatic arthritis
  - Arthritis and inflammatory bowel disease (enteropathic arthritis)
    - Crohn's, ulcerative colitis
## Reactive arthritis

- Photos of 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

- **Chondrocalcinosis**
- 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

Duchenne 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
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

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%)
  - Sulfur drugs, penicillin

Temporal Arteritis

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