

Arthritis I

Jason Ryan, MD, MPH



Arthritis

- Joint inflammation and swelling
- Many types
 - Osteoarthritis
 - Rheumatoid arthritis
 - Others
- Diagnosis may involve **arthrocentesis**
 - Aspiration of synovial fluid
 - Used for diagnosis in some cases
 - Also therapeutic for large effusions



Arthritis

Classification

- **Non-inflammatory**
 - Degenerative arthritis
 - Usually due to osteoarthritis
 - Joint pain without warmth or swelling
 - Low WBC in synovial fluid
 - May cause brief < 30 min morning stiffness
- **Inflammatory**
 - Warm, swollen joints
 - Elevated WBC in synovial fluid
 - Prolonged (>30 min) morning stiffness

Disease	White Blood Count (cells/mm ³)
Normal	< 200
Osteoarthritis	200-2000
Inflammatory	> 2000

Arthritis

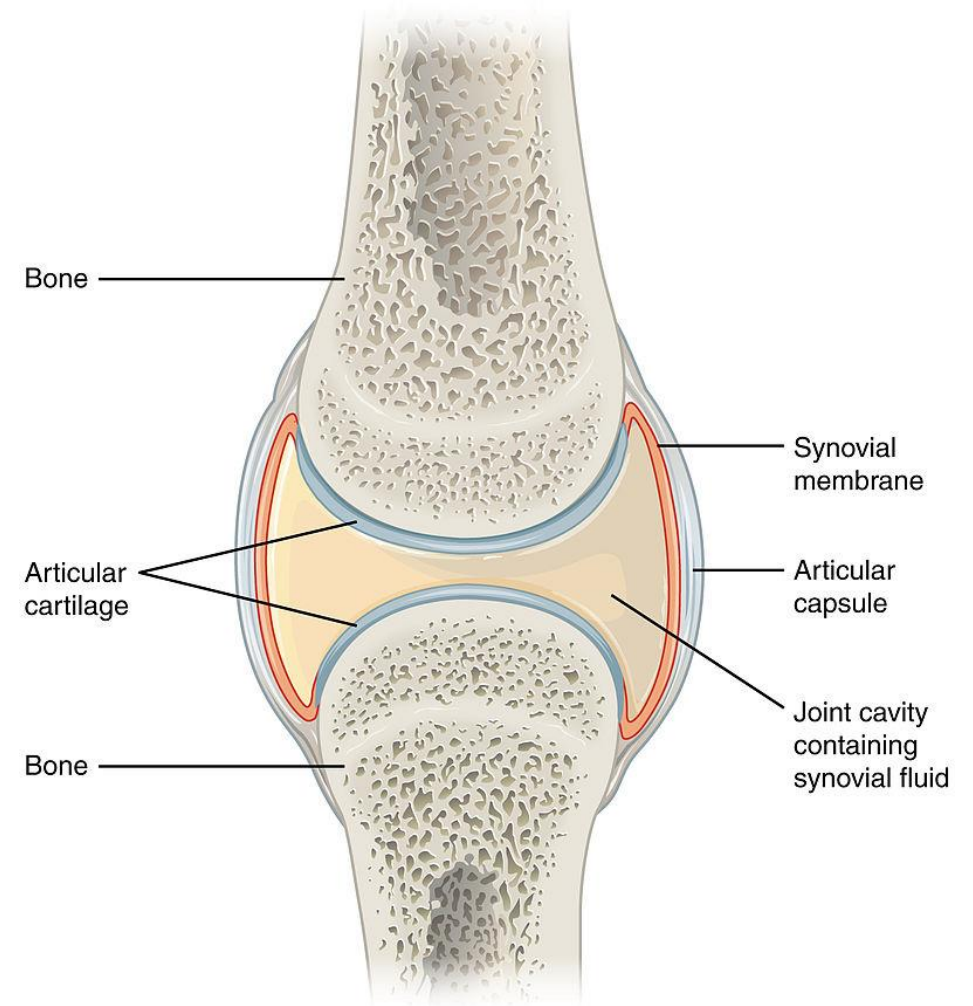
Classification

- **Number of joints**
 - One: monoarthritis
 - Two to four: oligoarthritis
 - More than five: polyarthritis



Osteoarthritis

- Degeneration of synovial joints
- **Hyaline cartilage breakdown**
 - Surrounds joint space
 - Provides smooth surface for gliding of bones
- **Hypertrophy of bone**
 - “Bone sclerosis” of subchondral bone
 - “Bone spurs” or osteophytes may form
 - Joint space narrows
- **Minimal inflammation of synovial fluid**
 - Non-inflammatory



Osteoarthritis

Clinical features

- **Insidious onset of joint pain**
 - Bone pain fibers irritated by movement
 - Deep, dull ache
 - Worsened by activity
 - Improved by rest
- **Stiffness**
 - In morning or after inactivity
 - Lasts < 30 minutes
- **Restricted motion**
 - Bony enlargement limits movement



Osteoarthritis

Clinical features

- Can affect any joint
- **Weight-bearing joints** most common
 - Hips
 - Knees
 - Cervical spine
 - Lumbar spine
- Monoarticular or polyarticular disease
 - May present as monoarticular symptoms



Osteoarthritis

Risk Factors

- Advanced age
 - 80% patients over 55 years old
- Obesity
 - Modifiable risk factor
 - Especially the knees
 - Hip
- Trauma
 - Major trauma to joint
 - Repeated microtrauma over time



Osteoarthritis

Diagnosis

- Clinical diagnosis
- Supportive evidence from **X-rays**
 - Joint space narrowing
 - Subchondral sclerosis
 - Osteophytes (bone spurs)
 - Subchondral cyst
- Low WBC in synovial fluid
 - “Non-inflammatory arthritis”
- All blood tests normal

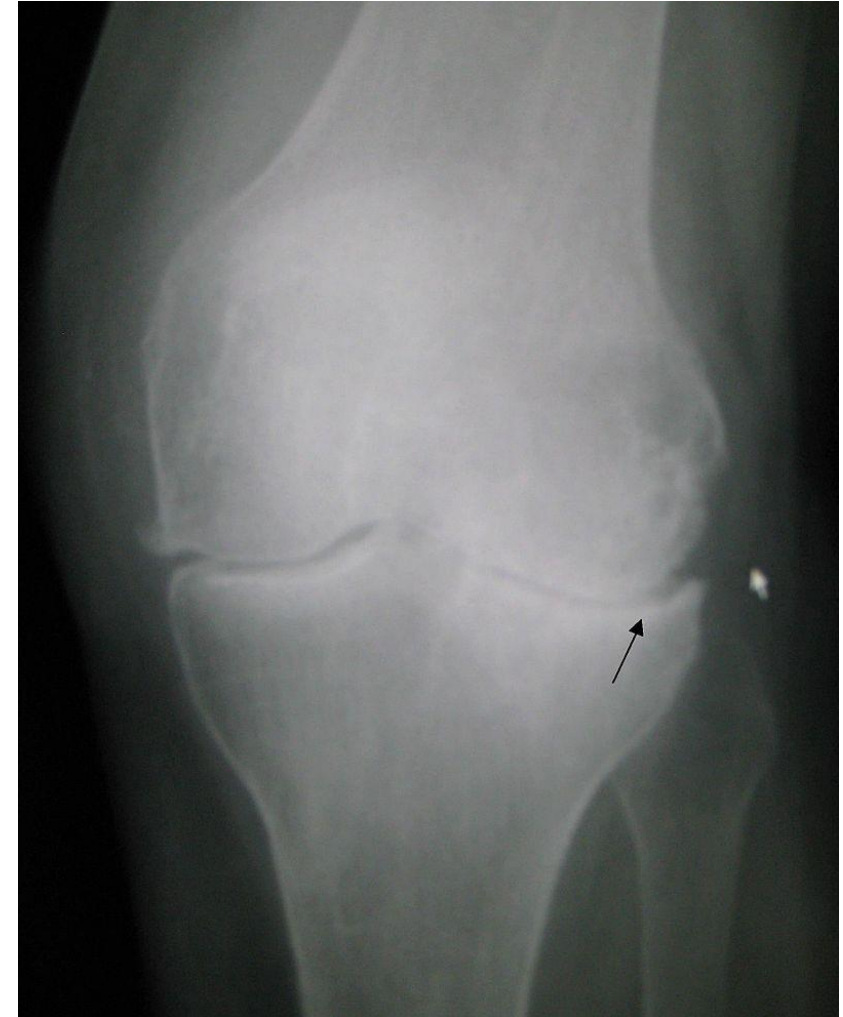


Joint Space Narrowing



Subchondral Sclerosis

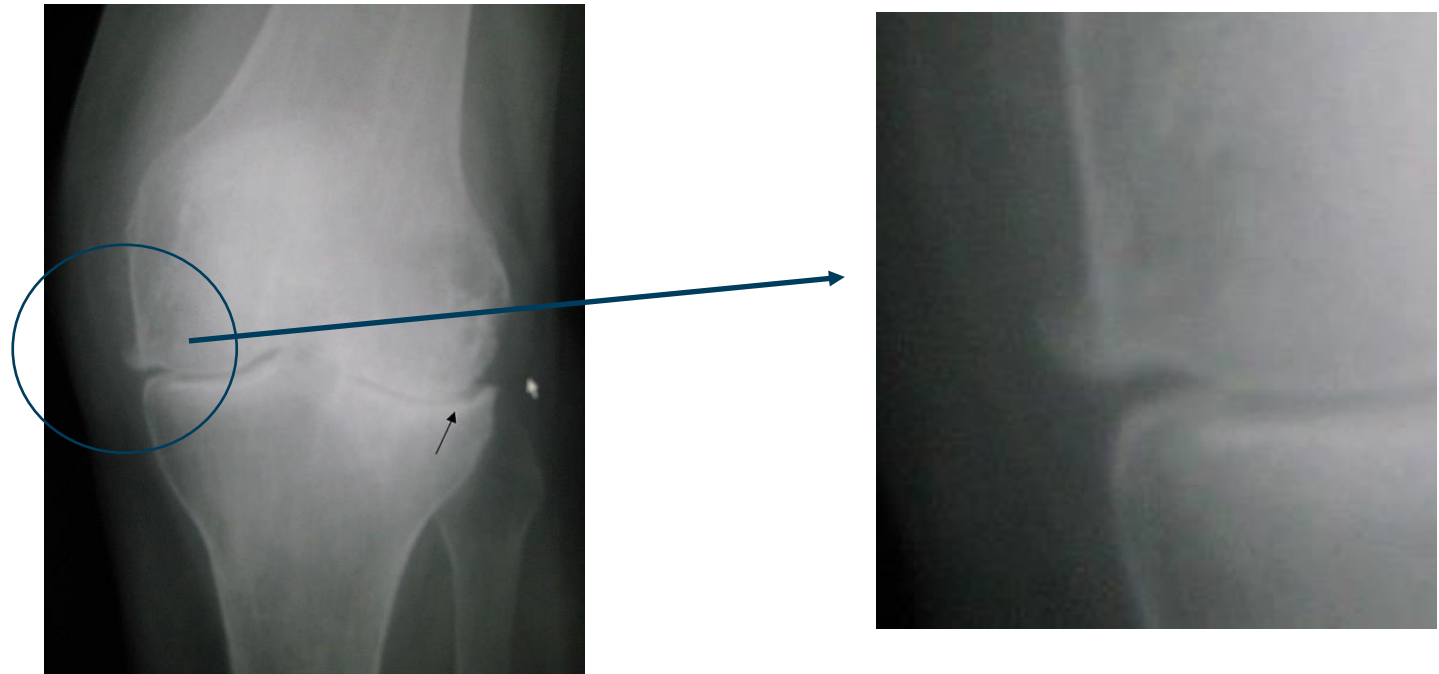
- Thickening of the subchondral bone
- ↑ collagen with abnormal mineralization



Osteophytes

Bone Spurs

- Thickening of the subchondral bone at joint margins
- Often insertion points of tendons or ligaments



Subchondral Cysts

- Fluid filled sack
- Bone cracks → synovial fluid accumulation



Osteoarthritis

Knee Involvement

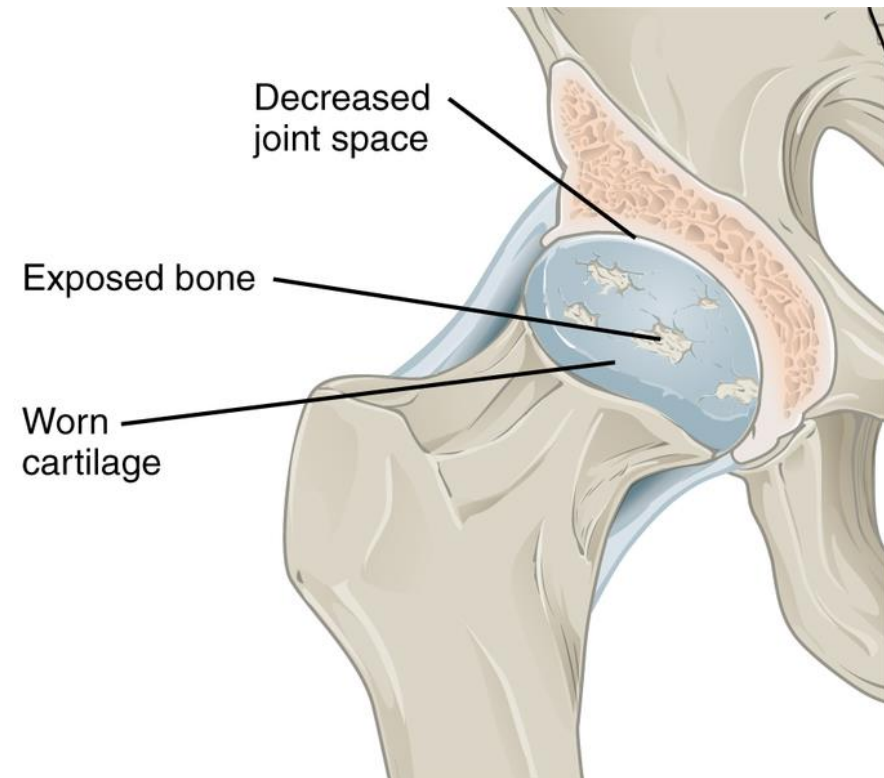
- Often involves **both knees**
- More weight-bearing medial knee
- Asymmetric narrowing may occur on medial side



Osteoarthritis

Hip Involvement

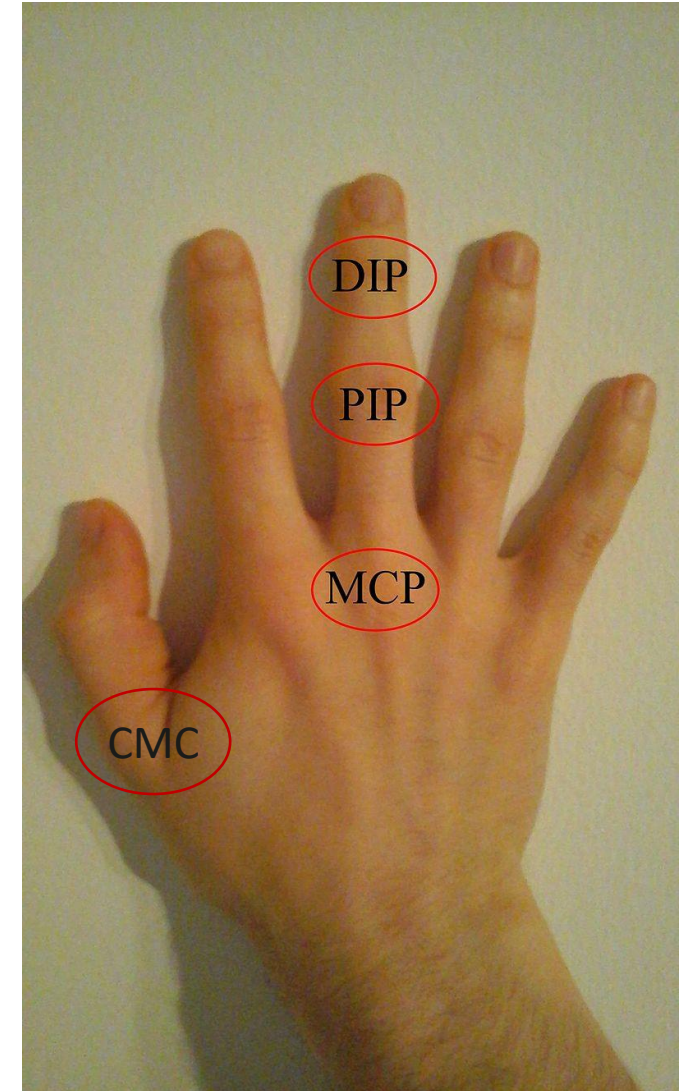
- Causes **groin, buttock or thigh pain**
- Reduced range of motion on exam
- Crepitus may be present
- Often unilateral
 - Contrast with knees - often bilateral



Osteoarthritis

Hand Involvement

- **Distal interphalangeal (DIP) joints**
 - Contrast with rheumatoid arthritis – DIP joints spared
- Proximal interphalangeal (PIP) joints
- Not MCP
- 1st Carpometacarpal (CMC) joint



Nodal Osteoarthritis

- Occurs in patients with interphalangeal OA of hands
- **Heberden's** (DIP) and **Bouchard's** (PIP) nodes
- Caused by bony overgrowth and osteophytes
- Over years, joints become less painful
- Inflammatory signs subside
- Swellings (nodes) remain
- Common at index and middle fingers



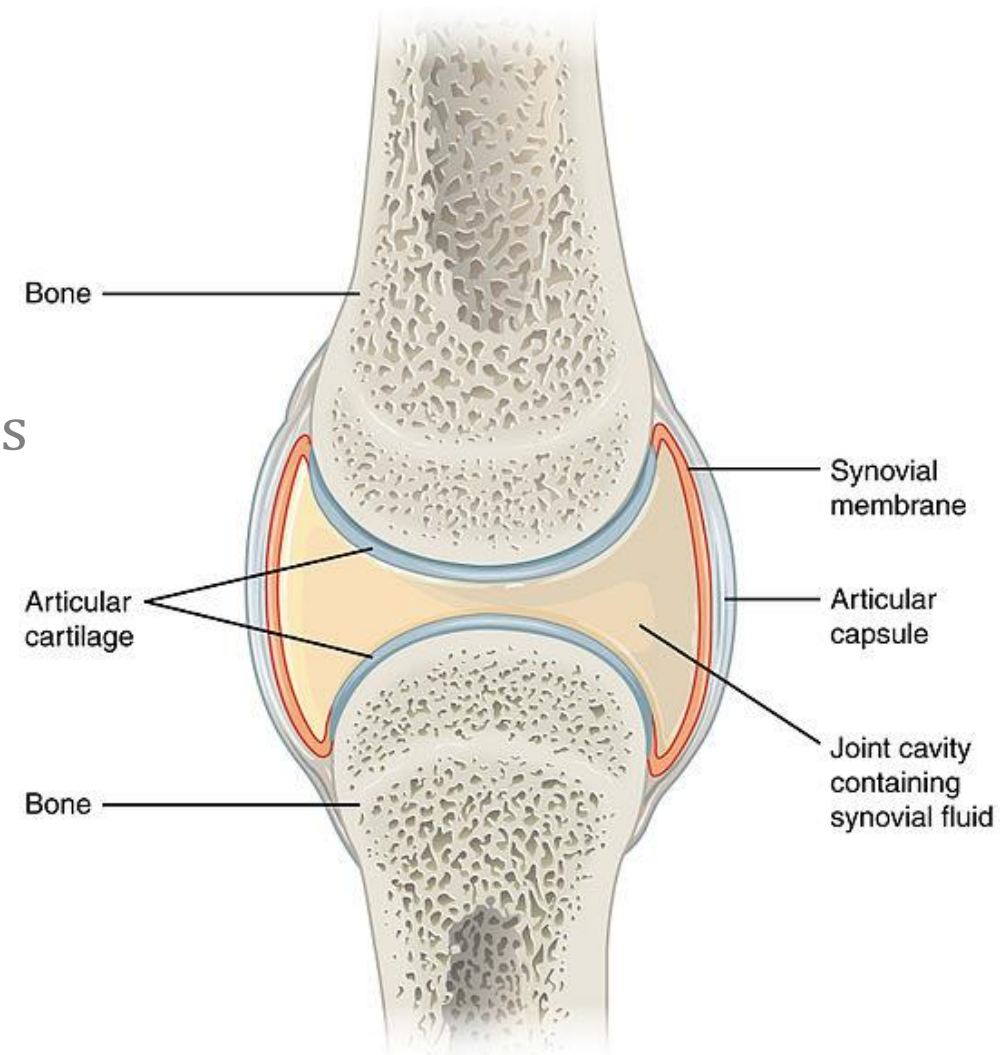
Osteoarthritis

Treatment

- **Weight loss**
- **Exercise and physical therapy**
 - Maintain range of motion and strength
- Topical or oral NSAIDs

Rheumatoid Arthritis

- **Autoimmune inflammation of synovium**
 - Thin layer of tissue (few cells thick)
 - Lines joints and tendon sheaths
 - Secretes hyaluronic acid to lubricate joint space
- Systemic disease with extraarticular complications
- More common in women
- Usual age of onset 20 to 40 years
- Disease course may wax and wane with flares



Rheumatoid Arthritis

Clinical features

- **Symmetric** joint inflammation
- Gradual onset
- Pain, stiffness, swelling
- Classically “**morning stiffness**”
 - Joint stiffness >1 hour after rising
 - Improves with use
- May have systemic symptoms
 - Fever, fatigue, weight loss

Rheumatoid Arthritis

Clinical features

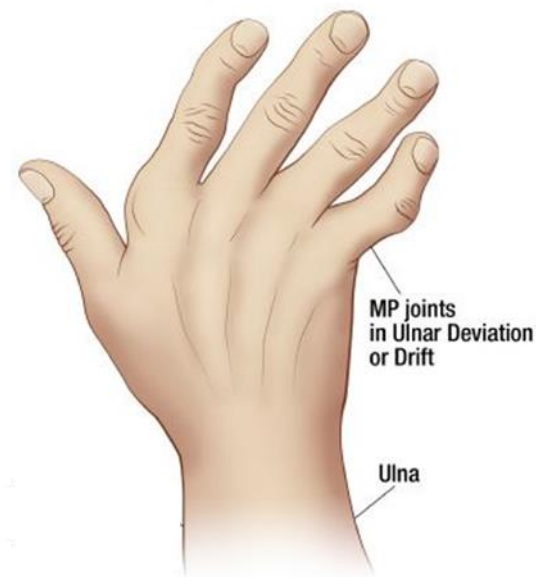
- Most often involves wrists and hands
- Classically affects **MCP and PIP** joints of hands
 - Often tender to touch
- **DIP joints spared**
 - Contrast with osteoarthritis – DIP joints involved
- Lumbar spine usually spared
 - Also a contrast with osteoarthritis



Rheumatoid Arthritis

Clinical features

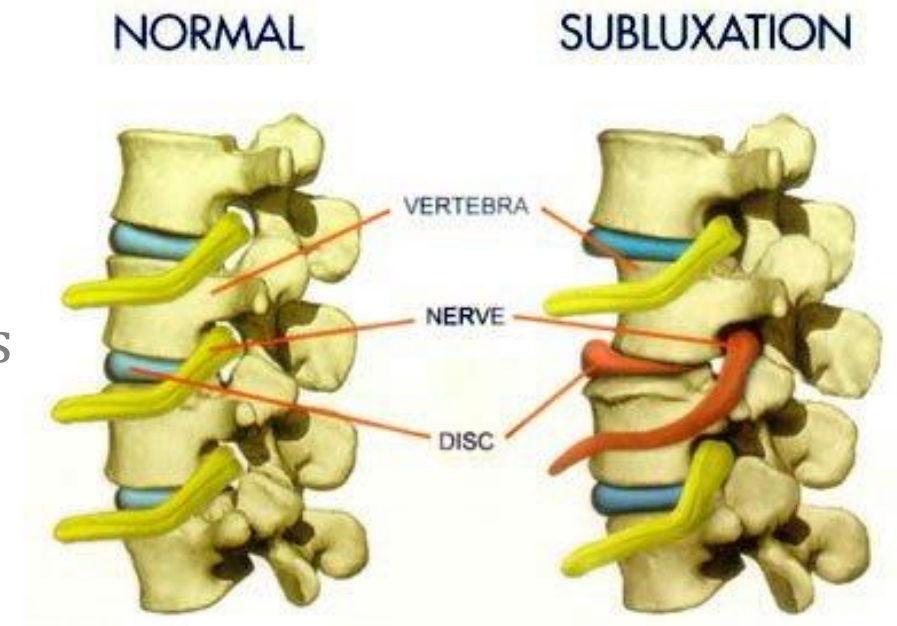
- Bones can erode and deviate
- **Ulnar deviation**
 - Swelling of MCP joints → deviation
- **Swan neck deformity**
 - Hyperextended PIP joint
 - Flexed DIP



Rheumatoid Arthritis

Clinical features

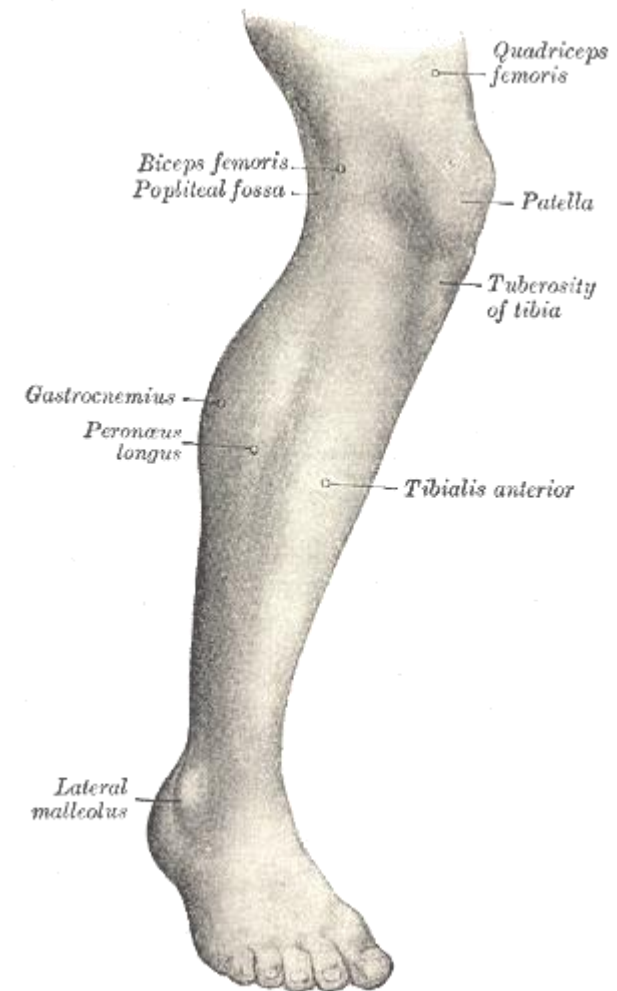
- Axial spine spared except **cervical region (usually C1 to C2)**
 - “Atlantoaxial joint”
 - Occurs with longstanding disease
 - Neck pain and stiffness
- **Cervical subluxation**
 - Possible life-threatening spinal cord compression
 - May require surgical treatment
- Limited by DMARD therapy
- Cervical spine X-ray before surgery in RA patients
 - Risk of neurologic injury with intubation



Rheumatoid Arthritis

Clinical features

- **Baker's cyst (popliteal cyst)**
 - Swelling of gastrocnemius-semimembranosus bursa
 - Synovium-lined sac at back of knee continuous with joint space
- Common in patients with **OA or RA of knee**
- Often asymptomatic bulge behind knee
- If ruptures → symptoms similar to DVT
 - Posterior knee pain, swelling, ecchymosis
- Usually a clinical diagnosis
- May need to rule out DVT

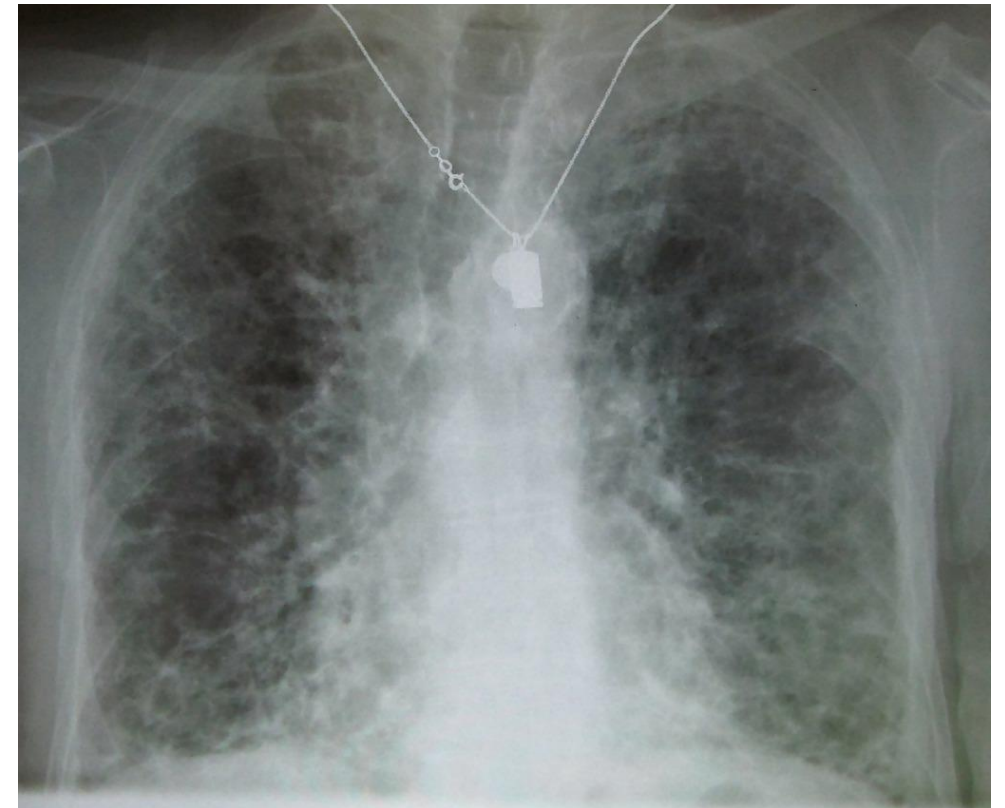


Rheumatoid Arthritis

Extraarticular features

- **Serositis** – inflammation of serosal surfaces
 - Pleuritis → pleural effusion
 - Pericarditis → pericardial effusion
- **Parenchymal lung disease**
 - Interstitial fibrosis
 - Pulmonary nodules
- **Carpal tunnel syndrome**
- **Anemia of chronic disease**

Interstitial Lung Disease



Rheumatoid Arthritis

Extraarticular features

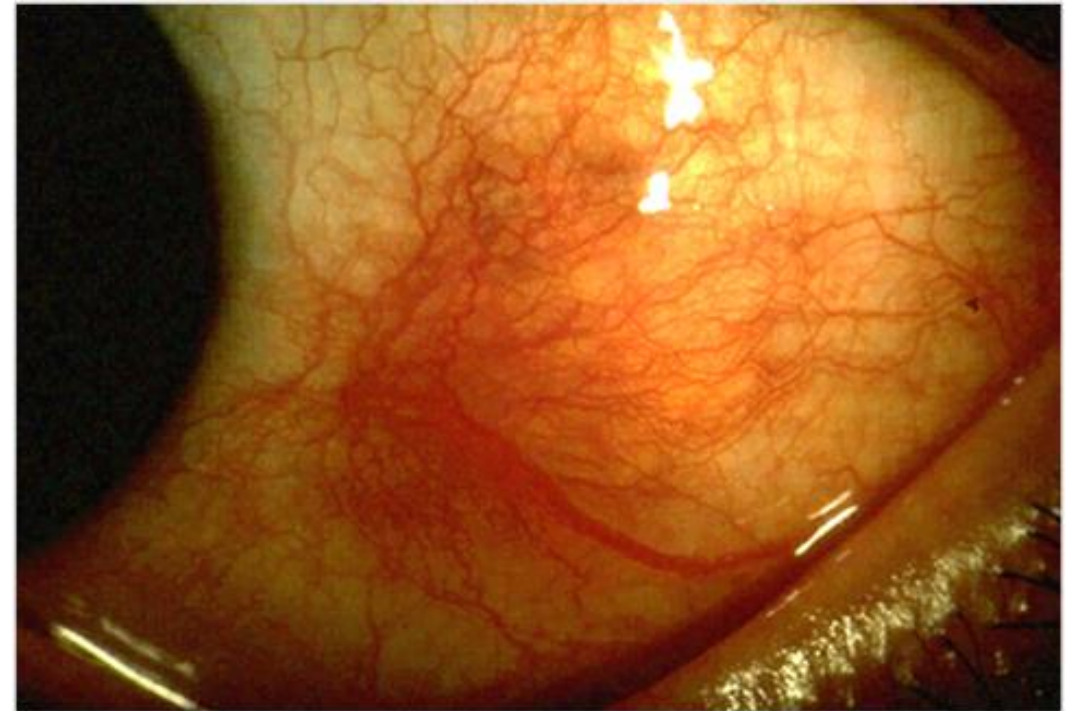
- Palpable nodules common (20 to 35% patients)
- Pathognomonic for rheumatoid arthritis
- Common on elbow although can occur anywhere
- Usually no specific treatment



Rheumatoid Arthritis

Extraarticular features

- Episcleritis and scleritis
 - Red eye
 - Eye pain
 - Discharge
- Sjogren's syndrome
 - Common in patient's with RA



Rheumatoid Arthritis

Osteoporosis

- Accelerated by RA
- Also often worsened by steroid treatment
- 30 percent ↑ risk of major fracture
- 40 percent ↑ risk hip fracture



Normal bone



Osteoporosis

Rheumatoid Arthritis

Diagnosis

- Inflammatory arthritis of 3 or more joints lasting more than 6 weeks
- **Rheumatoid factor (RF)** – 70 to 80% of patients
 - Low specificity – elevated in some normal patients and other conditions
- **Antibodies to citrullinated peptides (ACPA)**
 - More specific
- Acute phase reactants
 - Elevated C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR)

Rheumatoid Arthritis

Treatment

- Traditional **disease-modifying antirheumatic drugs (DMARDs)**
 - Protect joints from destruction
 - Provide long term reduction in disease progression and complications
 - Slow onset of effect over weeks
 - Usually given as oral drugs
- **Pain control**
 - Bridging therapy until DMARDs take effect
 - NSAIDs – drug of choice for pain control
 - Corticosteroids used if NSAIDs inadequate for pain control
 - Short term steroid treatment used for symptom flairs

DMARDs

Disease-modifying antirheumatic drugs

- **Methotrexate**

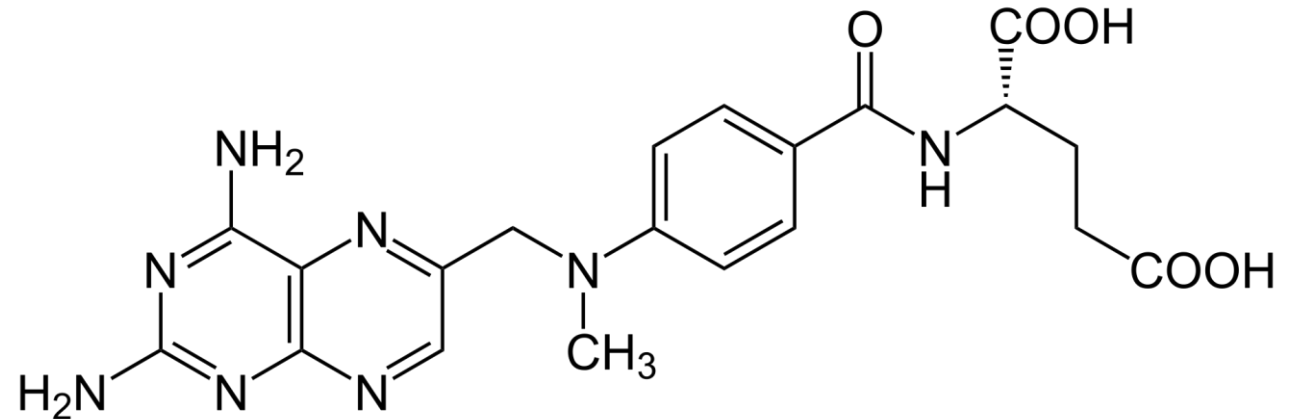
- Best initial DMARD
- May cause bone marrow suppression
- Co-administered with folic acid
- Also causes hepatotoxicity and stomatitis
- Monitor CBC, LFTs and creatinine

- Hydroxychloroquine

- Sulfasalazine

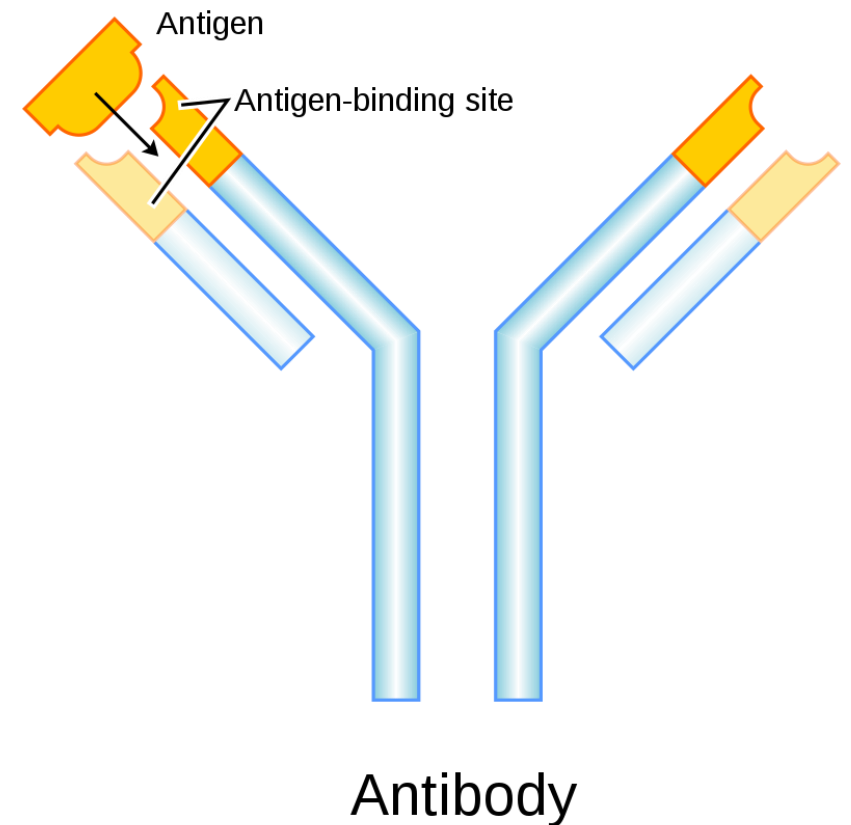
- Leflunomide

Methotrexate



Biologics

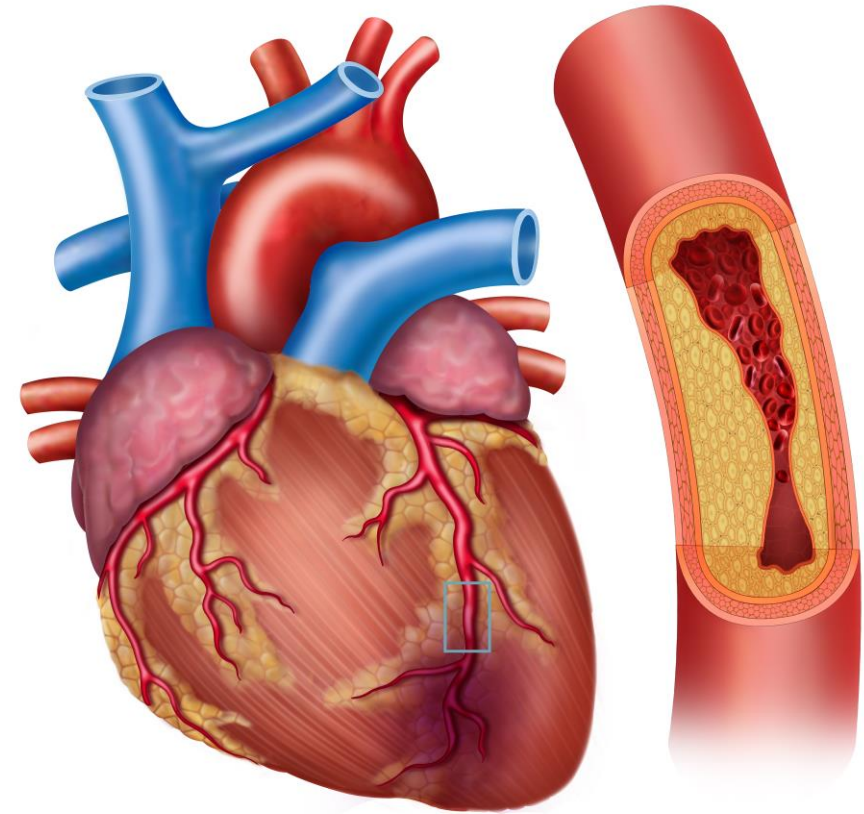
- Antibody-based treatments
- Infusions or injections
- Used when methotrexate does not control disease
- **Anti-TNF alpha therapy**
 - Etanercept and infliximab
- Non-TNF biologics
 - Abatacept, rituximab, tofacitinib
- **Pre-treatment screening for latent TB**
- Also hepatitis B and C



Rheumatoid Arthritis

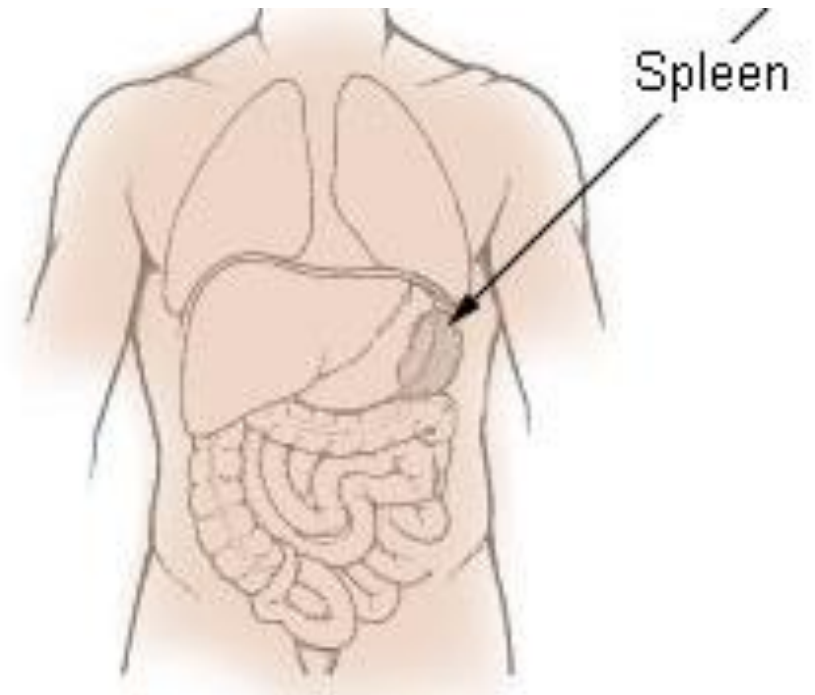
Long Term Complications

- Increased risk of **coronary disease**
 - Leading cause of mortality
- **Secondary (AA) amyloidosis**



Felty Syndrome

- Syndrome of **splenomegaly** and **neutropenia** in RA
 - Low WBC on blood testing
 - Increased risk for bacterial infections
 - Abdominal pain from enlarged spleen
- Classically occurs many years after onset RA
- Usually in patient with severe RA
 - Joint deformity
 - Extra articular disease
- Improves with RA therapy



Arthritis II

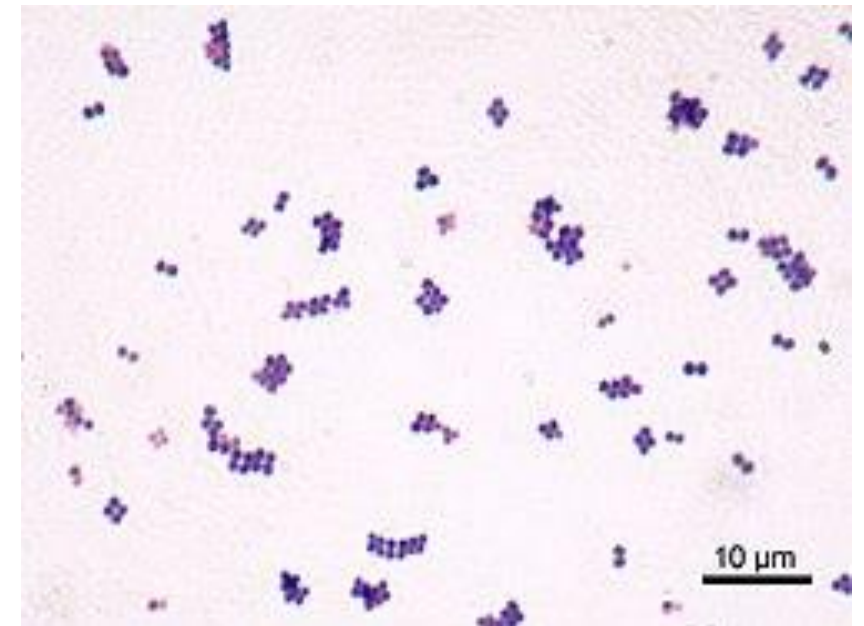
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Septic Arthritis

- Joint infection
- May be acquired through several mechanisms
 - Hematogenous spread
 - Contiguous spread (osteomyelitis)
 - Direct inoculation (trauma, surgery)
- Usually mono-bacterial
 - Most common cause: **Staph aureus including MRSA**
 - Streptococci
 - Gram negative rods

S. Aureus
(gram positive cocci)



Septic Arthritis

Clinical features

- **Acute onset** of arthritis symptoms
- Usually monoarthritis
 - Single swollen, painful joint
 - **Knee** is most common joint
 - Less commonly wrists, ankles or hips
- Fever



Septic Arthritis

Risk factors

- **Pre-existing joint disease**
 - Rheumatoid arthritis, osteoarthritis, gout
- Intravenous drug use
- Immunosuppression including diabetes



Septic Arthritis

Infants

- Usually involves hip or knee
- Fever, irritability, poor feeding
- Swollen, red, warm joint
- Joint tenderness to palpation



Septic Arthritis

Diagnosis and treatment

- **Blood cultures and synovial fluid analysis**
 - Should be sent before antibiotics
 - Synovial WBC usually 50,000 to 150,000 cells/microL
 - Mostly neutrophils
 - Purulent fluid
 - Gram stain and culture
- Joint drainage
 - Similar to management of an abscess
 - Serial aspiration for easily accessed joints (knee)
 - Arthroscopic drainage or arthrotomy
- Antibiotics

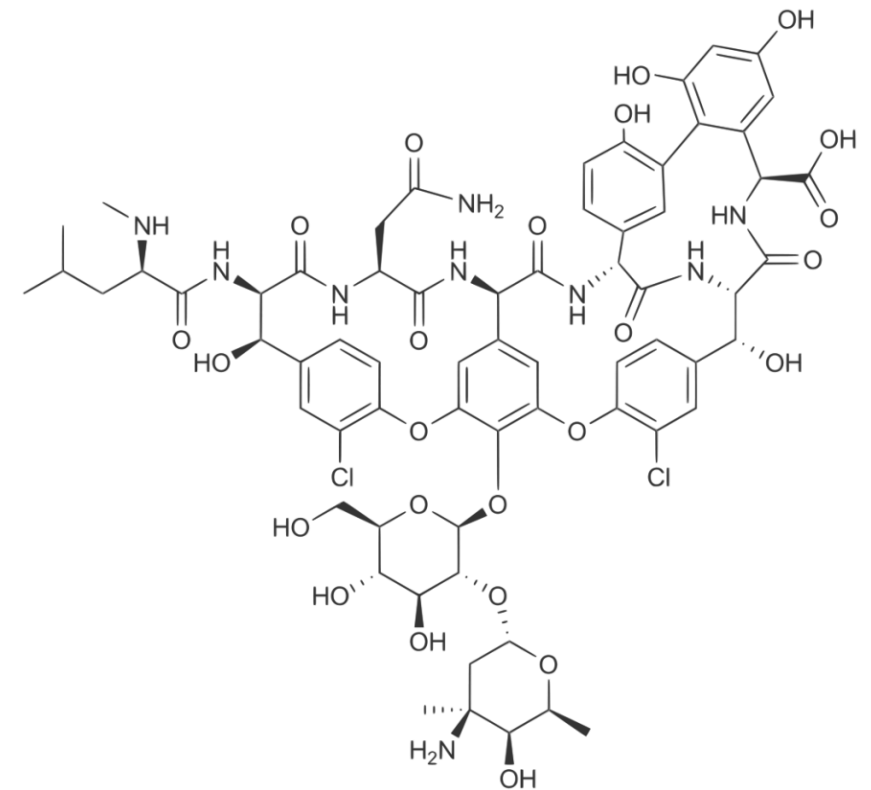
Disease	White Blood Count (cells/mm ³)
Normal	< 200
Osteoarthritis	200-2,000
Inflammatory	> 2,000
Septic	> 20,000 (PMNs)

Septic Arthritis

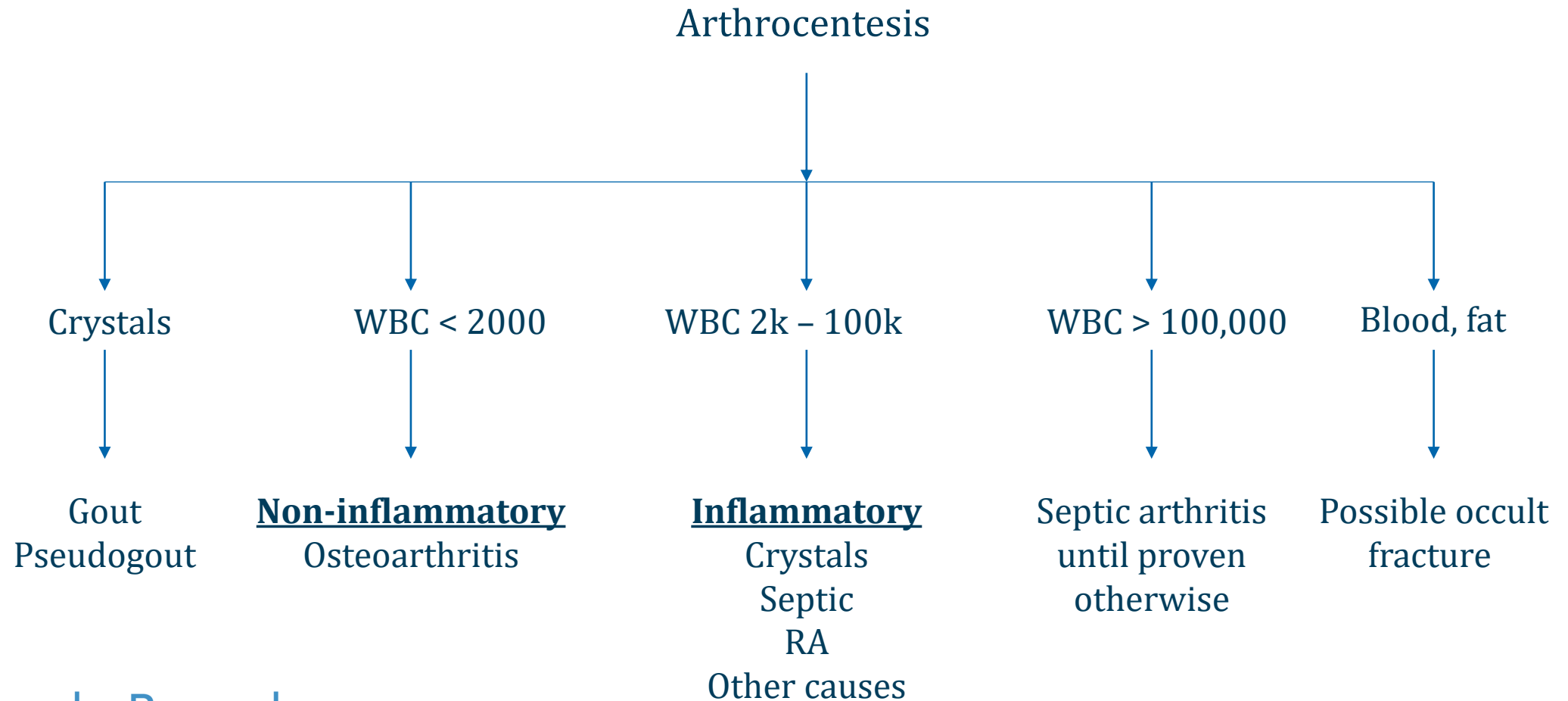
Antibiotics

- Gram positive cocci – **vancomycin**
- Gram-negative bacilli – **usually cephalosporins**
 - Ceftriaxone
 - Ceftazidime if concern for pseudomonas

Vancomycin



Acute Monoarthritis



Septic Arthritis

Prosthetic joint infection

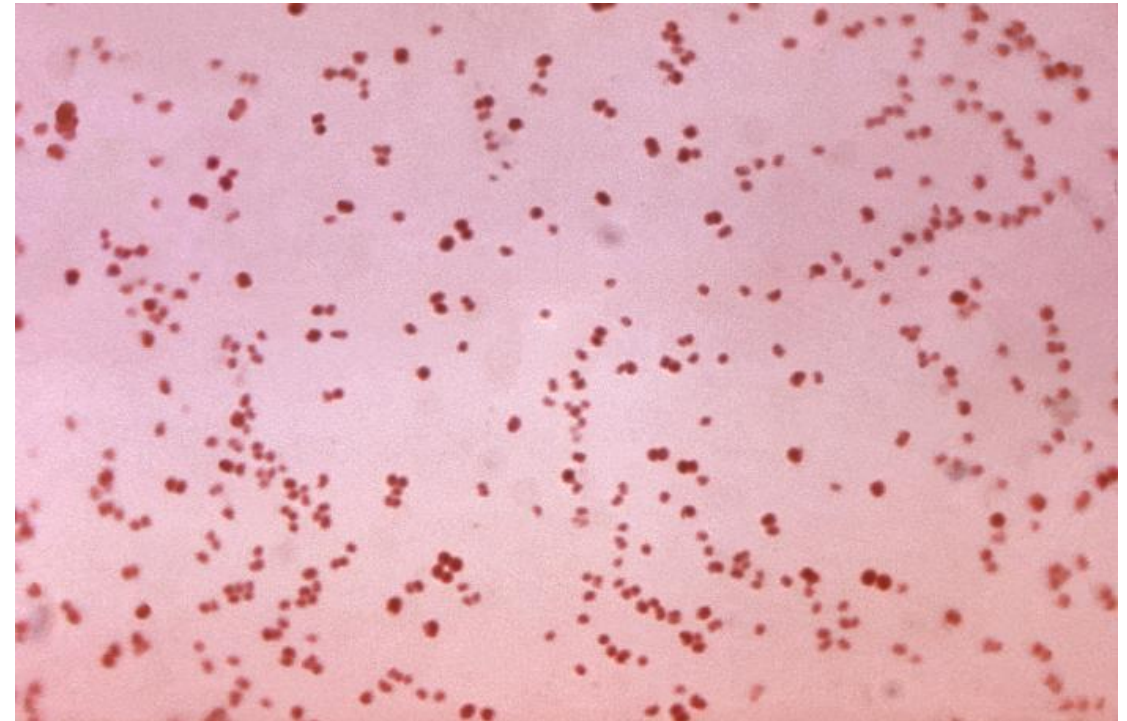
- Early onset (<3 months after surgery)
 - *S. aureus*, gram-negative rods
- Delayed onset (3 to 12 months after surgery)
 - **Coagulase-negative staphylococci** or enterococci
- Late onset (>12 months after surgery)
 - *S. aureus*, gram-negative bacilli, streptococci
- Broad antibiotic coverage until culture data available
- Often vancomycin plus broad-spectrum cephalosporin
- Surgery often required for debridement or re-implantation



Disseminated Gonococcal Infection

- Hematogenous spread of **Neisseria gonorrhoeae**
- Occurs among sexually-active adults
- Two classic patterns
 - Arthritis-dermatitis syndrome
 - Purulent arthritis
 - Patients may have elements of both (spectrum)

N. Gonorrhoeae



Disseminated Gonococcal Infection

Arthritis-dermatitis syndrome

- Fever, chills and malaise
- Polyarthralgia
 - Small or large joints
 - Migrates over time
- Tenosynovitis
 - Tendons of wrist, fingers, ankle and toes
- Dermatitis
 - Often **scattered pustules**



Disseminated Gonococcal Infection

Purulent arthritis

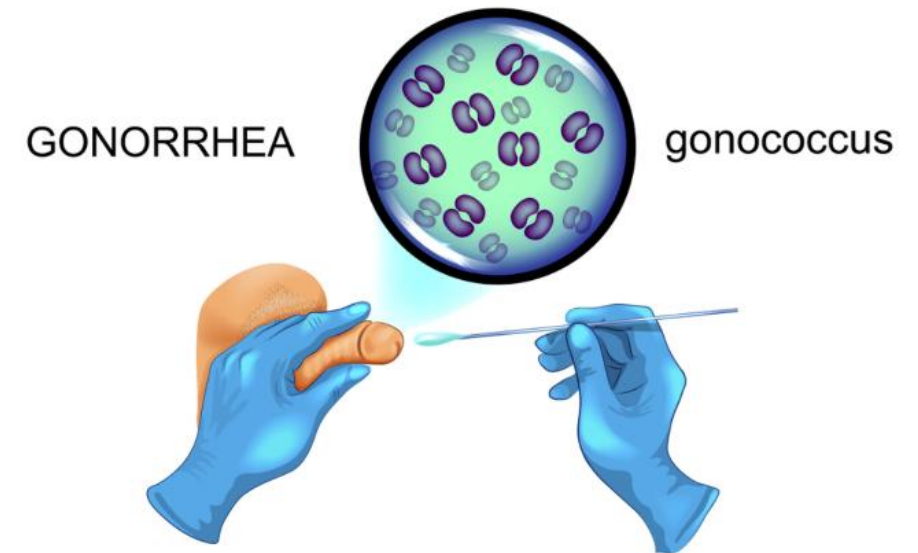
- Abrupt onset of monoarthritis or oligoarthritis
- Knees, wrists and ankles most common



Disseminated Gonococcal Infection

Diagnosis

- Blood cultures
- Mucosal testing
 - Urogenital, rectal, and pharyngeal swab
 - Nucleic acid amplification testing (NAAT)
- Arthrocentesis for synovial fluid testing
 - WBC ~ 50,000 cells/microL (but can be lower)
 - Gram stain and culture (can be negative)
 - NAAT testing - more sensitive than culture

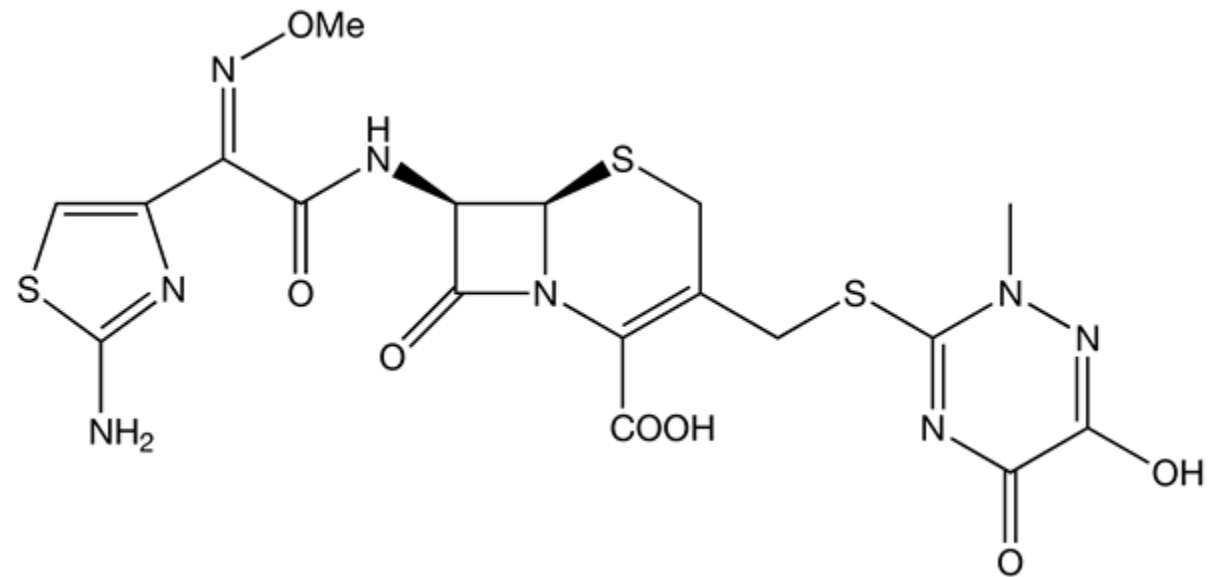


Disseminated Gonococcal Infection

Treatment

- **Intravenous ceftriaxone**
- Oral doxycycline or azithromycin
 - Treatment for chlamydia co-infection
 - Unless chlamydia infection ruled out by testing

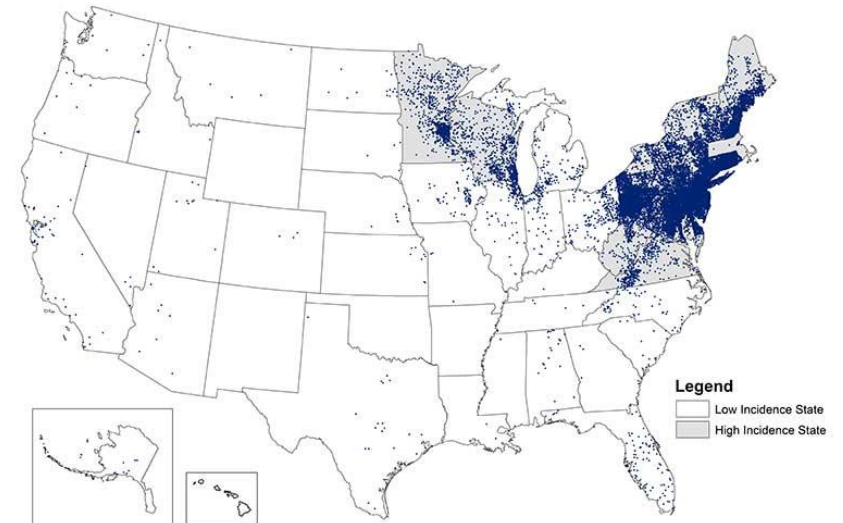
Ceftriaxone



Lyme Arthritis

- Occurs in **endemic areas** for Lyme (Northeast US)
- Suspect in patients with **possible exposure**
 - Endemic area
 - Prior tick bite
 - Hiking or camping
- Arthrocentesis: inflammatory findings
 - Negative gram stain and culture
- Diagnosis: Lyme serology
- Treatment: doxycycline, amoxicillin or ceftriaxone

Reported Cases of Lyme Disease
United States, 2018



Seronegative Spondyloarthritis

- Spondylo = spine
- Arthritis = joint inflammation
- Seronegative = negative rheumatoid factor
- Family of disorders with common features
- Ankylosing spondylitis
- Psoriatic arthritis
- Inflammatory bowel diseases
- Reactive arthritis



Parvovirus B19

- Erythema infectiosum in children
 - “Slapped cheek” rash
- In adults may cause arthralgia or arthritis
 - Acute, symmetric polyarthrititis
 - Small joints especially hands and wrists
- Diagnosis: clinical +/- anti-parvovirus IgM
- No specific treatment - self-limited
- Consider in **adults who work with children**
 - Daycare, schools



Wikipedia/Public Domain

Juvenile Idiopathic Arthritis

- Group of inflammatory disorders
- Occur in children under age 16 years
- All involve arthritis of ≥ 1 joint for ≥ 6 weeks
- Diagnosis: clinical
- Treatment: NSAIDs, steroids or DMARDs
- Major subtypes
 - Oligoarticular
 - Polyarticular
 - Systemic

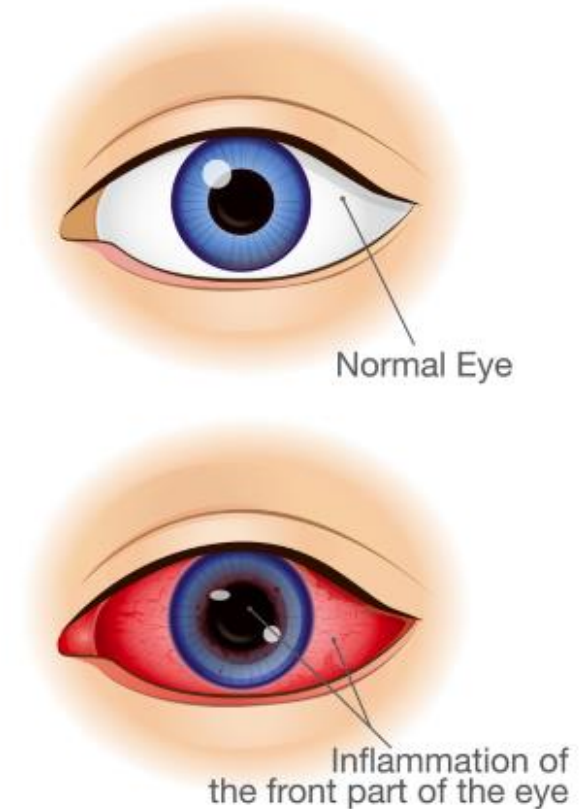


Juvenile Idiopathic Arthritis

Oligoarticular subtype

- Less than 5 joints affected
- Peak incidence 2 to 3 years
- Females > males
- Often knees or ankles
- Toddler with limp and swollen joint
- Usually negative RF
- Serious complication: uveitis (20 to 25% children)

Anterior Uveitis



Juvenile Idiopathic Arthritis

Polyarticular subtype

- Similar to oligoarticular but ≥ 5 joints affected
- Two peaks of incidence: 2 to 5 years and 10 to 14 years
- Females > males
- Uveitis may occur but less common

Juvenile Idiopathic Arthritis

Systemic subtype

- Previously called Still's disease
- Arthritis of ≥ 1 joint
- Occurs at any age < 16
- **High “quotidian fever”**
 - One high spike per day
 - Normal temp rest of day
- **Rash**
 - “Evanescent:” comes and goes
 - Usually pink and macular
- Hepatosplenomegaly
- Lymphadenopathy



Juvenile Idiopathic Arthritis

Systemic subtype

- Increased WBC
- Elevated platelets
- Elevated ESR
- ANA and RF usually negative



Adult Still's

- Similar to systemic JIA but occurs in adults
- Polyarthrititis
- Quotidian fever
- Rash
- ANA and RF usually negative
- Diagnosis of exclusion

Transient Synovitis

- Benign, self-limited condition
- Acute inflammation of synovium
- Commonly affects **hip joint in children**
- Usually **preceded by viral infection**
 - Upper respiratory, diarrheal
- Child usually well-appearing
- Low-grade fever may occur
- Low WBC, ESR and CRP
- Treatment: NSAIDs



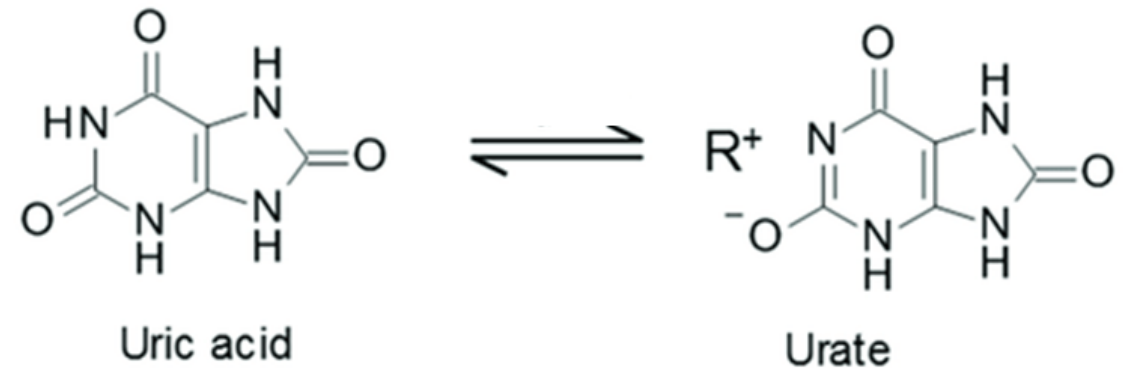
Gout

Jason Ryan, MD, MPH



Gout

- **Monosodium urate deposition** in joints
 - Most uric acid circulates as urate
 - Urate = uric acid after loss of proton (H^+)
- Triggers inflammatory response
- Recurrent attacks of **acute arthritis**
- Severe joint pain
- Redness, swelling, warmth



Acute Gouty Arthritis

- Hyperuricemia + genes + cool temperatures
- Usually **monoarthritis**
- Most common: **base of great toe (podagra)**
 - 1st metatarsophalangeal joint
- Also often occurs in knee
- More common in obese males
- Associated with hypertension



Gout

Clinical course

- **Gout flares**
 - Acute arthritis
 - Usually monoarticular
 - Often associated with a trigger
- Intercritical period
- **Tophaceous gout**



Chronic Tophaceous Gout

- **Tophi:** urate collections in connective tissue
- Ears, tendons, bursa
- Slowly-enlarging hard masses
- Usually **not painful or tender**
- May cause erosion of surrounding bone
- Seen with longstanding hyperuricemia
- Don't confuse with RA nodules
 - History of symmetric polyarthritis in RA
 - History of recurrent bouts of monoarthritis in gout



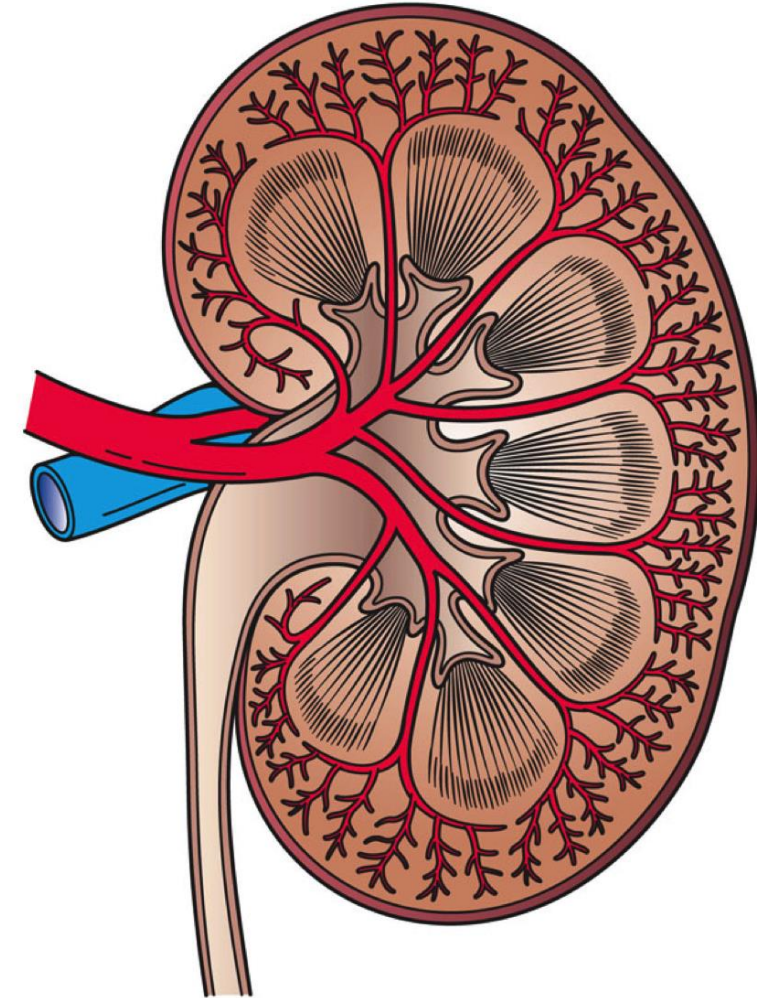
Herbert L. Fred, MD/Hendrik A. van Dijk



Apoorv Jain/Slideshare

Urate Nephropathy

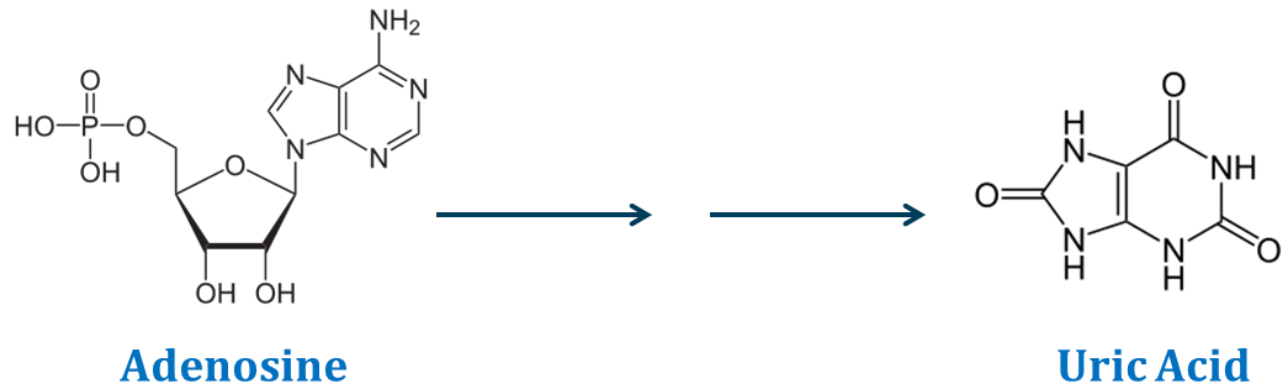
- Consequence of longstanding hyperuricemia
- Uric acid crystals in urine
- Uric acid kidney stones
- Chronic renal failure



Gout

Triggers

- Increased serum uric acid levels
 - Overproduction
 - Decreased excretion by kidneys
 - Rare genetic enzyme defects
- Uric acid produced from metabolism of **purine nucleotides**
 - Excess purines → increased uric acid



Gout

Triggers

- Purine sources
- Red meat, seafood
- Trauma/surgery (tissue breakdown)



Gout

Triggers

- Myeloproliferative disorders
 - Chronic myeloid leukemia
 - Essential thrombocytosis
 - Polycythemia vera
- Associated with high cell turnover
- Hyperuricemia → gout



Gout

Triggers

- Urate excreted mostly via **kidneys and urine**
- Any reduction in GFR → ↓ uric acid excretion
 - Renal failure
 - Volume depletion
 - **Diuretics**
- Commonly cause gout attacks
- Diuretics also ↓ uric acid secretion in urine
 - Thiazides, loop diuretics



Gout

Triggers

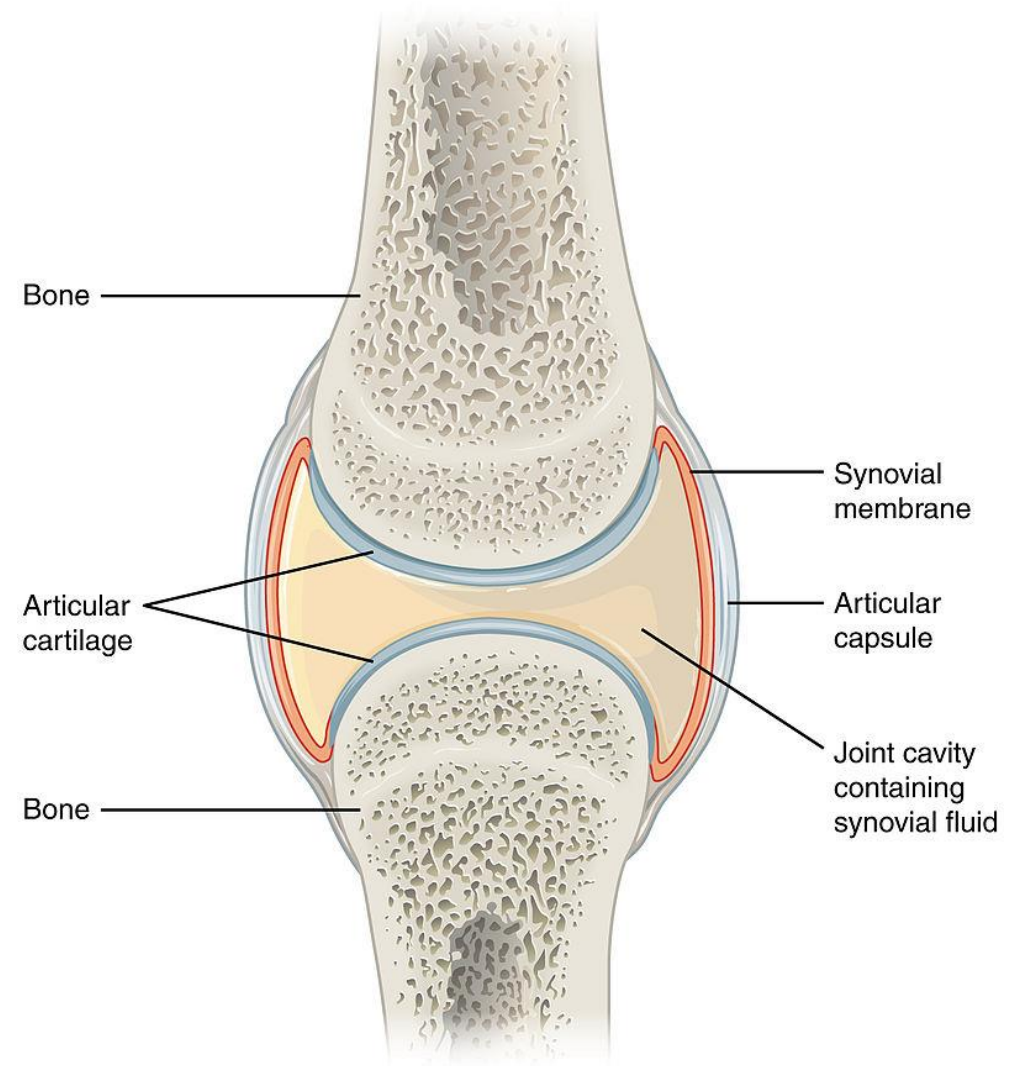
- Alcohol: classic trigger for gout
- Metabolism leads to lactic acid production
- Lactic acid increases renal reabsorption of urate



Gout

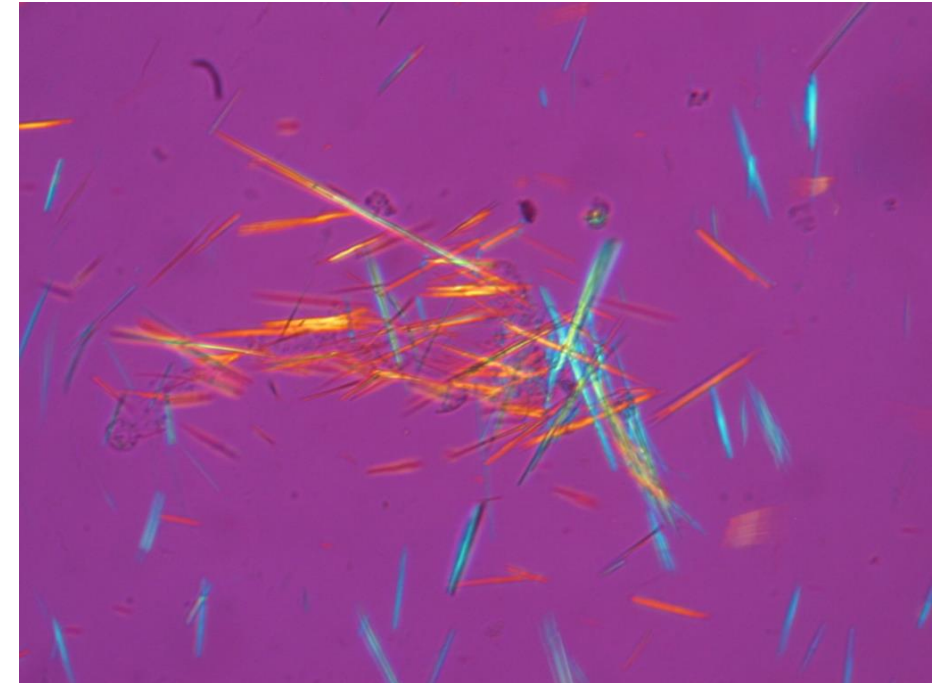
Diagnosis

- **Arthrocentesis**
 - Sampling of synovial fluid
 - WBC 20k to 50k
 - Crystals seen by polarized light microscopy
- X-rays
 - May show evidence of joint destruction
 - Particularly in advanced, chronic disease



Gout Crystals

- **Needle-shaped, “negatively birefringent” crystals**
 - Two reflections of polarized
 - Change in index of refraction is negative
- **Yellow** when **parallel** to axis of the polarization
- **Blue** when **perpendicular** to polarization axis



Hyperuricemia

- All patients with gout have some degree of hyperuricemia
- Most hyperuricemic patients never develop gout
- **Normal or low serum urate** may be present during gout flares
 - Cytokines may lower urate levels
 - Urate deposits in joints
- Testing for serum urate not helpful for diagnosis of gout
- Most accurate testing for urate is two weeks or more after a flare

Gout Treatment

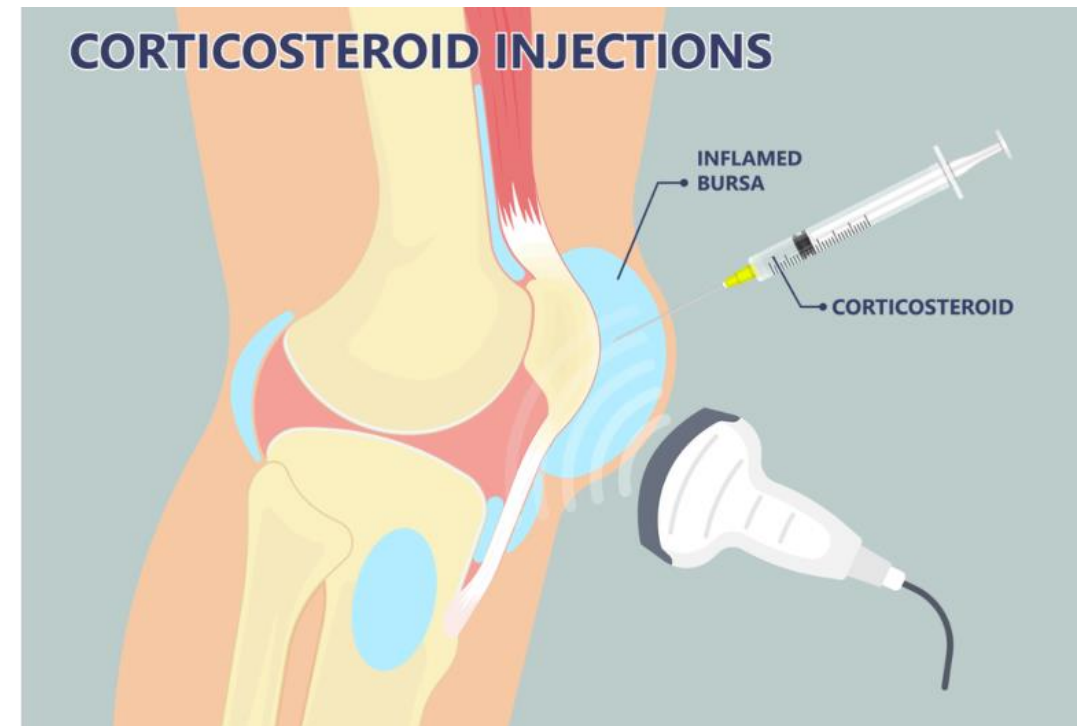
Acute attacks

- **Oral glucocorticoids**
 - Usually prednisone or prednisolone
 - Avoided with infection, post-op (wound healing), brittle diabetes
- **NSAIDs**
 - Usually high-dose potent NSAIDs
 - Naproxen or indomethacin
 - Avoided with high bleeding risk (anticoagulant use), CKD, peptic ulcer disease

Gout Treatment

Acute attacks

- Colchicine
 - Anti-inflammatory: inhibits white blood cell activity
 - Alternative to glucocorticoids or NSAIDs
- Glucocorticoid intraarticular injection
 - Used when flare involves only one or two joints



Aspirin

- Not used for treatment of acute gout flares
- Doses up to 1 to 2 grams/day inhibit urate excretion
- Low-dose daily aspirin can be used in patients with gout
 - Benefits > Risks for prevention of vascular disease



Gout Treatment

Prevention of acute attacks

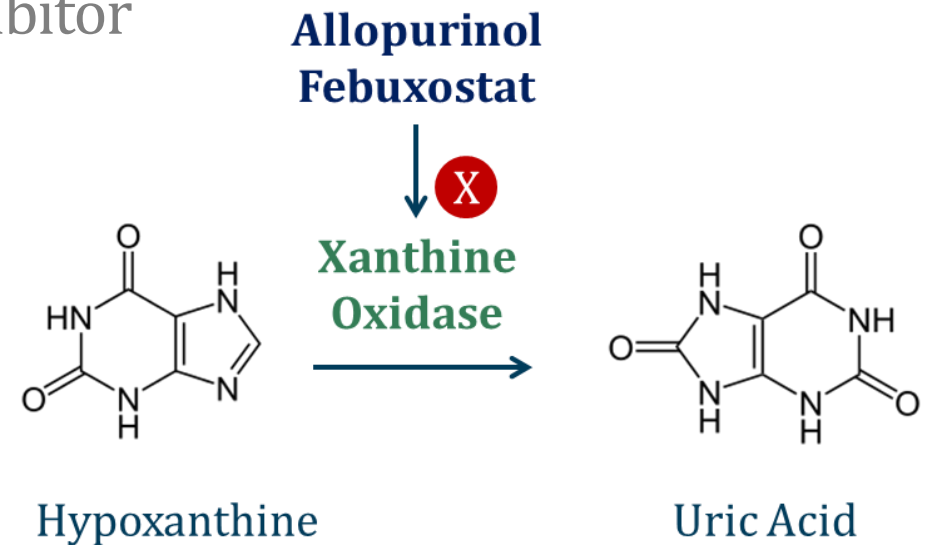
- **Lifestyle modification**
 - Weight loss and exercise: ↓ serum urate and risk of flares
 - Moderation of animal/seafood protein intake and alcohol
- Pharmacologic therapy indications
 - Frequent or disabling attacks
 - Tophi or structural joint damage
 - Renal insufficiency ($\text{CrCl} < 60 \text{ mL/minute}$)



Gout Treatment

Prevention of acute attacks

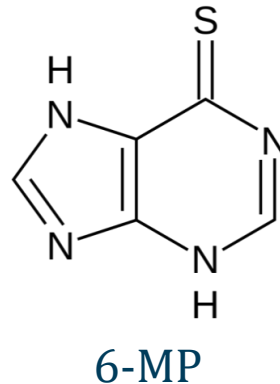
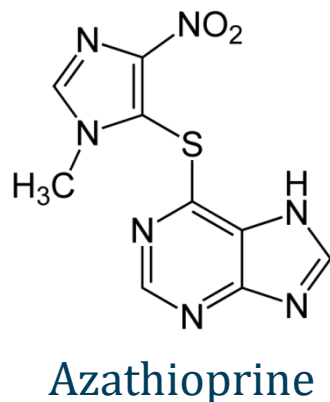
- Usual first-line therapy: **allopurinol**
 - Xanthine oxidase inhibitor
 - Goal urate level < 6 mg/dL (normal 3 to 8)
 - May cause rash, leukopenia/thrombocytopenia or diarrhea
 - Alternative: febuxostat
- Must administer **colchicine** when starting XO inhibitor
 - Given for first few months of treatment
 - Prevents triggering a gout flare



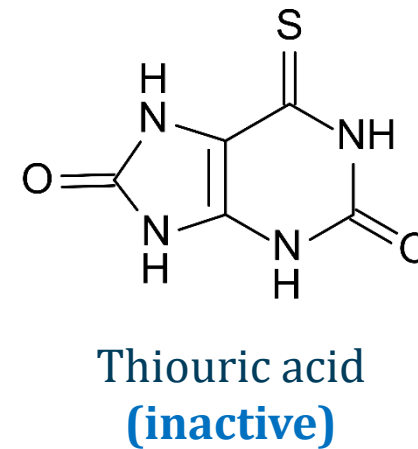
Xanthine Oxidase Inhibitors

Allopurinol, Febuxostat

- Interact with azathioprine and 6-MP
- Both metabolized by **xanthine oxidase**
- Caution with XO inhibitors
- May boost effects
- May increase toxicity



Xanthine
Oxidase



Gout Treatment

Other drugs

- Probenecid
 - Uricosuric drug – promotes urate excretion
- Pegloticase
 - Recombinant form of uricase
 - Enzyme that breaks down urate
 - Intravenous drug given as infusion every two weeks
 - Used for severe, refractory gout
- Rasburicase
 - Also a recombinant uricase
 - Used only in tumor lysis syndrome

Lesch-Nyhan Syndrome

- Enzyme defect in purine salvage pathway
- **X-linked absence of HGPRT**
 - Hypoxanthine-Guanine phosphoribosyltransferase
- **Excess uric acid** and “juvenile gout”
- Neurologic impairment (mechanism unclear)
- Hypotonia, chorea
- Self-mutilating behavior
- Classic presentation
 - Male child with motor symptoms, self-mutilation, gout

Nail Biting in Lesch-Nyhan



Von Gierke's Disease

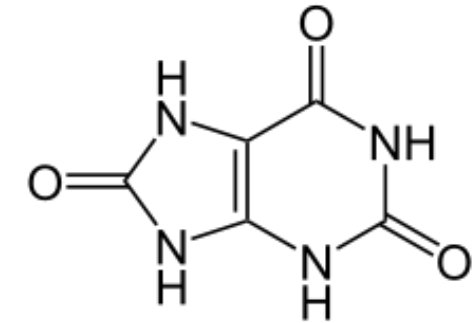
Glycogen Storage Disease Type I

- Glucose-6-phosphatase deficiency
- Presents in infancy: 2-6 months of age
- Severe **hypoglycemia** between meals
- May lead to seizures
- Associated with **lactic acidosis**
 - Promotes urate reabsorption
 - May lead to gout attacks

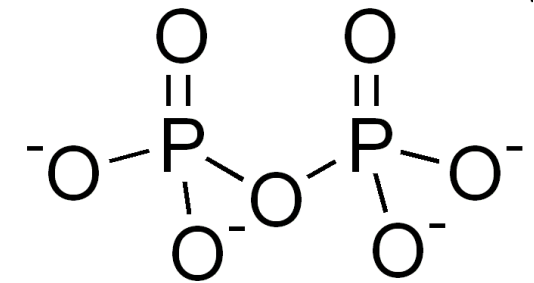
CPPD

Calcium Pyrophosphate Deposition Disease

- **“Pseudogout”**
- **Calcium pyrophosphate** deposition in joints
- Occurs in **older patients** (average age: 72)
- Common in patients with **hemochromatosis**
 - Arthropathy often involves pyrophosphate
- Associated with **hypercalcemia and hyperparathyroidism**



Uric Acid

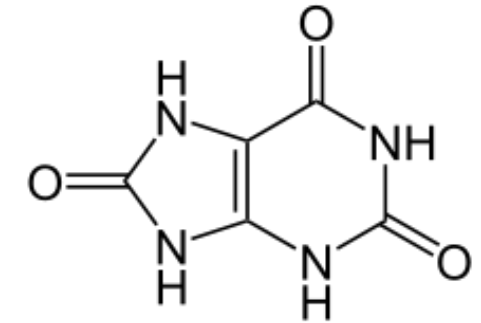


Pyrophosphate

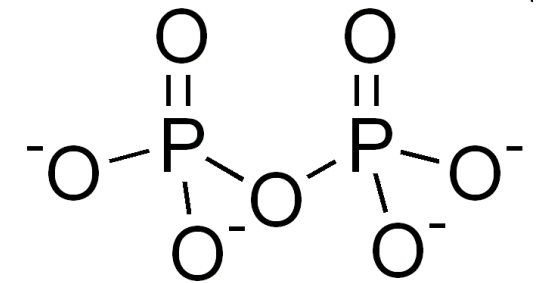
CPPD

Major clinical manifestations

- Asymptomatic (discovered on imaging)
- Acute arthritis (similar to gout)
- Chronic joint disease (similar to OA)



Uric Acid



Pyrophosphate

Asymptomatic CPPD

- Most joints with CPPD have no symptoms
- Crystal deposits discovered on imaging
- **Chondrocalcinosis:** calcification of cartilage



Pseudogout

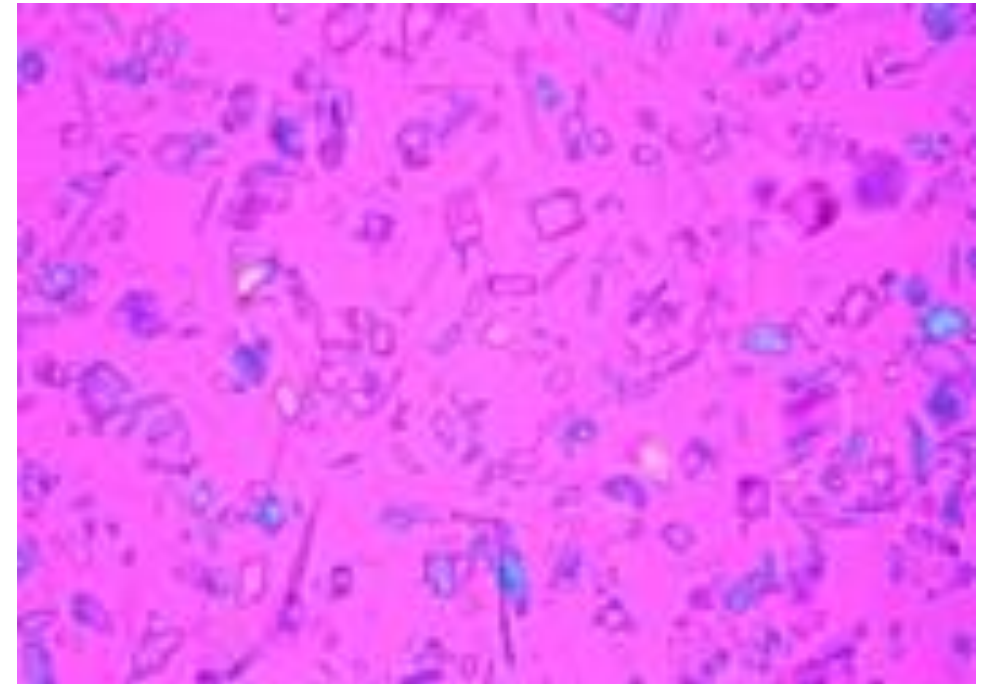
- Acute attacks of **inflammatory arthritis**
- Resemble attacks of gout
- **Knee involved in 50% of cases**
 - Pain, redness, warmth, swelling
- Provoked by trauma, surgery, medical illness
- Many flares reported after **parathyroidectomy**



Pseudogout

Polarized Light Microscopy

- **Rhomboid crystals**
- Positively birefringent
- **Blue when parallel** to light (yellow for gout)



Harriet Ribbons/Caroline Hoernig

Chronic Joint Disease

- Pseudo-osteoarthritis
- Progressive joint degeneration
- Occurs in ~50% of patients with CPPD joints
- Progressive cartilage deterioration
- Bony enlargement, tenderness similar to OA



CPPD

Treatment

- Acute pseudogout attack
 - Intraarticular glucocorticoid injection
 - NSAIDs
 - Colchicine
- Prophylaxis for pseudogout: colchicine
- Chronic joint disease: same treatment as OA

Systemic Lupus Erythematosus

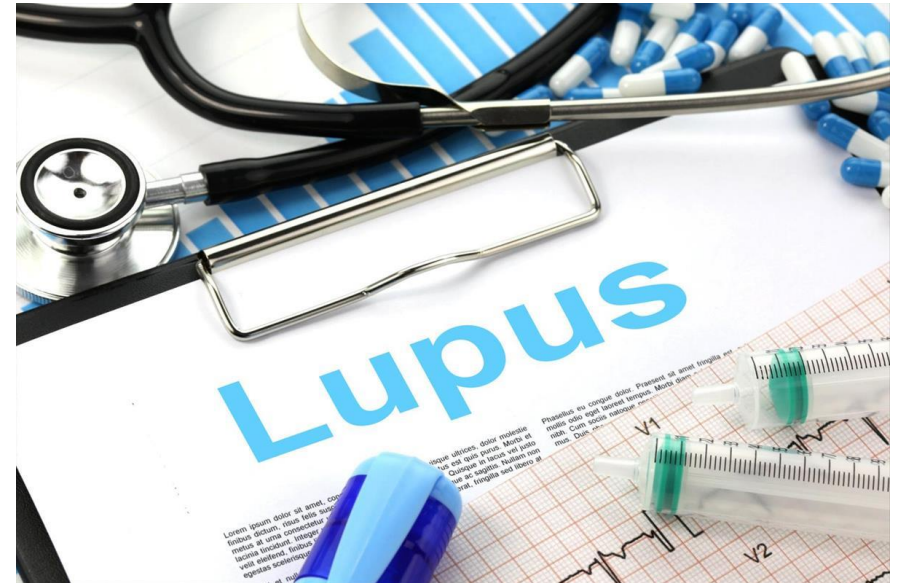
Jason Ryan, MD, MPH



SLE

Systemic Lupus Erythematosus

- Autoimmune disease
- **Antibody-antigen complexes** circulate in plasma
 - Type III hypersensitivity reaction
 - Deposit in MANY tissues → diffuse symptoms
- Most patients (90%) are women
- Usually develops age 15 to 45



SLE

Clinical features

- **Flares** and remissions common
- Fever, weight loss, fatigue, lymphadenopathy
- **Malar rash**
 - Classic lupus skin finding
 - “Butterfly” rash
 - Common on **sunlight** exposure
- Can also see “**discoid**” **skin lesions**
 - Circular skin patches
 - Classically on forearm



SLE

Raynaud Phenomenon

- White/blue fingertips
- Painful on **exposure to cold**
- Vasospasm of the artery → ischemia
- Can lead to **fingertip ulcers**



SLE

Raynaud Phenomenon

- Seen in other conditions
 - Isolated
 - Other autoimmune disorders (RA, scleroderma)
- Treatments: avoid cold
- **Dihydropyridine calcium blockers (amlodipine)**



SLE

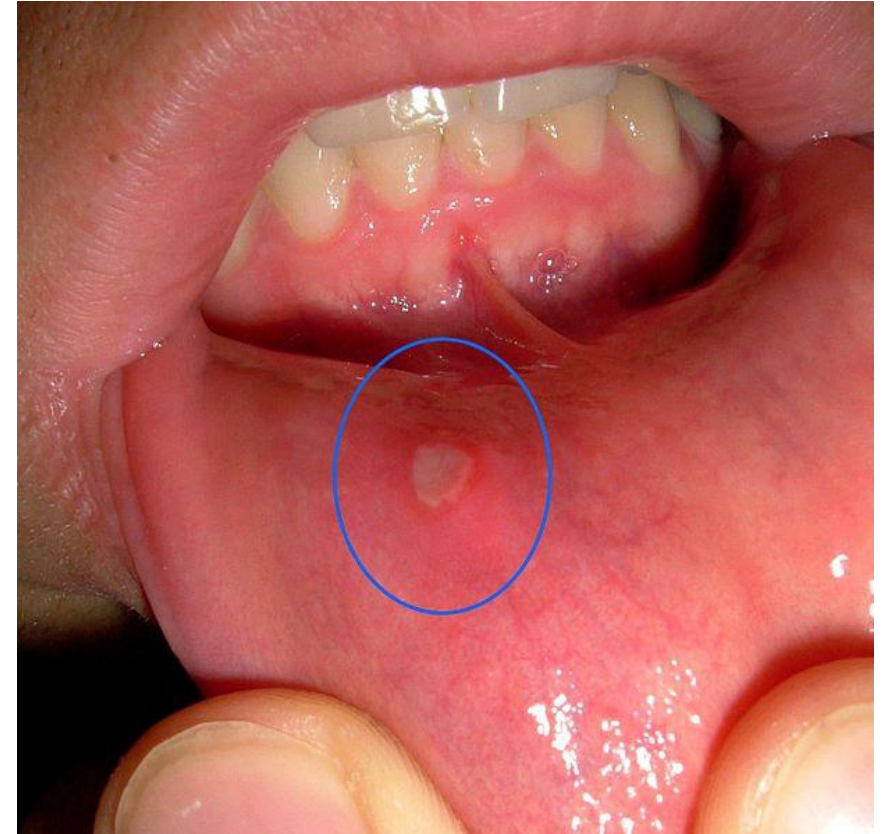
Clinical features

- **Polyarthrititis** (monoarthrititis unusual)
- Symmetric
- **Migratory**
 - Symptoms come/go over 24 hours
- Brief morning stiffness (< RA)
- Knees and hands most common
- Pain out of proportion to objective findings
 - Mild swelling, minimal X-ray abnormalities

SLE

Clinical features

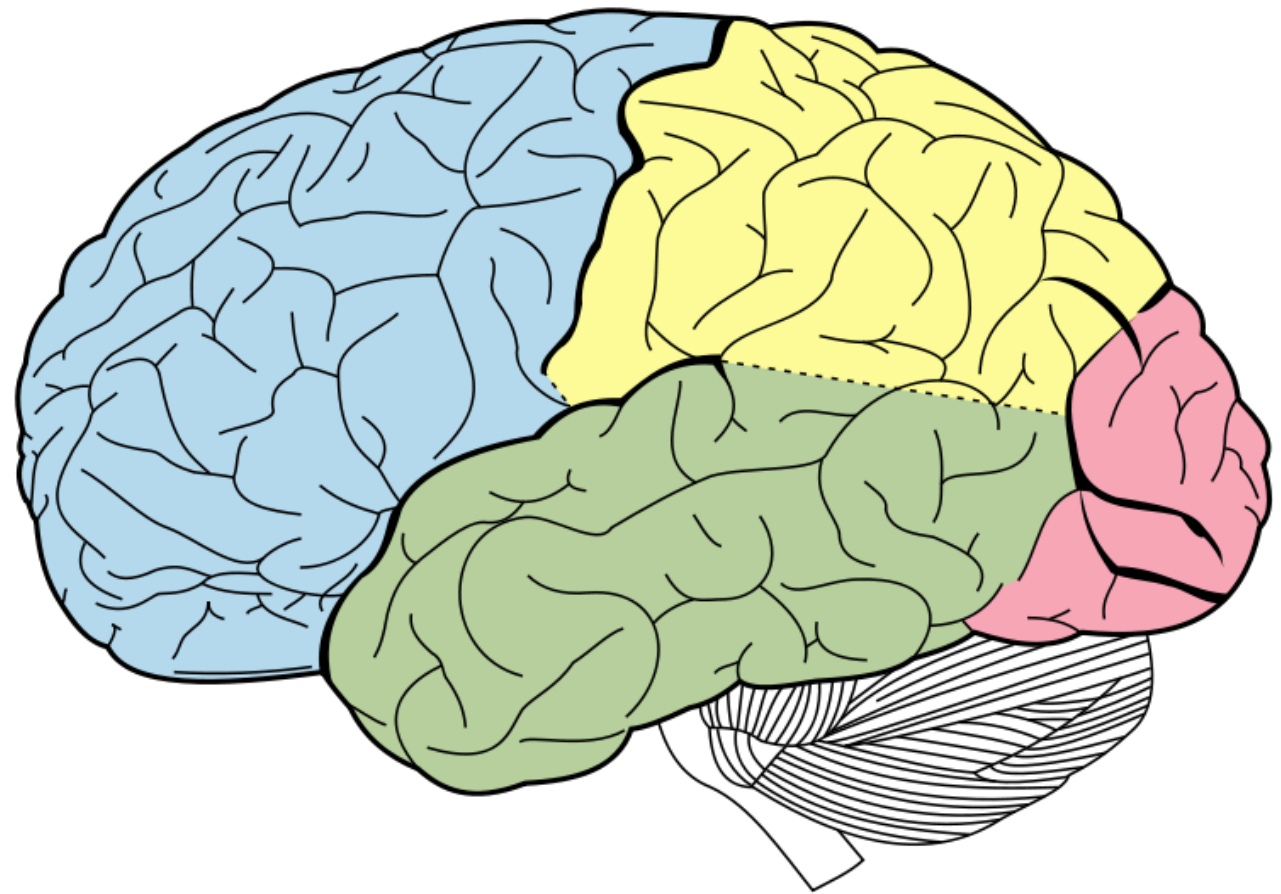
- **Oral or nasal ulcers**
- Serositis
 - Inflammation of pleura (pain with inspiration)
 - Inflammation of pericardium (pericarditis)
- **“Penias”**
 - Anemia, thrombocytopenia, leukopenia
 - Antibody deposition on blood cells → destruction
- Immune dysfunction and ↑ infection risk



Lupus Cerebritis

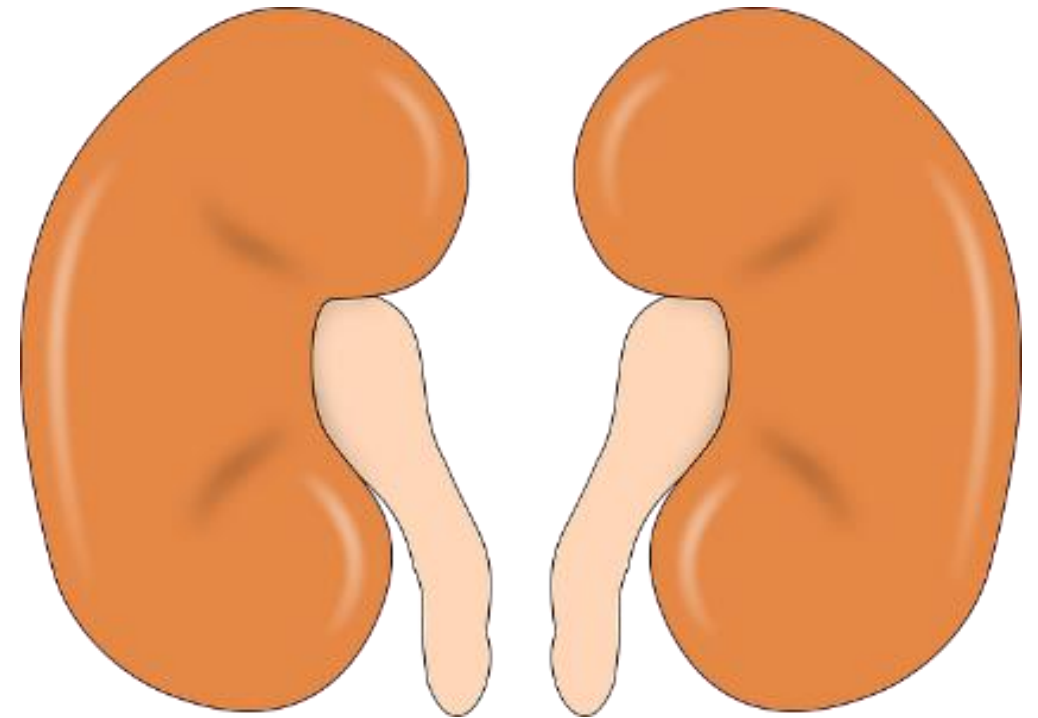
CNS Involvement

- Cognitive dysfunction
 - Confusion
 - Memory loss
- Stroke
- **Seizures**



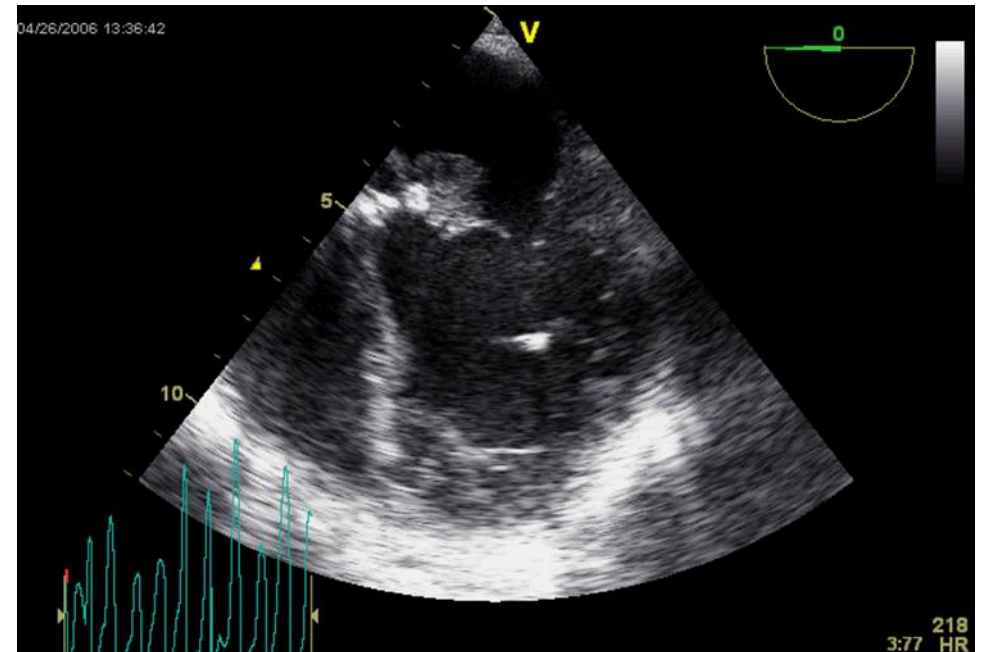
Lupus Nephropathy

- Nephritic or nephrotic syndrome or both
- Common cause of death in lupus
- **Diffuse proliferative glomerulonephritis**
 - Most common SLE renal syndrome
 - Nephritic syndrome
- **Membranous glomerulonephritis**
 - Nephrotic syndrome



Cardiac Manifestations

- Libman-Sacks (marantic) endocarditis
 - Nonbacterial inflammation of valves
- Increased risk of coronary artery disease



SLE

Laboratory findings

- **Anti-nuclear antibodies (ANA)**
 - Present in serum of lupus patients
 - Also present in 5% normal patients
 - Also present in many other autoimmune disorders
 - **Sensitive** but not specific
 - Negative test = disease very unlikely
 - Reported as titer: 1:20 or 1:200
 - Often 1:160 considered positive



SLE

Laboratory findings

- **Anti-double stranded DNA (anti-dsDNA)**
 - Specific for SLE
 - Associated with disease activity (↑ in flares)
 - Associated with renal involvement (glomerulonephritis)
- **Anti-smith (anti-Sm)**
 - Specific for SLE



Extractable Nuclear Antigens

ENA Panel

- Panel of blood tests against nuclear antigens

Antibody	Features
Anti-RNP	MCTD, SLE, Scleroderma
Anti-Sm	Specific for Lupus
Anti-SS-A (Ro)	Sjogren's syndrome, SLE, Scleroderma
Anti-SS-B (La)	Sjogren's syndrome, SLE, Scleroderma
Scl-70	Specific for scleroderma
Anti-Jo-1	Polymyositis

SLE

Laboratory findings

- **Antiphospholipid antibodies**
 - Antibodies against proteins in phospholipids
 - Can lead to antiphospholipid syndrome
 - May cause venous or arterial thrombosis with ↑ PTT
- **Low complement levels**
 - Low C3/C4 levels (hypocomplementemia)
 - Antibody-antigen complexes activate complement
 - Also low CH50

SLE

Diagnosis

- Need four of 11 criteria per American College of Rheumatology (ACR) criteria
- Or four of 17 Systemic Lupus International Collaborating Clinics (SLICC) criteria

ACR Criteria

1. Malar Rash	2. Discoid Rash
3. Photosensitivity	4. Oral ulcers
5. Arthritis	6. Serositis
7. Cerebritis	8. Renal disease
9. "Pienias"	10. + ANA
11. Anti-dsDNA or Anti-Sm or anti-phospholipid	

SLE

Treatment

- Avoid sunlight
 - Many patients photosensitive
 - Can trigger flares
 - Wear sun protection
- Pregnancy counseling
 - May exacerbate disease
 - Higher risk of complications
 - Usually avoided until disease quiescent 6 months



SLE

Treatment

- **Hydroxychloroquine**
 - Anti-malarial drug with immunosuppressant properties
 - Common first line therapy
 - Rare, feared adverse outcome: retinopathy, corneal deposits and vision loss
 - Routine eye exams required
- **Glucocorticoids**
 - Added to hydroxychloroquine for more severe forms
 - Oral prednisone or intravenous methylprednisolone
- Other immunosuppressants

Avascular Necrosis

Osteonecrosis

- Bone collapse
- Most commonly **femoral head**
- Mechanism poorly understood
 - Interruption of blood flow (infarct)
 - Demineralization/bone thinning
 - Collapse
- Associated with **glucocorticoid use and SLE**
- Also occurs in sickle cell disease

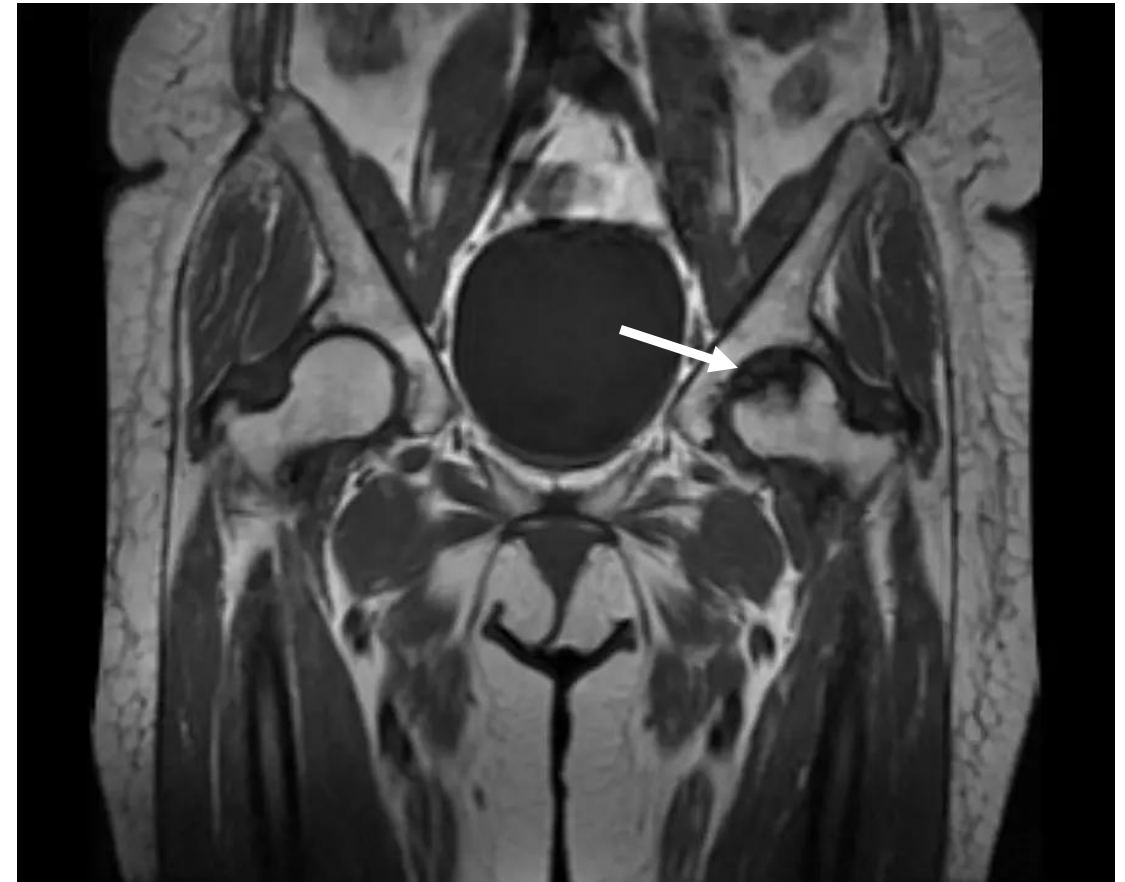


Avascular Necrosis

Osteonecrosis

- Groin, thigh or buttock pain
- Reduced range of motion
- Diagnosis: **x-ray or MRI**
- X-ray can be normal in early disease
- Often requires surgery

Avascular Necrosis by MRI



Drug-Induced Lupus

- Lupus-like syndrome after taking a drug
- Classic drugs: **isoniazid, hydralazine, procainamide**
- Often rash, arthritis, penias, ANA+
- Kidney or CNS involvement rare
- Key features: **anti-histone antibodies**
- Resolves on stopping the drug



Mixed Connective Tissue Disease

- Overlap syndrome of SLE, scleroderma and polymyositis
- Often presents with Raynaud's
- Arthritis
- Myalgias
- Pulmonary disease (ILD, PH)
- Absence of renal disease
- Hallmark: **anti-U1 ribonucleoprotein (RNP)**
- Treatment: glucocorticoids



Scleroderma and Sjogren's Syndrome

Jason Ryan, MD, MPH



Scleroderma

Systemic Sclerosis

- Autoimmune disorder
- Fibroblast activation → excess collagen deposition
- Stiff, hardened tissue (sclerosis)
- Skin, other organ systems involved
- Most common demographic is **women**
- Peak onset **30-50 years old**
- Presents along a spectrum of clinical syndromes
 - Diffuse
 - Limited (CREST)

Scleroderma

Diffuse form

- Diffuse **skin thickening**
- Face: lip thinning and retraction
- **Hands:**
 - **Fibrosis of skin of hands**
 - Puffy fingers, hard to bend
 - Skin often becomes shiny
 - Thickened skin (can't pinch)
 - Loss of wrinkles
 - Severe form: hands like claws
 - Also occurs in limited form



@Rheumatologistt



Harsh shaH/Slideshare

Scleroderma

Diffuse form

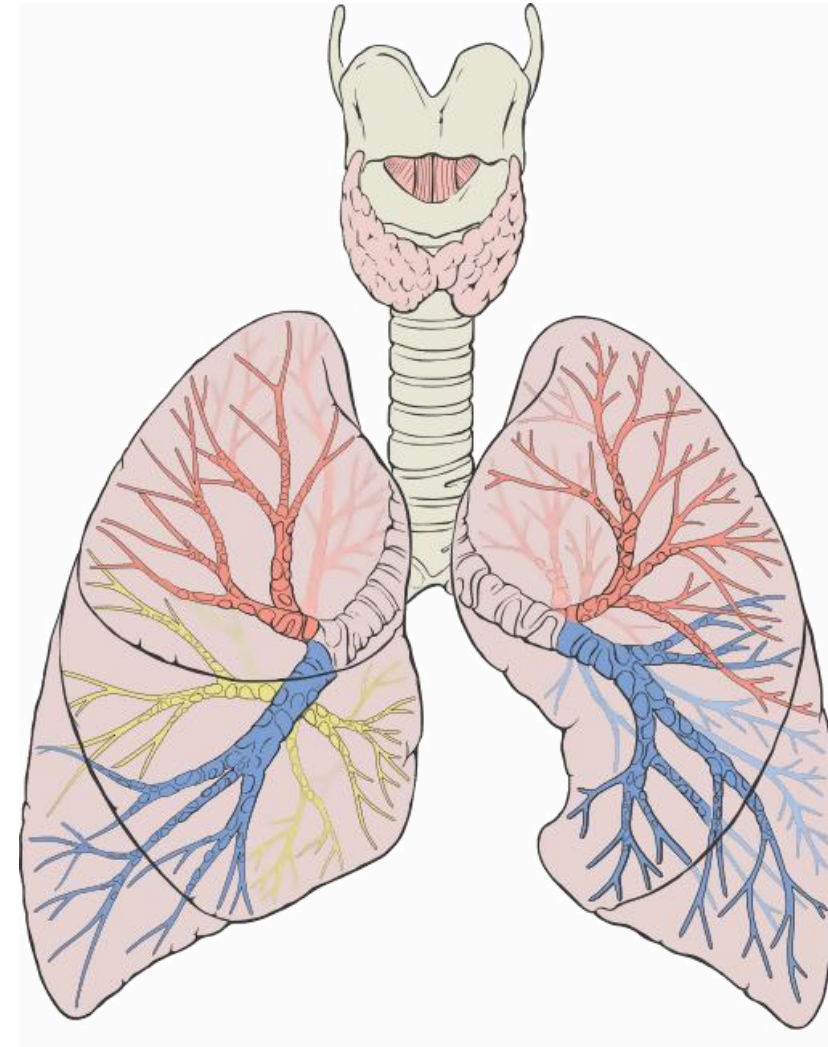
- **Raynaud's phenomenon**
 - Often initial sign
 - Followed ~ 1 year with other signs/symptoms
- Early involvement of visceral organs
 - Renal disease – renal failure
 - GI tract – dysmotility, heartburn
 - Heart: pericarditis, myocarditis, conduction disease
 - Joints/muscles: arthralgia, myalgias



Scleroderma

Diffuse form

- **Pulmonary hypertension**
 - Can progress to right heart failure
 - RV heave
 - Elevated jugular veins
 - Pitting edema
 - Routine monitoring: echocardiography
- **Interstitial lung disease**



Scleroderma

Diffuse form

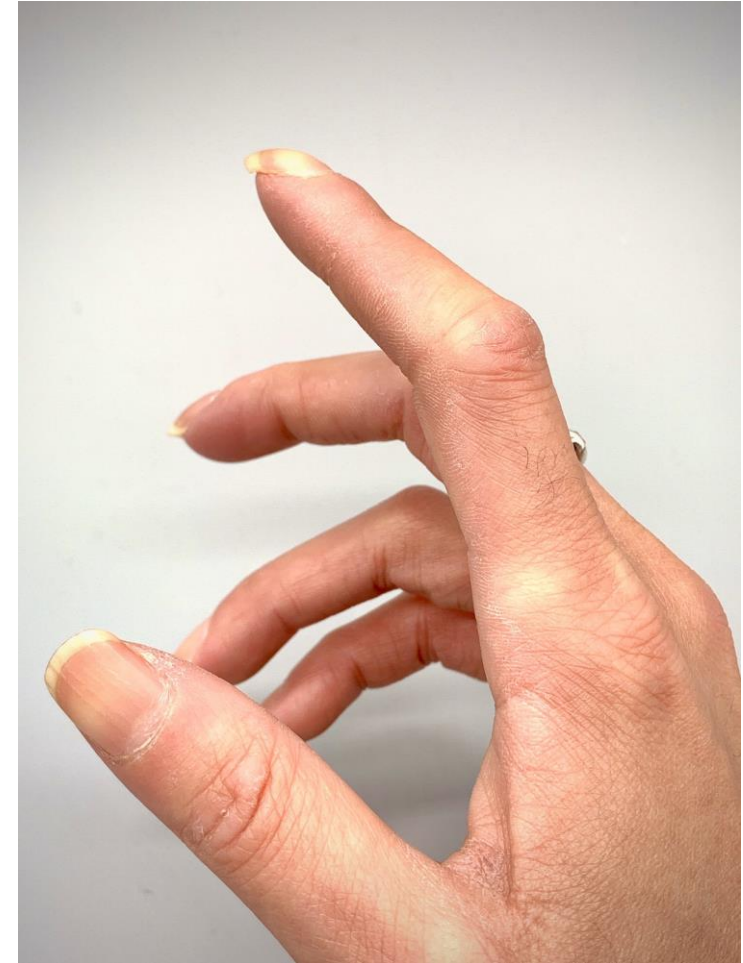
- Scleroderma renal crisis
- Life-threatening complication of diffuse scleroderma
- Acute onset of oliguric renal failure
- Marked hypertension
- MAHA: anemia, schistocytes, thrombocytopenia
- Responds to **ACE inhibitors**
 - Most studies with captopril
 - Used even if creatinine is elevated



Scleroderma

Limited form/CREST

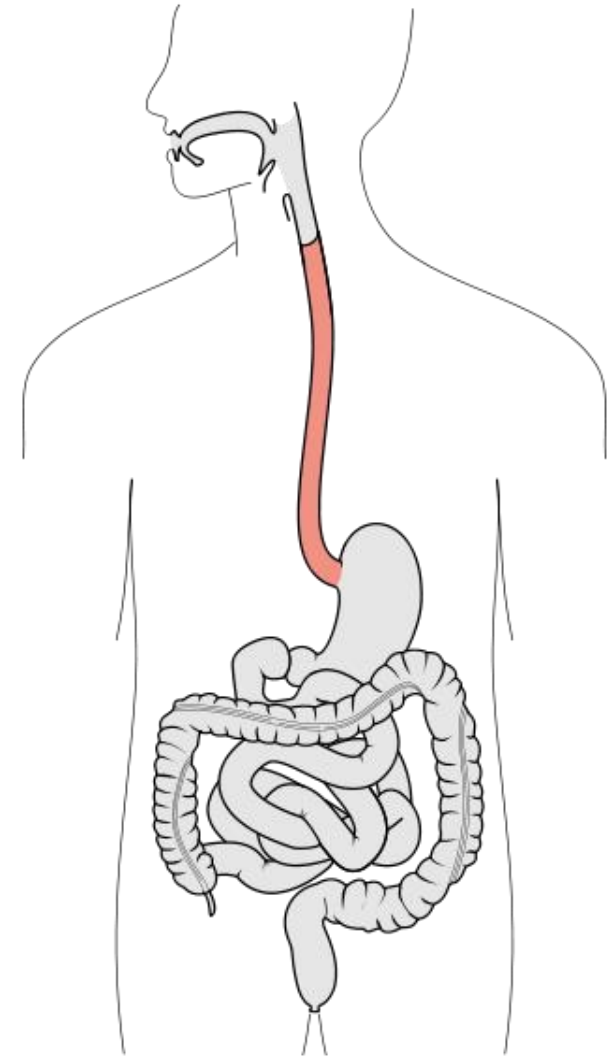
- **“Limited” skin involvement**
 - Skin sclerosis restricted to hands
 - Sometimes distal forearm, face or neck
 - Trunk and proximal extremities not involved
- **CREST**
 - Calcinosis
 - Raynaud’s phenomenon
 - Esophageal dysmotility
 - Sclerodactyly
 - Telangiectasias



Scleroderma

Limited form/CREST

- **Calcinosis**
 - Calcium deposits in subcutaneous tissue
 - Bumps on elbows, knees and fingers
 - Can break skin, leak white liquid
 - X-rays of hands may show soft tissue calcifications
- **Esophageal dysmotility**
 - Difficulty swallowing
 - Reflux/heartburn
 - Manometry: hypomotility and incompetence of LES
 - Heartburn + Raynaud's or skin thickening → CREST



Scleroderma

Limited form/CREST

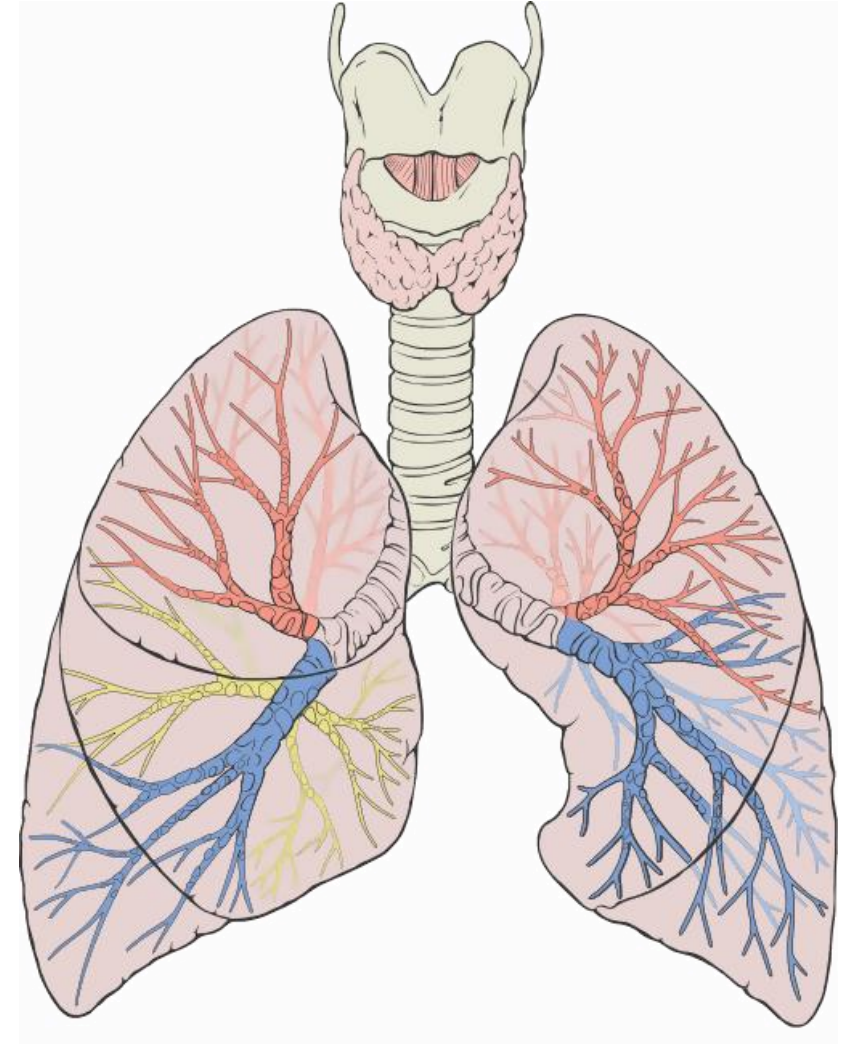
- **Telangiectasias**
 - Skin lesions
 - Dilated capillaries
 - Face, hands, mucous membranes
- Classic features of CREST
- Also occur in diffuse scleroderma



Scleroderma

Limited form/CREST

- Generally more benign course than diffuse
 - Rarely involves heart, kidneys
- Main risk is **pulmonary disease**
- Leading cause of death
- Pulmonary hypertension
- Interstitial lung disease
- Similar features to diffuse scleroderma
- Regular screening echocardiograms for PH



Scleroderma

Diagnosis

- Antinuclear antibody (ANA) – positive in most but not specific
- **Anti-topoisomerase I (anti-Scl-70) antibody**
 - Diffuse disease (**T**otally diffuse)
- **Anti-centromere antibody (ACA)**
 - Limited disease
 - CREST = centromere
- **Anti-RNA polymerase III antibody**
 - Diffuse disease
 - Associated with rapidly progressive skin involvement
 - Also increased risk for renal crisis



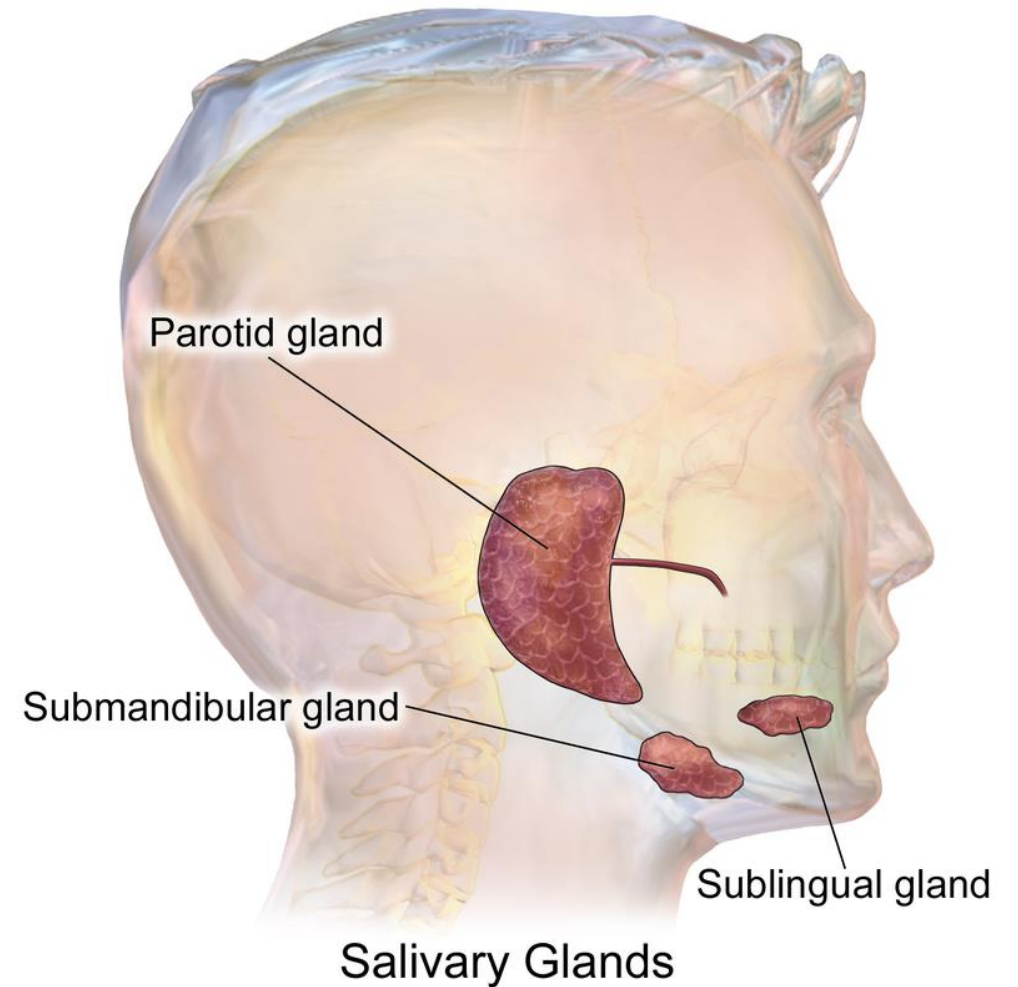
Scleroderma

Treatment

- Treatment usually aimed at organ system
 - GI tract: proton pump inhibitors
 - Raynaud's: calcium channel blockers
 - Pulmonary: pulmonary hypertension drugs
- Immunosuppressants have limited role
 - Little proven benefit
 - Used in rare, special cases

Sjogren's Syndrome

- Autoimmune disorder
- Destruction of **salivary and lacrimal glands**



Sjogren's Syndrome

Clinical features

- **Dry eyes (keratoconjunctivitis sicca)**
 - May present as feeling of dirt/debris in eyes
- **Dry mouth (xerostomia)**
 - Difficulty chewing dry foods (e.g., crackers)
 - Dysphagia
 - Cavities
 - Bad breath
- Vulvovaginal dryness, pruritus and dyspareunia



Sjogren's Syndrome

Clinical features

- Xerosis
 - Dry, scaly skin
 - Often lower extremities and axilla
- Joints: arthralgias or arthritis
- Raynaud's phenomena
- Many, many other potential symptoms



Sjogren's Syndrome

Demographics

- More common among women
- Age of onset usually in 40s
- Don't confuse with **age-related sicca syndrome**
 - Occurs in elderly patients
 - Caused by age-related changes to lacrimal and salivary glands
 - Dry mouth, dry eyes
 - Not due to Sjogren's
 - Antibody tests and/or biopsy = normal

Sjogren's Syndrome

Classification

- May be a primary disorder
- Often **secondary** to another condition
 - Rheumatoid arthritis
 - SLE
 - Primary biliary cirrhosis

Sjogren's Syndrome

Diagnosis

- No single diagnostic test
- Usually a combination of clinical features plus other testing
- Antibodies
- Eye and salivary gland testing
- Lip biopsy



Sjogren's Syndrome

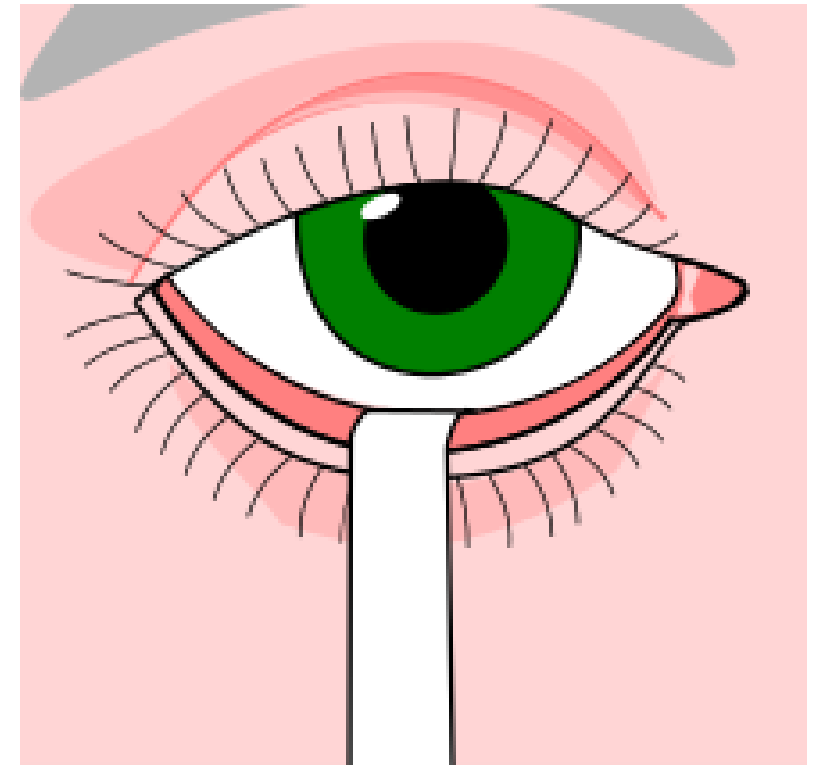
Diagnosis – antibodies

- ANA and RF often positive
- **Anti-Ro/SSA antibodies**
 - Sjogren's Syndrome A (SSA) antigen
 - Also called Ro antigen
- **Anti-La/SSB antibodies**
 - Sjogren's Syndrome B (SSB) antigen
 - Also called La antigen
- Antibodies alone insufficient for diagnosis
- Need objective evidence of glandular dysfunction

Sjogren's Syndrome

Diagnosis

- **Schirmer Test**
 - Tests reflex tear production
 - Filter paper placed near lower eyelid
 - Patient closes eyes
 - Amount of wetting (mm) measured over 5 minutes
- **Labial salivary gland biopsy** (lips)
 - Focal lymphocytic sialadenitis
 - Lymphocytes in glandular tissue



Sjogren's Syndrome

Diagnosis

- Salivary gland scintigraphy
 - Nuclear test
 - Low uptake of radionuclide in patients with SS
- Whole sialometry
 - Measurement of saliva production
 - Patient collects all saliva over 15 minutes
 - Sample weighed
- Salivary gland imaging

Sjogren's Syndrome

Treatment

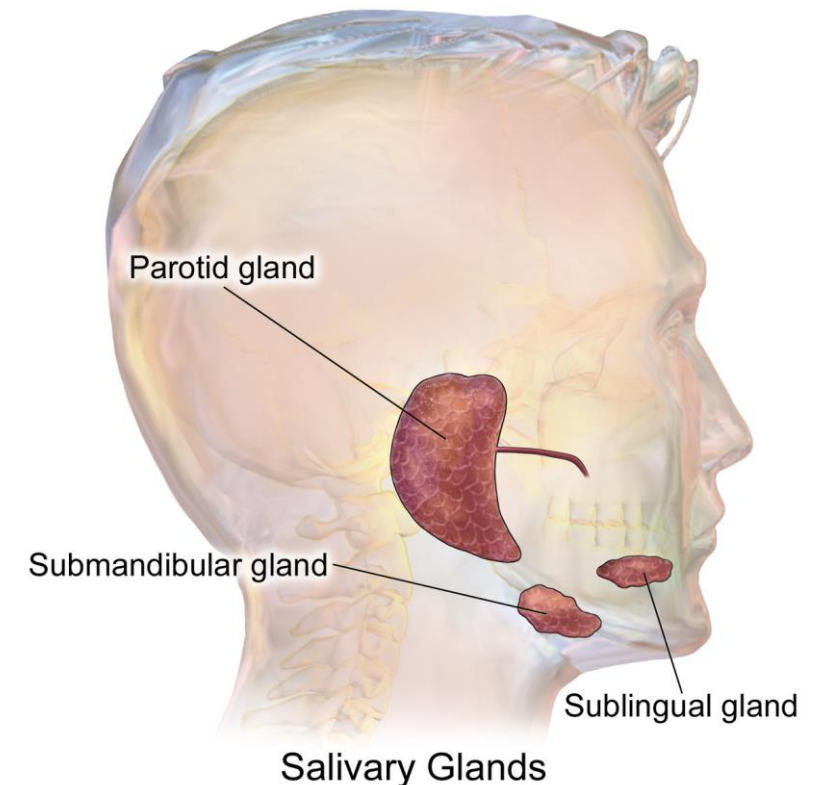
- May involve rheumatologist, ophthalmologist, dentist
- **Behavioral modification**
 - Good oral hygiene
 - Artificial tears
 - Sips of water
 - Avoid coffee, smoking (desiccants)
- **Secretagogues**
 - Pilocarpine or cevimeline (muscarinic agonists)
- Severe cases: glucocorticoids or immunosuppressants



Sjogren's Syndrome

B cell Lymphoma

- Increased risk among Sjogren's patients - 5-10% of patients
- Non-Hodgkin's B-cell lymphoma
- Usually marginal zone lymphoma
- May present as persistent **unilateral swollen gland**



Neonatal Lupus

- Maternal antibodies → fetus
- Occurs in mothers with **Ro/SSA or La/SSB antibodies**
 - Some mothers have SLE or Sjogren's
 - Others asymptomatic with antibodies
- Mothers with autoimmune disease screened for antibodies
- Major risk to baby involves **skin and heart**



Neonatal Lupus

- At birth or first few weeks of life
- **Rash**
 - Multiple red, circular lesions on face, scalp
 - Usually resolves over months
- **Congenital complete heart block**
 - Fetal bradycardia ($<110/\text{min}$) during pregnancy
 - Bradycardia at birth
 - May require pacemaker after birth



Ariyanto Harsono, MD, PhD/Slideshare

3rd degree AV block



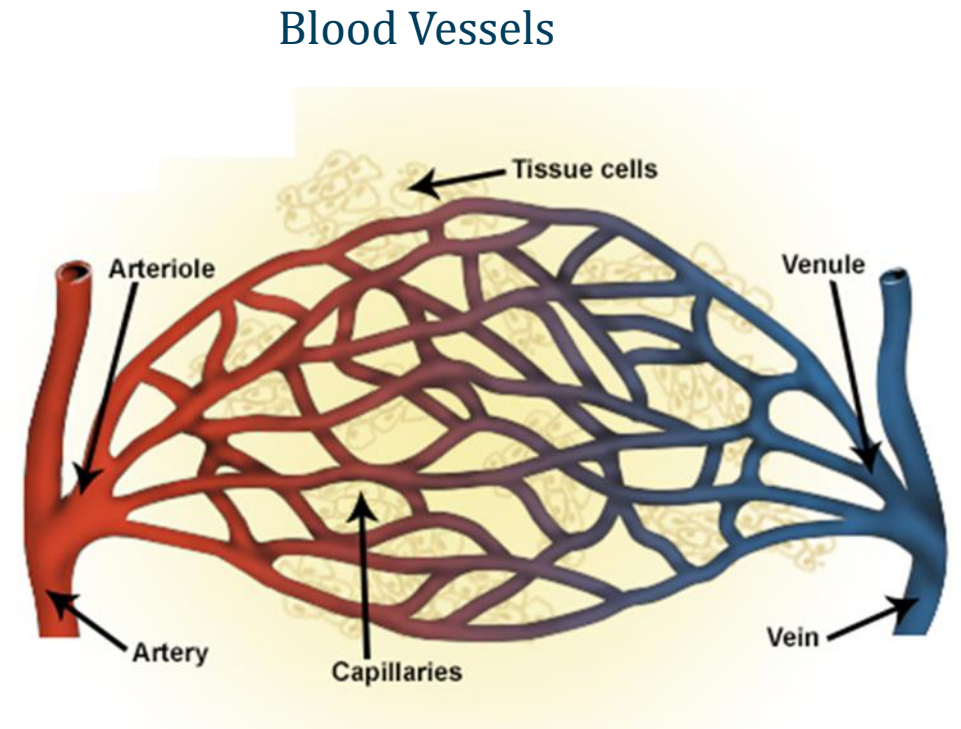
Vasculitis

Jason Ryan, MD, MPH



Vasculitis

- Rare autoimmune disorders
- Inflammation of **blood vessels**
- Typical inflammation symptoms
 - Fever
 - Myalgias
 - Arthralgias
 - Fatigue
- Organ/disease specific symptoms
 - Vessel lumen narrows or occludes from inflammation



Purpura

- Purpura: red-purple skin lesions
- Extravasation of blood into the skin
- Does not blanch when pressed
- **Palpable purpura**
 - Occurs in vasculitis
 - Raised

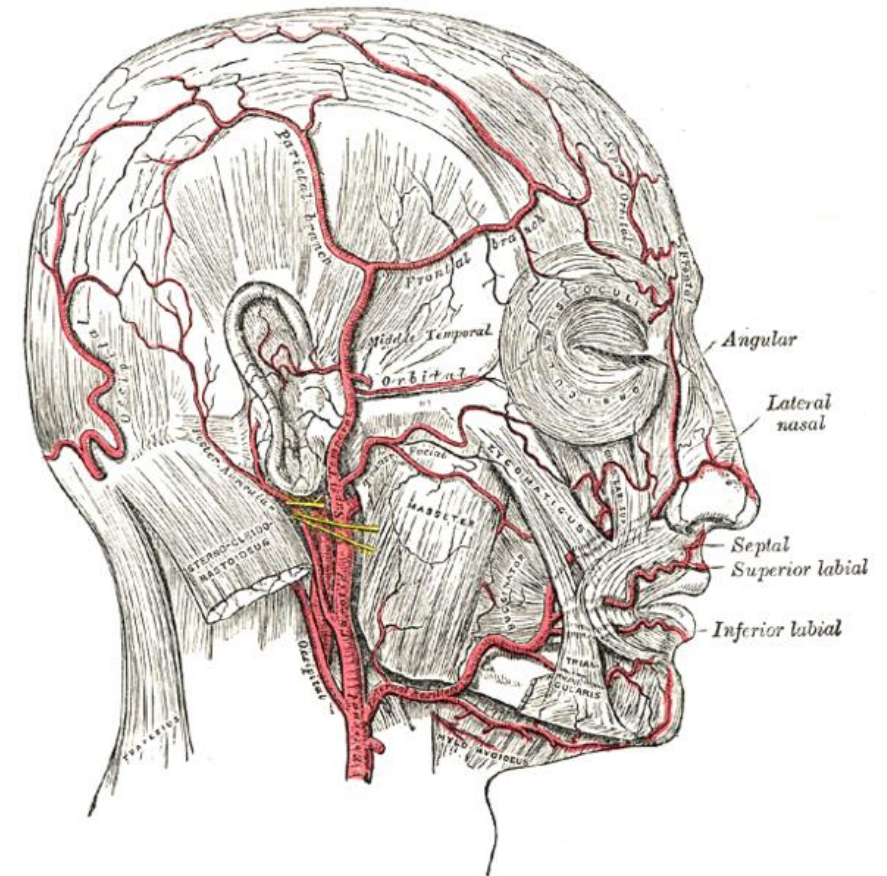


Dr. James Heilman/ Wikipedia

Temporal Arteritis

Giant Cell Arteritis

- Inflammation of **temporal artery system** of head and neck
- Fever, fatigue, weight loss
- **Headache**
- Jaw claudication - pain on chewing
- Vision loss
 - Ophthalmic artery occlusion
 - Transient vision loss or permanent **blindness**
- May lead to **aortic aneurysm**



Temporal Arteritis

Clinical features, diagnosis and treatment

- More common among women
- Almost all patients over age 50
- Key clinical clue: **high ESR**
- Diagnosis: **biopsy temporal artery**
 - Removal of segment of superficial temporal artery
 - Granulomas present in temporal arteritis
- Treat with **high dose glucocorticoids**
 - Don't wait for biopsy
 - Treat any patient with high suspicion
 - ESR should fall with therapy



Dr. Ryan's Grandmother

Takayasu's Arteritis

- Granulomatous thickening of **aortic arch and branches**
- Up to 90% of cases occur in women
- Occurs in young adults ages 20 to 40
- Shares many features with temporal arteritis
 - Large vessel granulomatous inflammation
 - Similar vessels can be involved
 - Major difference is age of onset
 - Age < 50 = Takayasu's arteritis
 - Age > 50 = temporal arteritis
- Found worldwide with greatest prevalence in Asia



Public Domain

Takayasu's Arteritis

Clinical features

- Fever, fatigue, weight loss
- ↑ ESR and CRP
- Aorta or any branch may become narrowed
- “Pulseless disease”
 - Proximal great vessel inflammation/narrowing
 - Weak carotid pulses
 - BP difference between arms/legs
 - Bruits over arteries
- Vision loss



Takayasu's Arteritis

Diagnosis and treatment

- **Angiography**
 - Usually MRA or CTA
 - Visualization of aorta and branches
 - Will demonstrate vessel narrowing
- Biopsy rarely done
- Treatment: **high dose glucocorticoids**
- Vascular stent placement



Kawasaki Disease

Kawasaki disease

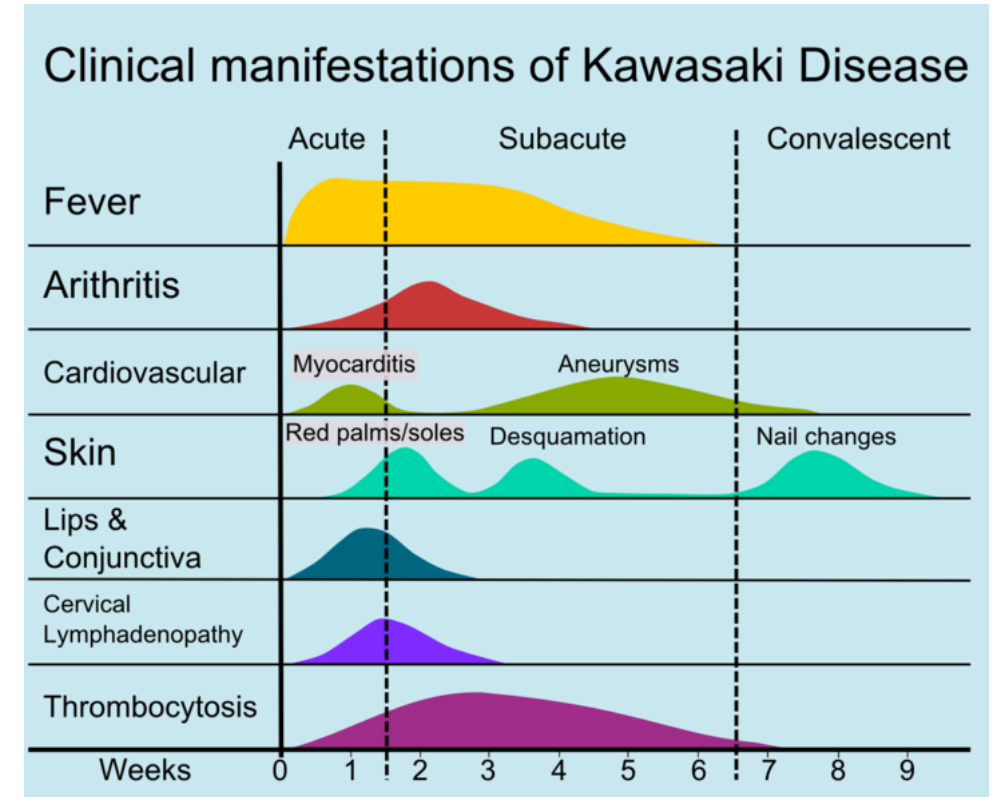
- Mostly a disease of children 1 to 5 years of age
- ↑ ESR/CRP, leukocytosis and thrombocytosis
- Classic involvement: **skin, lips, tongue**
 - Diffuse, red rash
 - Palms, soles → later desquamates
 - Changes in lips/oral mucosa: "strawberry tongue"
- Feared complication: **coronary aneurysms**
 - Lymphocytic myocarditis occurs
 - Coronary artery rupture → myocardial infarction



Kawasaki Disease

Clinical criteria

- **Fever > 5 days** plus 4/5 additional criteria
- Bilateral conjunctivitis
- Cervical lymphadenopathy
- Mucositis
 - Erythema of lips and pharynx
 - **Strawberry tongue**
- Extremity changes in hands and feet
- Rash



Kawasaki Disease

Clinical criteria

- Extremity changes
 - Erythema of palms, soles, hands, feet
 - **Edema of hands and feet**
 - **Periungual desquamation** (near nails)
- Rash
 - **Perineal erythema and desquamation**
 - Diffuse macular or morbilliform rash

Periungual Desquamation

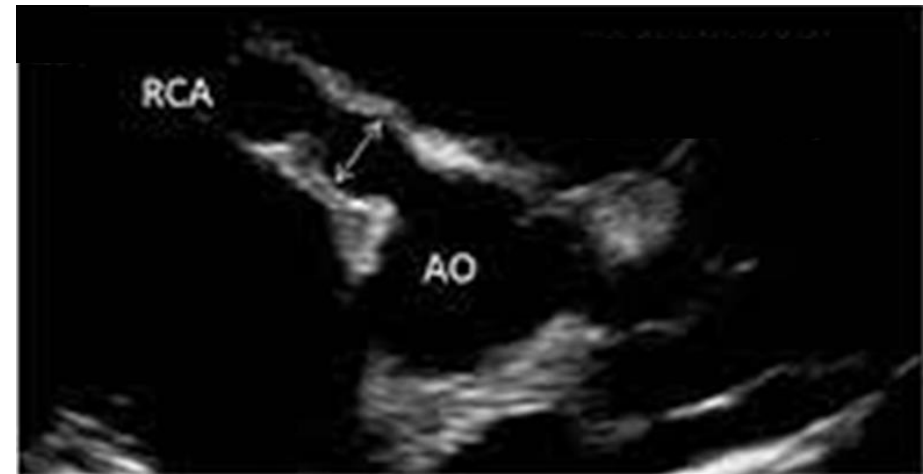


Kawasaki Disease

Diagnosis and treatment

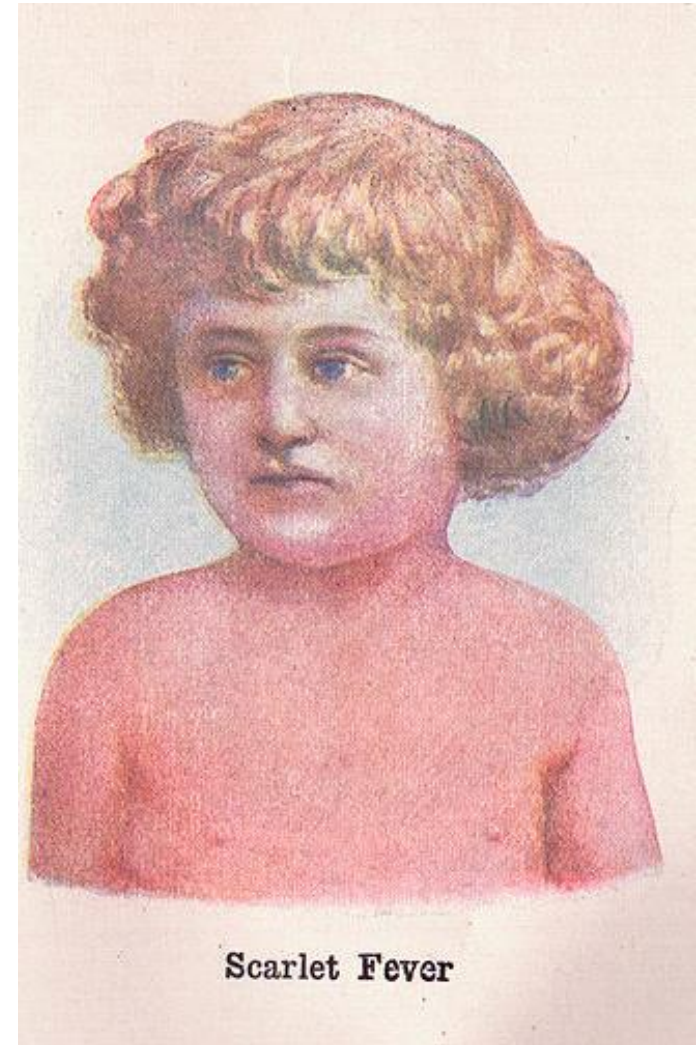
- Clinical diagnosis
- **Echocardiography**
 - Screen for coronary aneurysms
 - At diagnosis then repeated ~2 and ~6 weeks
- Treatment: **IVIG plus aspirin**
 - IVIG = pooled antibodies
 - Poorly understood immunosuppressive effect
 - Reduces risk of aneurysms
 - Aspirin used in children (risk of Reye's)

RCA by Echocardiography



Scarlet Fever

- Fever, diffuse red rash
- Follows strep infection of throat or skin
- Often preceded by **sore throat**
- Many small papules (“sandpaper” skin)
- Classic finding: strawberry tongue
- Eventually skin desquamates



Reye's Syndrome

- Liver failure, fatty infiltration and encephalopathy
- Symptoms: vomiting, confusion, seizures, coma
- Often follows viral illness
 - Influenza, varicella
- Associated with aspirin use in children
 - Generally, aspirin not used for kids
- Exception is Kawasaki



Buerger's Disease

Thromboangiitis obliterans

- Inflammation of small to medium arteries and veins of extremities
- Formation of inflammatory occlusive thrombi
- Triggered by **cigarette smoking**
- Occurs in **younger patients < 45 years**
- Poor blood flow to hands/feet
 - Raynaud's phenomenon
 - Superficial thrombophlebitis (pain, erythema over veins)
 - Gangrene or autoamputation of digits



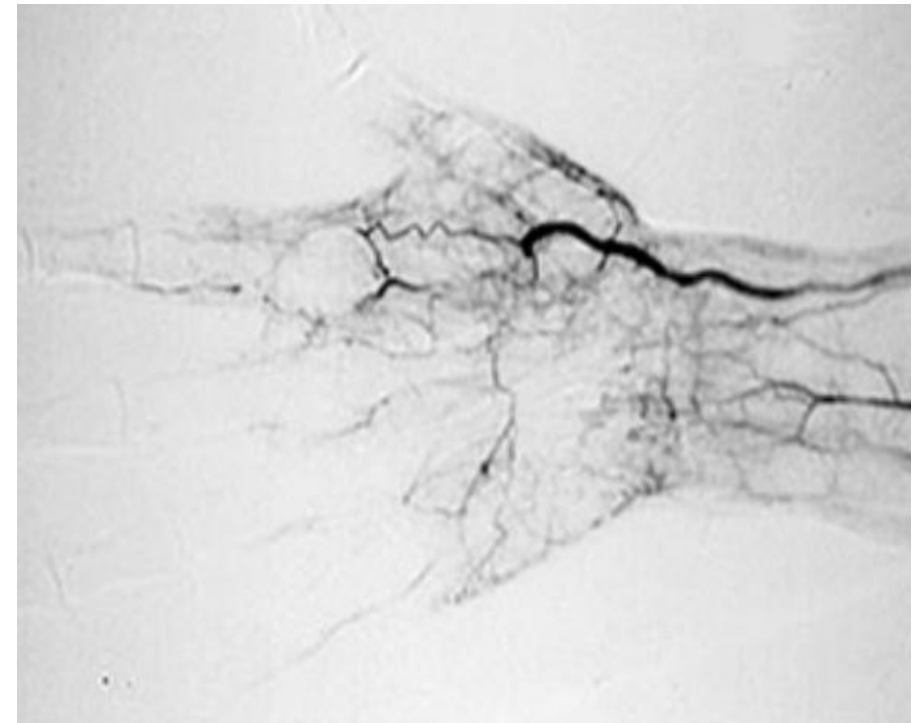
Dr. James Heilman/Wikipedia

Buerger's Disease

Diagnosis and treatment

- Often a **clinical diagnosis**
 - Age < 45 years with tobacco use
 - Distal extremity ischemia
 - Exclusion of other causes (e.g., negative ANA)
 - Angiography sometimes used
- Treatment:
 - **Smoking cessation**
 - Calcium channel blockers (nifedipine)
 - Intravenous iloprost (prostaglandin)

Angiography



Polyarteritis Nodosa

PAN

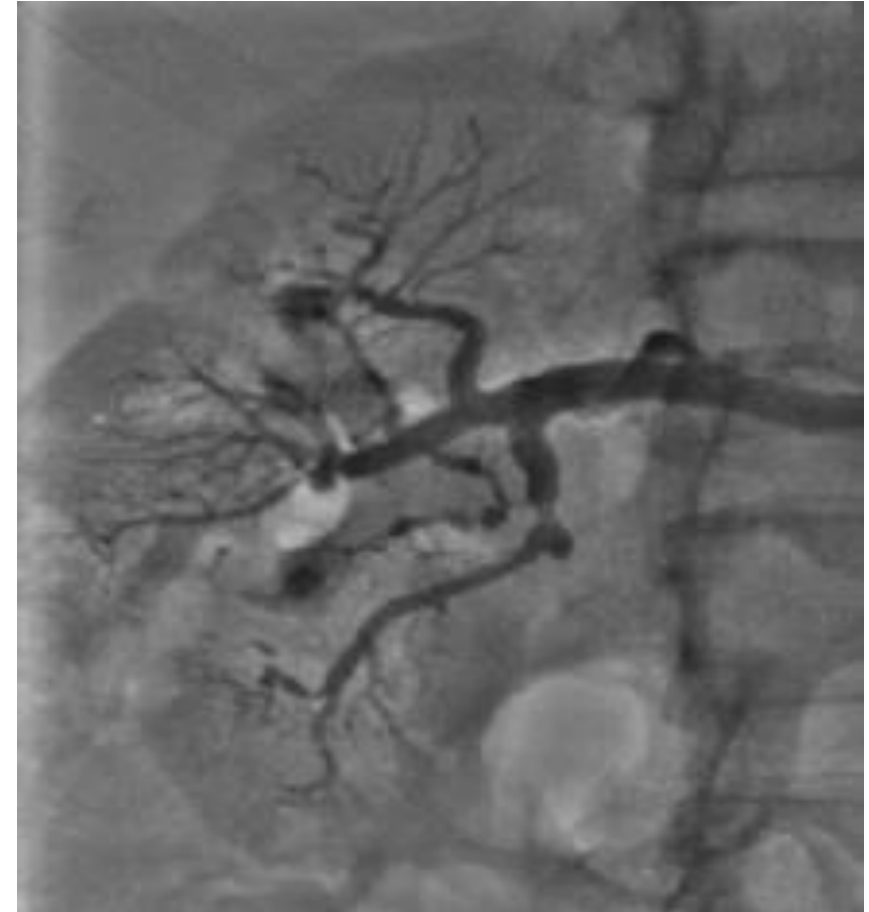
- Inflammation of medium-sized vessels
- Clinical features involve many vascular beds
- About 30% of patients have **hepatitis B**
- Renal arteries: **hypertension, renal insufficiency**
- Mesenteric arteries: abdominal pain, bloody diarrhea
- Nerves: **motor or sensory deficits**
- Skin: **nodules**, purpura

B b

Polyarteritis Nodosa

- Suspected based on clinical findings
 - Systemic symptoms: fever, fatigue, weight loss
 - Hypertension, renal failure, ↑ ESR/CRP
 - Negative testing for other conditions (ANCA)
- **Angiogram:** aneurysms and constrictions
 - Kidney, liver, and mesenteric arteries
 - Rosary sign
- **Biopsy of affected organ**
 - Transmural inflammation of medium vessel wall
 - Fibrinoid necrosis
- Treatment: glucocorticoids +/- immunosuppressants

Renal Angiogram
(aneurysms)



Malhotra R, et al. The role of renal angiography in Hepatitis B-related polyarteritis nodosa. Images in Nephrology 2018 28(1) 81-82

IgA vasculitis

Henoch-Schonlein purpura

- Associated with **IgA antibody deposition** in tissues and vessels
- Mostly occurs in **children**
- Often follows **upper respiratory syndrome**
- Palpable purpura of legs and buttocks
- Abdominal pain and GI bleeding
- Arthralgias
- Hematuria usually with no casts/protein

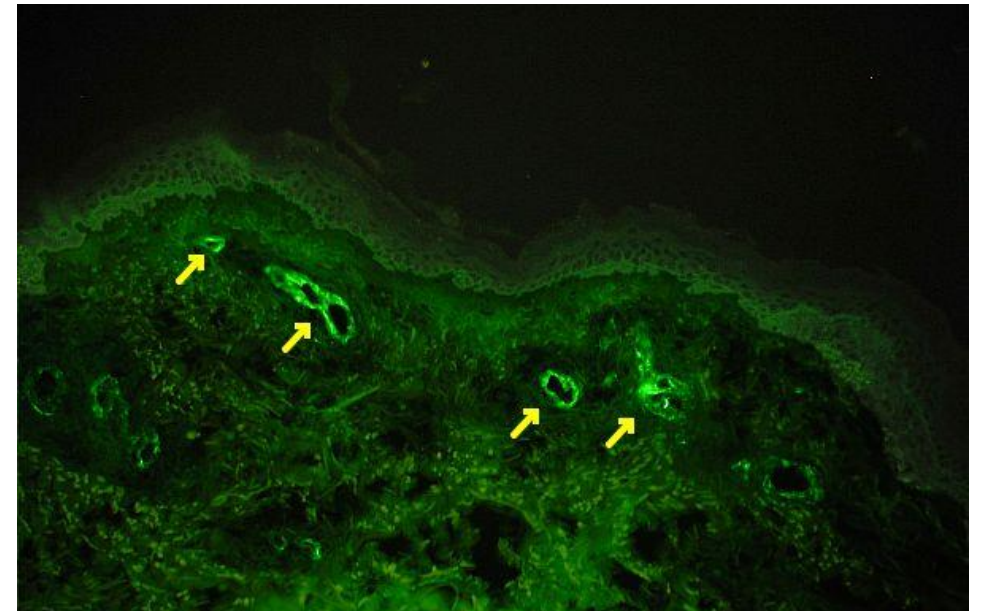


IgA vasculitis

Diagnosis and treatment

- Clinical diagnosis if classic features present
- **Skin or renal biopsy**
 - Leukocytoclastic vasculitis
 - IgA deposition
- Supportive care - usually self-limited
 - Fluids, NSAIDs for joint pain, monitor BUN/Cr
- Feared result: renal failure
 - More common adults
- Severe cases treated with glucocorticoids

Immunofluorescence Staining for IgA

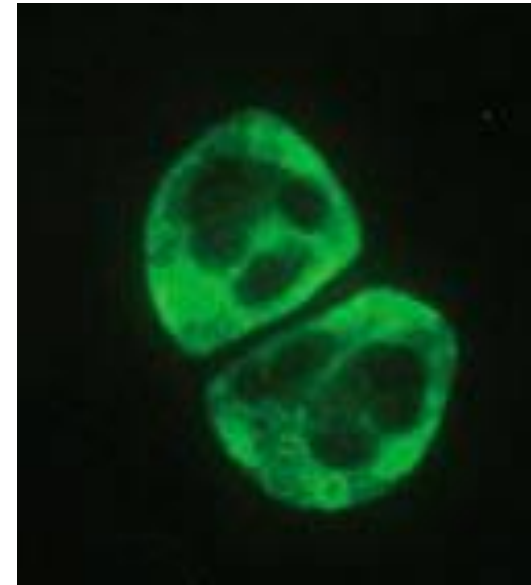


ANCA-associated Vasculitis Syndromes

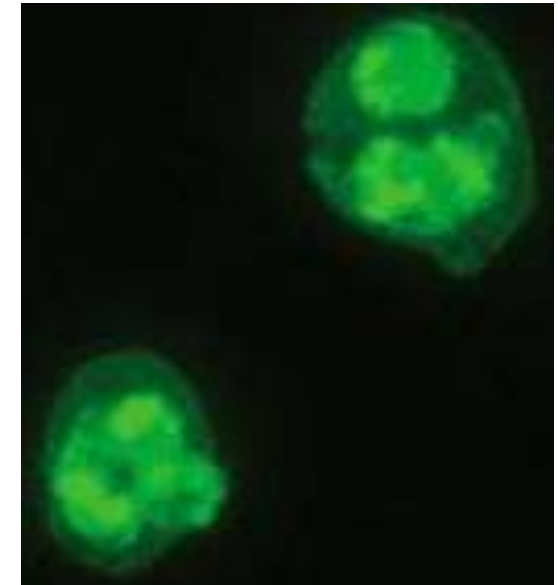
Anti-neutrophil cytoplasmic antibodies

- Group of disorders
- All have **anti-neutrophil antibodies**
 - c-ANCA – cytoplasmic antibodies
 - p-ANCA – perinuclear antibodies
- All have **pulmonary involvement**
- All have **renal involvement**
 - Crescentic RPGN
 - Nephritic syndrome
 - Proteinuria, hematuria, red cell casts

p-ANCA



c-ANCA

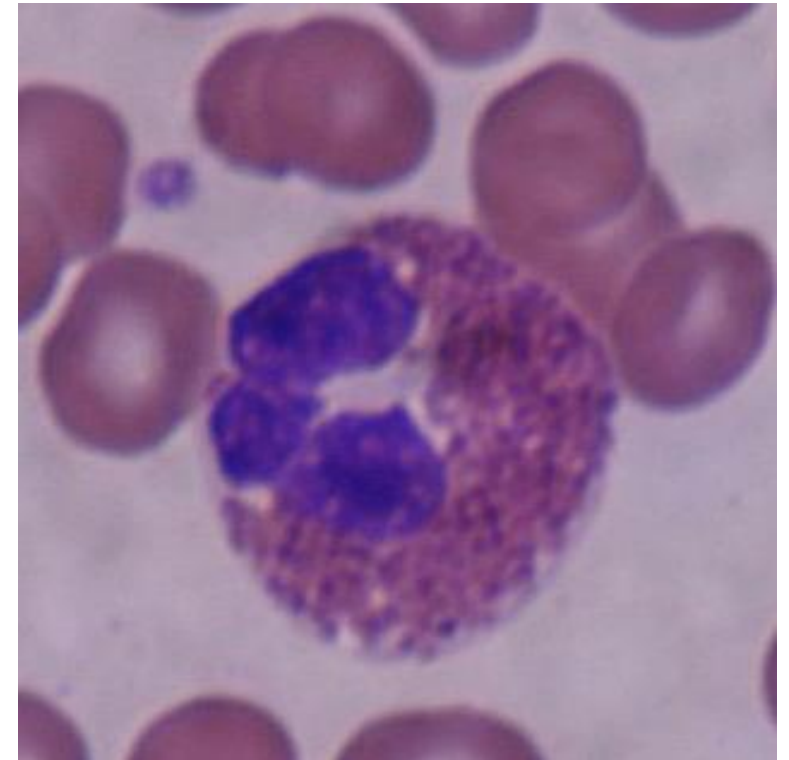


Eosinophilic Granulomatosis with Polyangiitis

EGPA or Churg-Strauss syndrome

- Vasculitis with allergic features
- Classic presentation: **asthma with eosinophilia**
 - Asthma symptoms plus lung opacities on imaging
 - Eosinophils > 10% total leukocyte count
- Skin lesions: **palpable purpura**
- GI tract: abdominal pain or bleeding
- Myocarditis and renal involvement
- Glomerulonephritis

Eosinophil

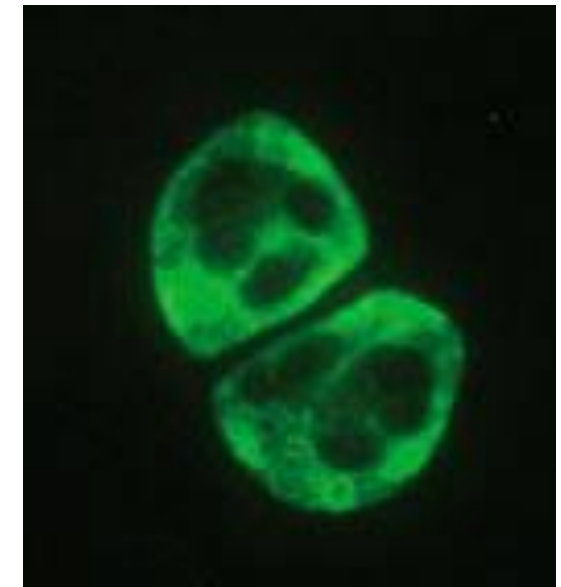


Eosinophilic Granulomatosis with Polyangiitis

EGPA or Churg-Strauss syndrome

- Positive **p-ANCA in 50% cases**
- ↑ ESR and CRP
- Biopsy of any involved site may be performed
- Blood vessels show eosinophils
- Treatment: glucocorticoids +/- immunosuppressants

p-ANCA

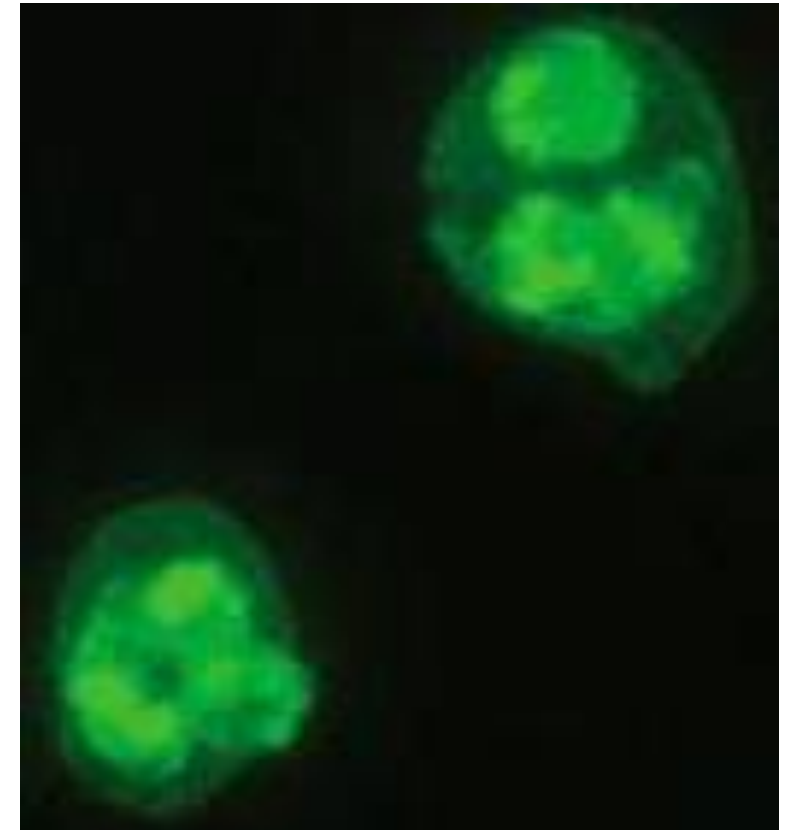


Granulomatosis with Polyangiitis

GPA or Wegener's Granulomatosis

- **Sinusitis, hemoptysis or otitis media**
 - Upper and lower airway disease
- Glomerulonephritis
- Purpura
- Granulomas on biopsy
- **c-ANCA**
- Treatment: glucocorticoids +/- immunosuppressants

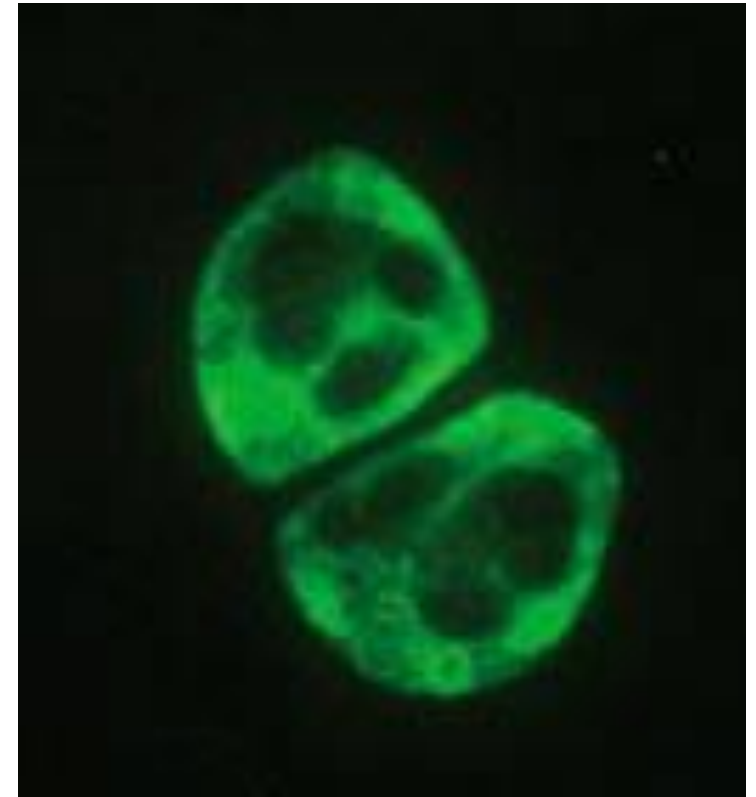
c-ANCA



Microscopic Polyangiitis

- Hemoptysis, glomerulonephritis, purpura
- Similar to GPA except
 - No upper airway disease (sinusitis)
 - p-ANCA not c-ANCA
 - Absence of granulomas on biopsy
- Treatment: glucocorticoids +/- immunosuppressants

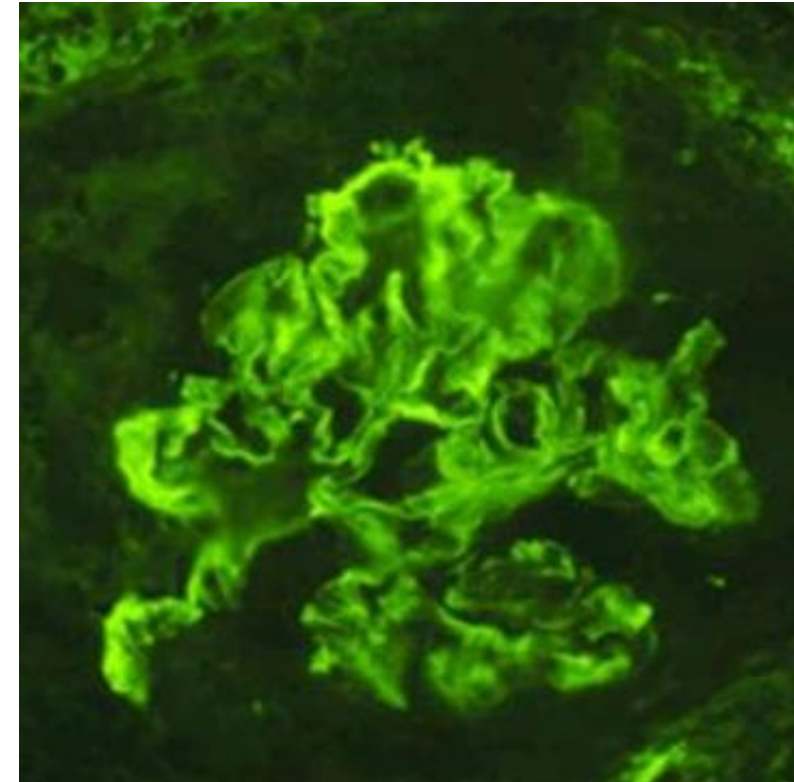
p-ANCA



Goodpasture's Syndrome

Anti-GBM disease

- Antibodies to **type IV collagen**
 - Found in glomeruli and alveoli
- **Hemoptysis and nephritic syndrome**
- Clinical features can resemble GPA or ANCA disease
- Negative ANCA
- Positive serum anti-GBM antibodies
- Biopsy: linear IF antibody staining (IgG, C3)
- Treatment: plasmapheresis plus immunosuppressants
 - Often glucocorticoids plus cyclophosphamide



Pulmonary-Renal Syndromes

Disorder	Nickname	Features
Eosinophilic granulomatosis with polyangiitis (EGPA)	Churg Strauss syndrome	Asthma Eosinophilia p-ANCA
Granulomatosis with polyangiitis (GPA)	Wegener's granulomatosis	Upper and lower airways c-ANCA
Microscopic Polyangiitis	--	Lower airways only p-ANCA
Anti-glomerular-basement-membrane (anti-GBM) disease	Goodpasture's syndrome	Lower airways only anti-GMB antibodies

Spondyloarthritis

Jason Ryan, MD, MPH



Seronegative Spondyloarthritis

- **Spondylo = spine**
- Arthritis = joint inflammation
- Seronegative = negative rheumatoid factor
- Family of autoimmune disorders with common features
 - Ankylosing spondylitis
 - Psoriatic arthritis
 - Inflammatory bowel diseases
 - Reactive arthritis



Terminology

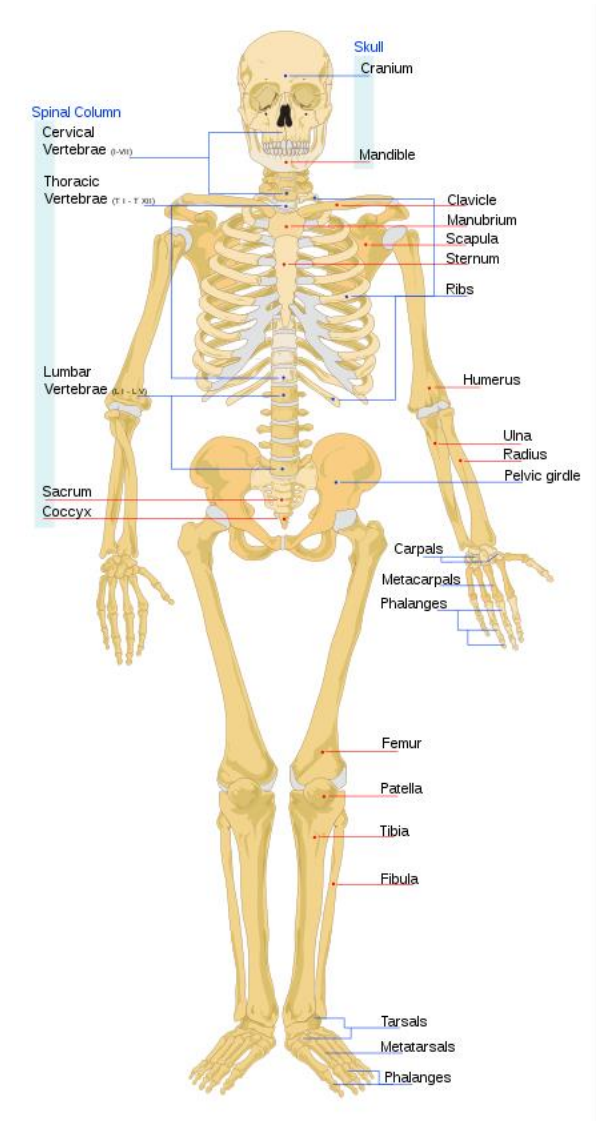
- Monoarthritis = 1 joint
- Oligoarthritis = 2-4 joints
- Polyarthritis = >5 joints



Seronegative Spondyloarthritis

Common Features

- **Asymmetric oligoarthritis**
 - Acute attacks of joint pain and swelling
 - Often lower extremities
- Contrast with rheumatoid arthritis
 - Symmetric
 - Polyarthritis
 - Often hands



Wikipedia/Public Domain

Seronegative Spondyloarthritis

Common Features

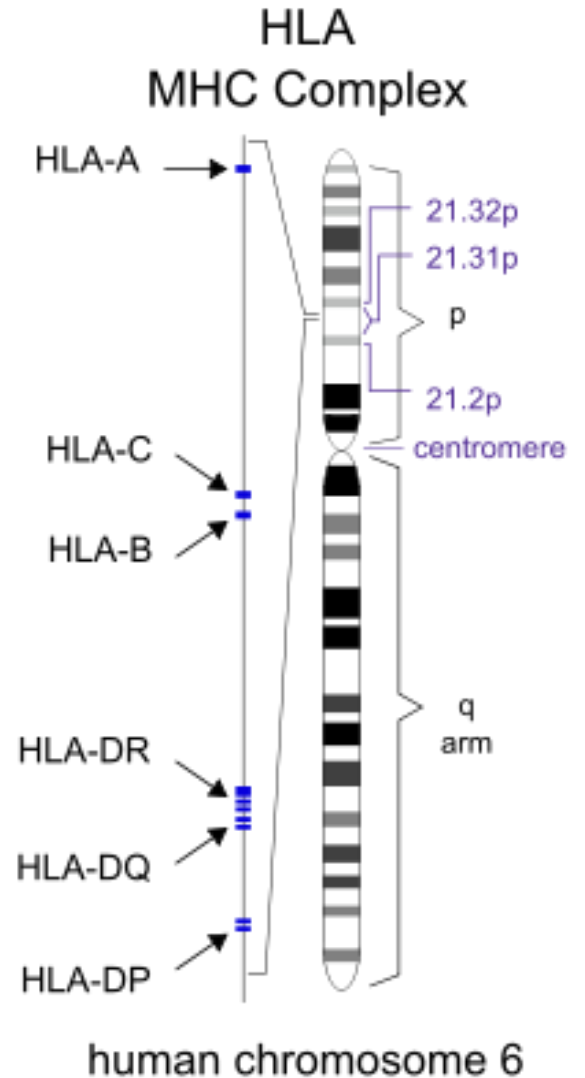
- Axial spine inflammation
 - Commonly sacroiliac (SI) joints
- Dactylitis
 - Inflammation of entire digit
 - Creates “sausage digits”
- Enthesitis
 - Inflammation of ligament/tendon attachment to bone

Dactylitis



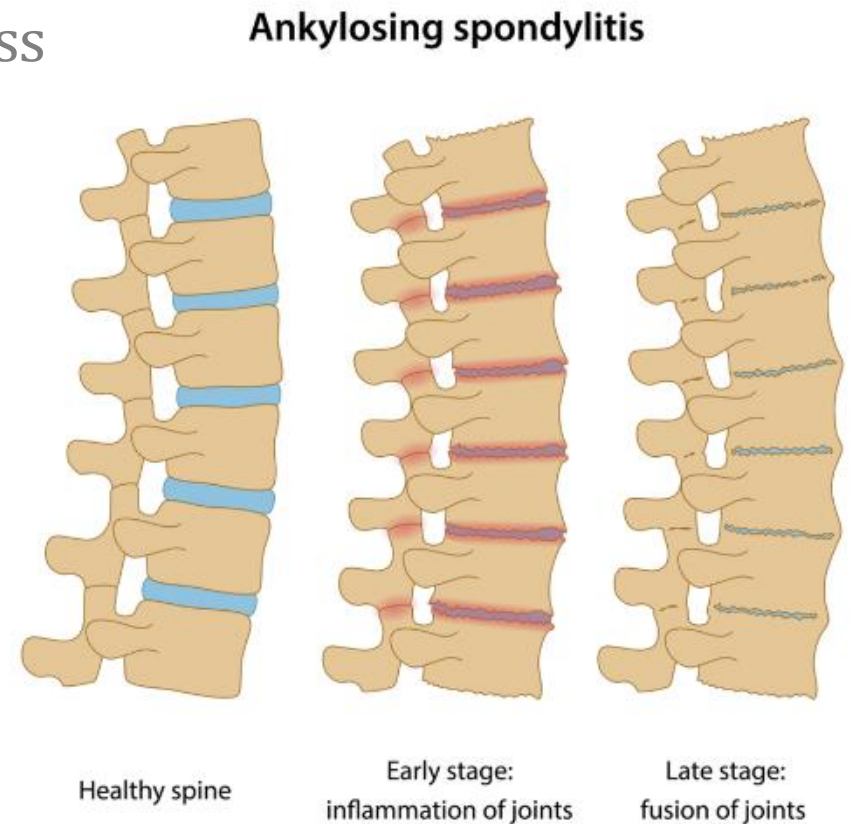
HLA B27

- Human Leukocyte Antigens
- Antigens that make up MHC class I and II molecules
- Genes on chromosome 6 determine “HLA type”
- MHC Class I Genes: HLA-A, HLA-B, HLA-C
- HLA B27: Common in spondyloarthritis disorders
 - **90% of ankylosing spondylitis cases**
 - **50% of psoriatic arthritis cases**
- Most people with B27 never develop AS
- **Minimal utility as a diagnostic test**
- Sometimes helpful in equivocal cases



Ankylosing Spondylitis

- Classic form of seronegative spondyloarthritis
- Ankylosis = new bone formation in spine → stiffness
- More common in **males**
- Usually **20-30 years old**



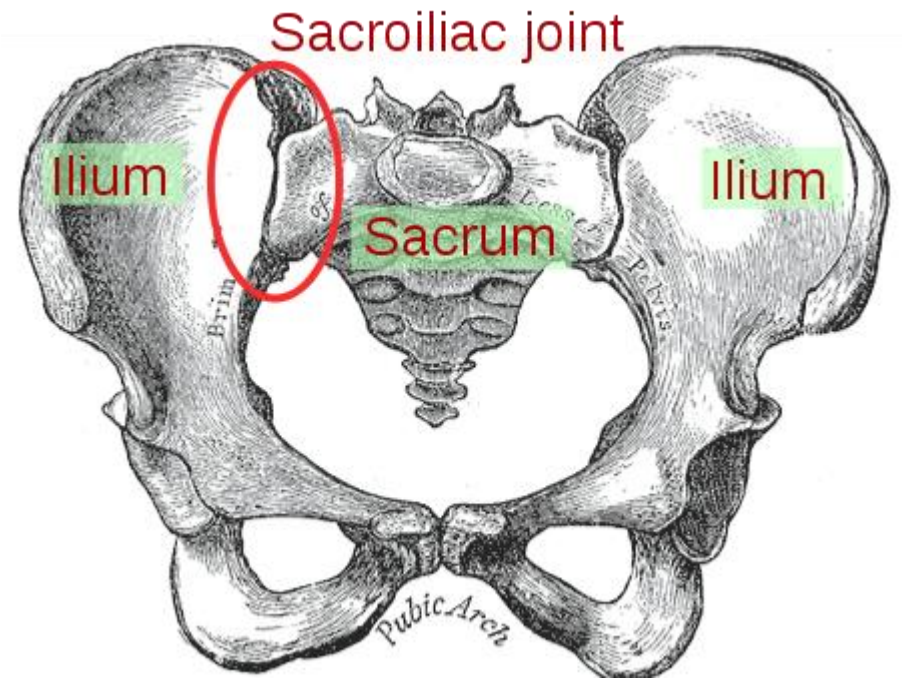
Ankylosing Spondylitis

- **“Inflammatory” back pain** (~75% of patients)
 - Younger age (<40 years)
 - Slow, insidious onset
 - Improves with exercise
 - Does NOT improve with rest
 - Pain at night (better with awakening/movement)



Ankylosing Spondylitis

- Classically involves the **sacroiliac (SI) joint**
 - Sacroiliitis and low back pain
 - Abnormal SI joint space on x-ray from erosion
- **Impaired spinal mobility**
 - Stiffness of spine
 - Impaired chest wall expansion
 - May lead to restrictive lung disease
- May lead to osteoporosis and vertebral fractures
- Classic x-ray finding: **bamboo spine**
 - Calcium deposition in spine



Bamboo Spine

Normal

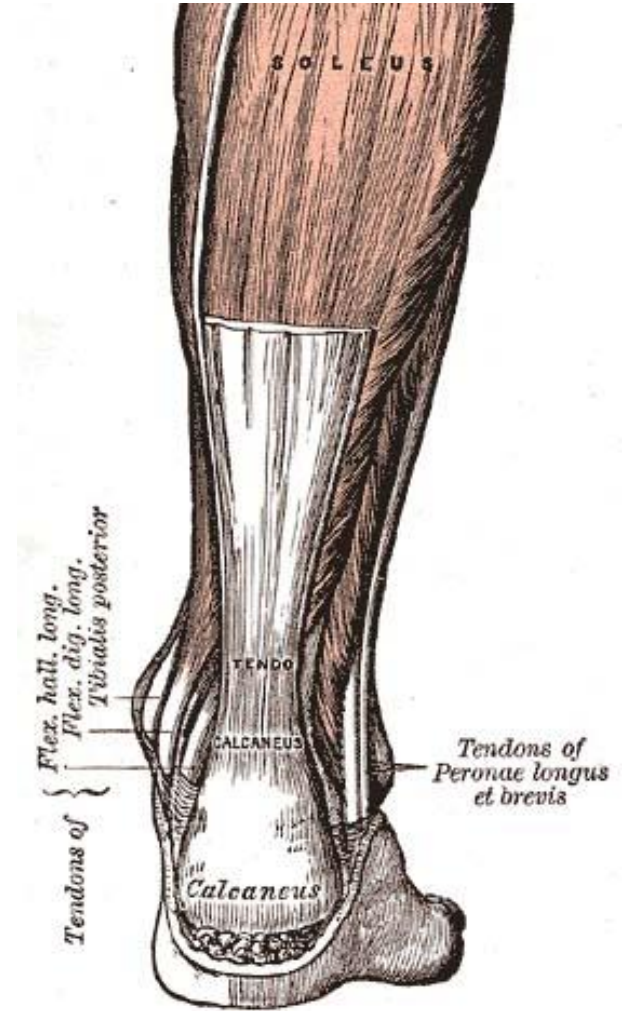


Bamboo



Enthesitis

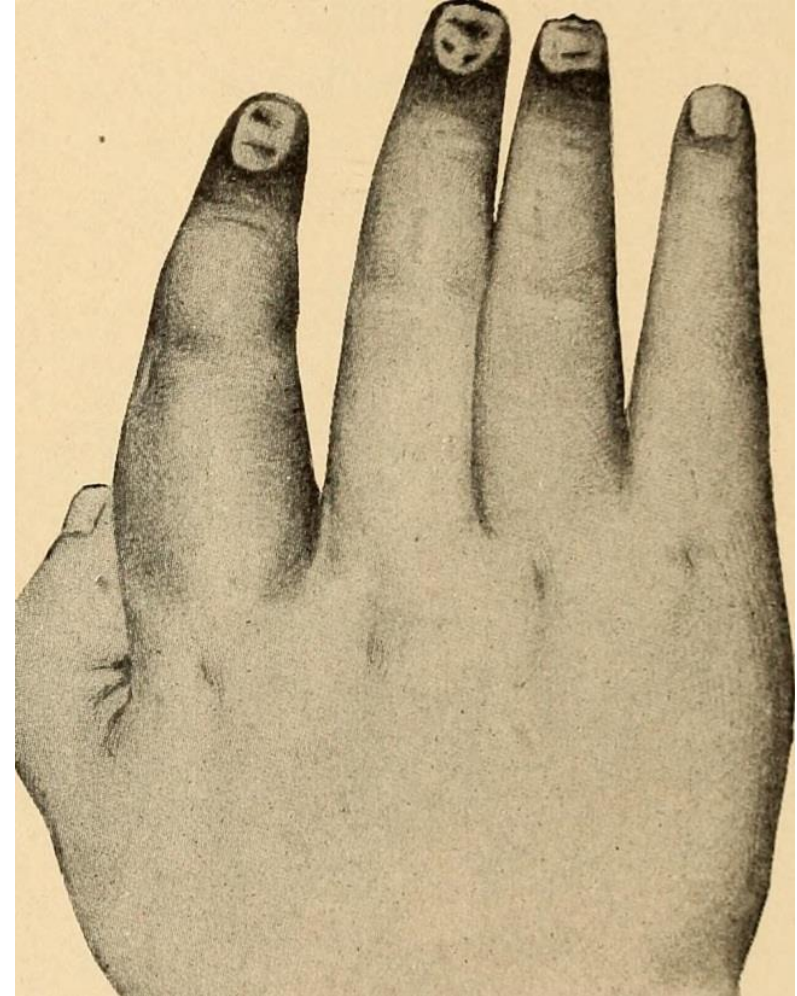
- Inflammation of tendon or ligaments
- Classically insertion of Achilles tendon
- Or plantar fascia
- Causes **heel pain**
- Common presenting feature



Ankylosing Spondylitis

Other features

- Dactylitis
 - Swelling of fingers and toes
 - Caused by tendon and soft tissue inflammation
- Uveitis
- Aortitis
 - Often leads to **aortic regurgitation**



Ankylosing Spondylitis

Diagnosis and treatment

- **Clinical diagnosis**
 - Symptoms and exam findings
 - **X-ray or MRI of SI joints and spine**
 - Most patients have ↑ESR and ↑CRP
- Initial treatment: **usually NSAIDs**
 - Pain relief plus inhibition of disease progression
- **TNF inhibitors**
 - Adalimumab or infliximab
 - Used in more advanced disease
- DMARDs (methotrexate) not often used



Ankylosing Spondylitis

Classic case

- 25-year-old male
- Inflammatory back pain
- Heel pain
- Swollen fingers and toes
- Elevated ESR and CRP
- HLA B27 positive
- Treatment: anti-inflammatory drugs
 - NSAIDs
 - Anti-TNF antibodies (infliximab)

Classic

Psoriatic Arthritis

- Arthritis associated with psoriasis
- Occurs in less than 1/3 of psoriasis patients



Psoriatic Arthritis

Common features

- Asymmetric polyarthrititis
 - Mimics RA but not symmetric
 - Morning stiffness
 - Improves with use
- **Distal interphalangeal (DIP) arthritis**
 - DIP spared with RA
- Sacroiliitis
- Dactylitis
- Heel pain (enthesitis)



Psoriasis

Nail findings

- Nail pitting
- Onycholysis - separation of nail from nailbed
- Subungual hyperkeratosis
- 46% of uncomplicated psoriasis cases
- **90% of psoriatic arthritis cases**

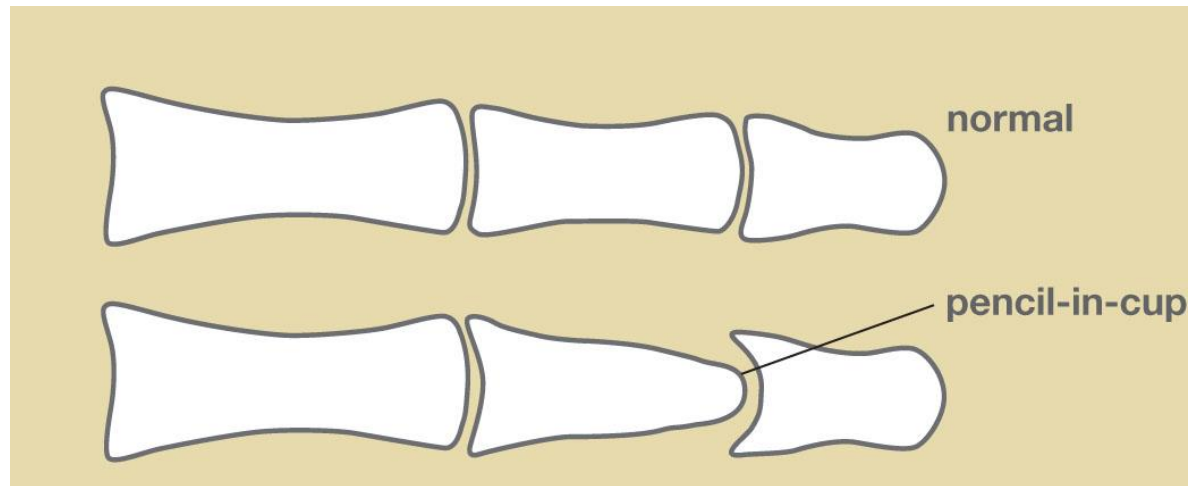


Alborz Fallah/Wikipedia

Psoriatic Arthritis

Imaging findings

- Often involves distal interphalangeal (DIP) joints
- Classic finding: **“pencil in cup”** deformity DIP joint



Public Domain

Psoriatic Arthritis

Diagnosis

- Clinical diagnosis
- Must be distinguished from other causes of arthritis
- Differences with RA
 - Most patients with PsA have **negative RF or anti-CCP antibodies**
 - Only PsA has **DIP involvement**, spondyloarthritis, sausage digits
 - PsA usually asymmetric; RA usually symmetric
- No preceding infection to suggest reactive arthritis
- No history of IBD

Psoriatic Arthritis

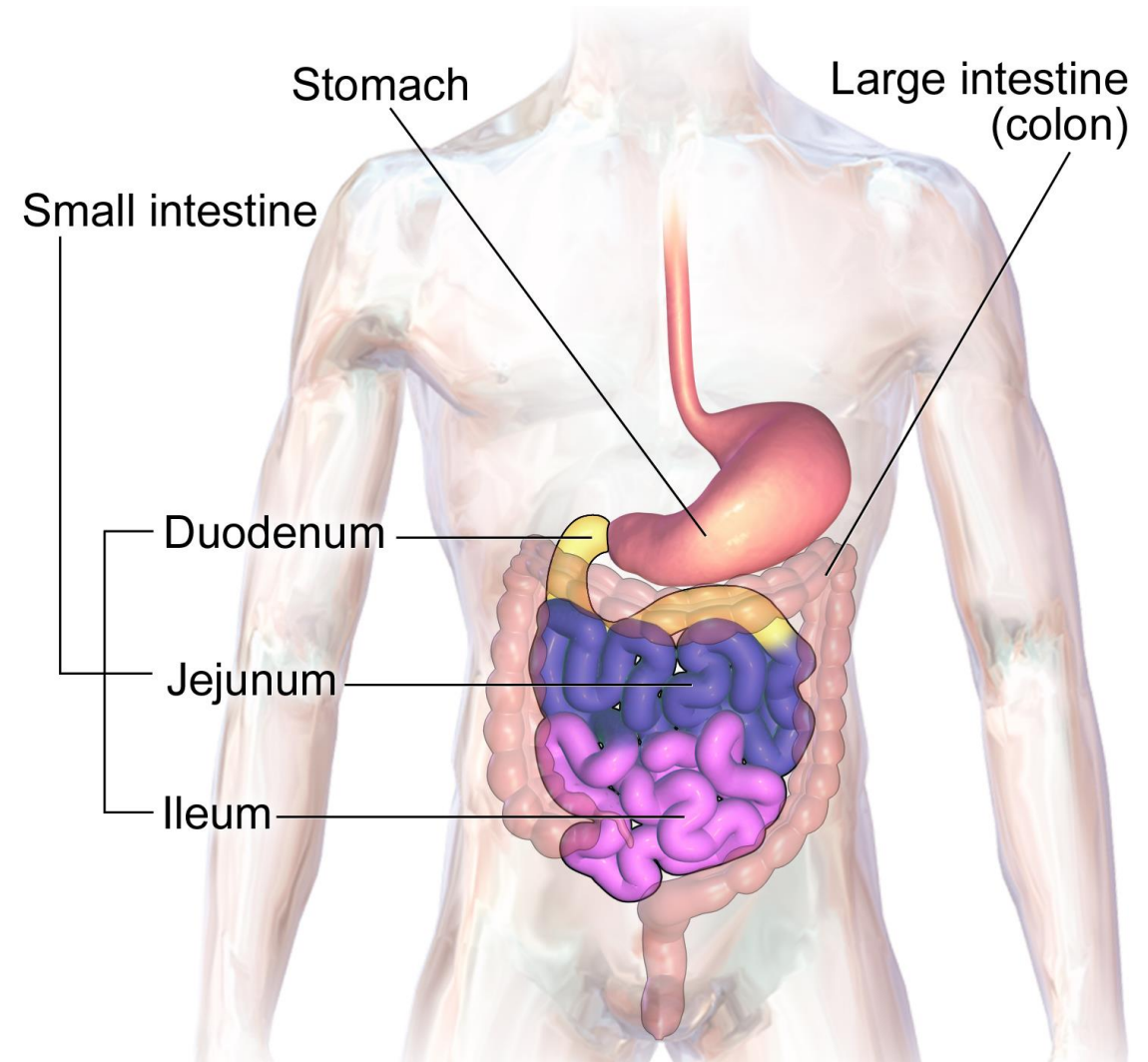
Treatment

- Mild disease without joint damage: NSAIDs
- More severe disease or refractory disease: DMARDs
 - Usually methotrexate
 - Alternative: leflunomide
- Biologics (TNF inhibitors) also used

Inflammatory Bowel Disease

Crohn's disease and Ulcerative colitis

- Frequently complicated by arthritis
- Type 1 pattern
 - < 5 joints
 - Usually large joints: knees, hips, shoulders
 - Symptoms often with flare of GI disease
- Type 2
 - >5 joints
 - Small joints of the hands
 - Independent of GI disease
- Can see spondylitis and sacroiliitis
- Rarely enthesitis and dactylitis



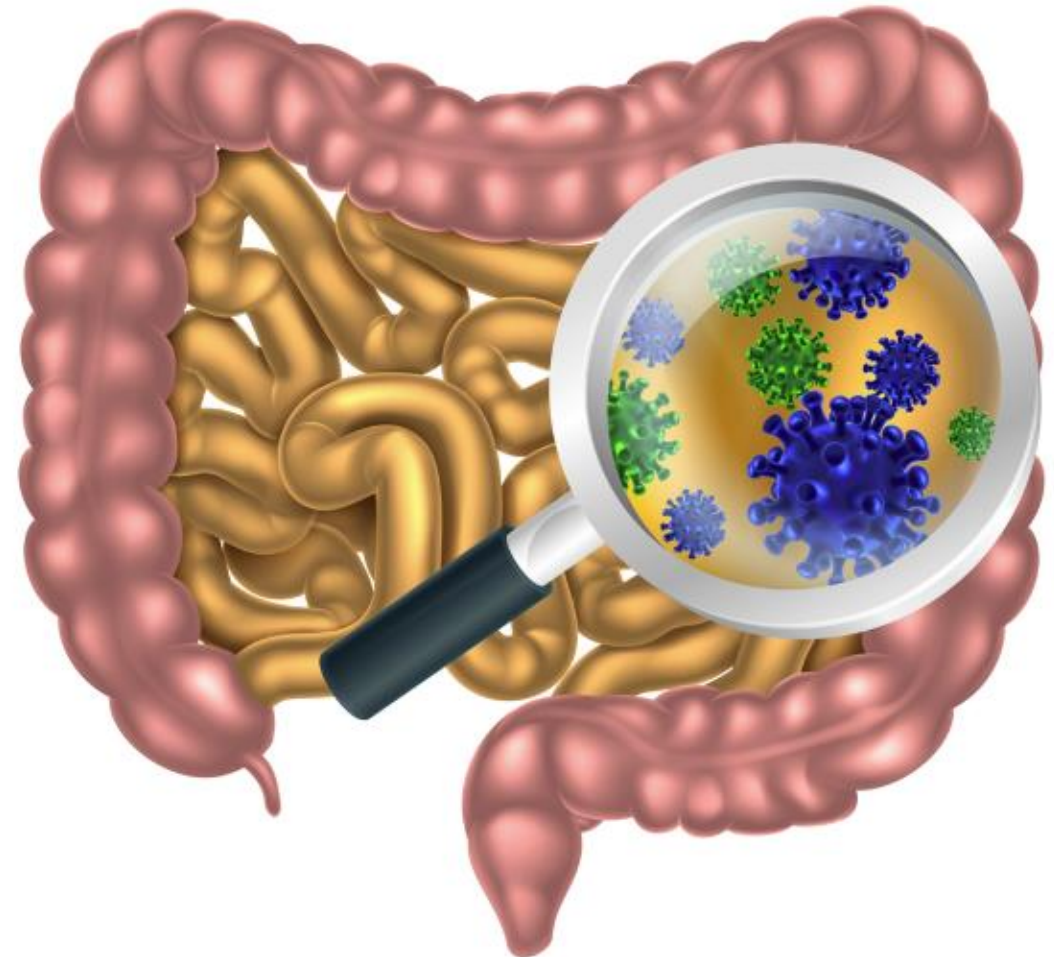
Reactive Arthritis

- Arthritis following **infection**
- Form of autoimmune spondyloarthritis
- Occurs **days to weeks after an infection**
- One or multiple joints affected
- Sometimes occurs with dactylitis and enthesitis
- Symptoms usually resolve in 6-12 months

Reactive Arthritis

Triggering infections

- GI bacteria:
 - Salmonella
 - Shigella
 - Yersinia
 - Campylobacter
 - Clostridium difficile
- Urogenital: **Chlamydia trachomatis**



Reactive Arthritis

Clinical features

- **Asymmetric oligoarthritis**
 - Usually 1 to 4 weeks after infection
 - Most commonly affects lower extremities often knees
- Enthesitis (heel pain)
- Dactylitis
- Inflammatory low back pain

Reactive Arthritis

Clinical features

- **Conjunctivitis**
- Urethritis (dysuria)
- Oral ulcers
- Reiter syndrome
 - Older term
 - Arthritis, urethritis, conjunctivitis following infection

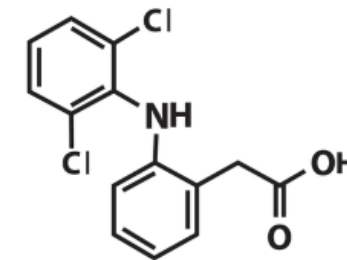


Reactive Arthritis

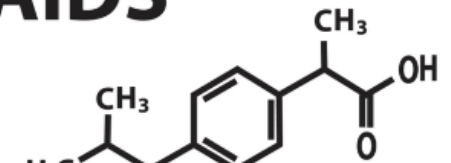
Diagnosis and treatment

- Clinical diagnosis
 - Must exclude other diagnoses
 - Most patients have **negative RF or anti-CCP antibodies**
- Treat underlying infection
- Arthritis symptoms:
 - NSAIDs
 - Intraarticular or systemic glucocorticoids
 - Rarely requires DMARDs (sulfasalazine, MTX)

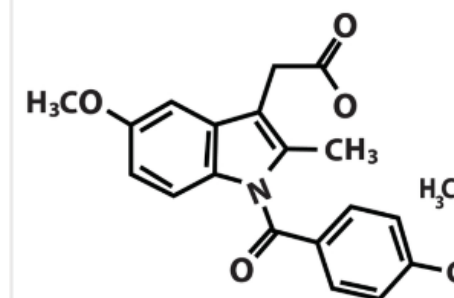
NSAIDs



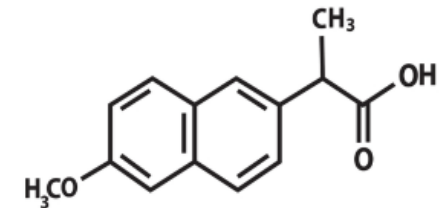
Diclofenac



Ibuprofen



Indomethacin



Naproxen

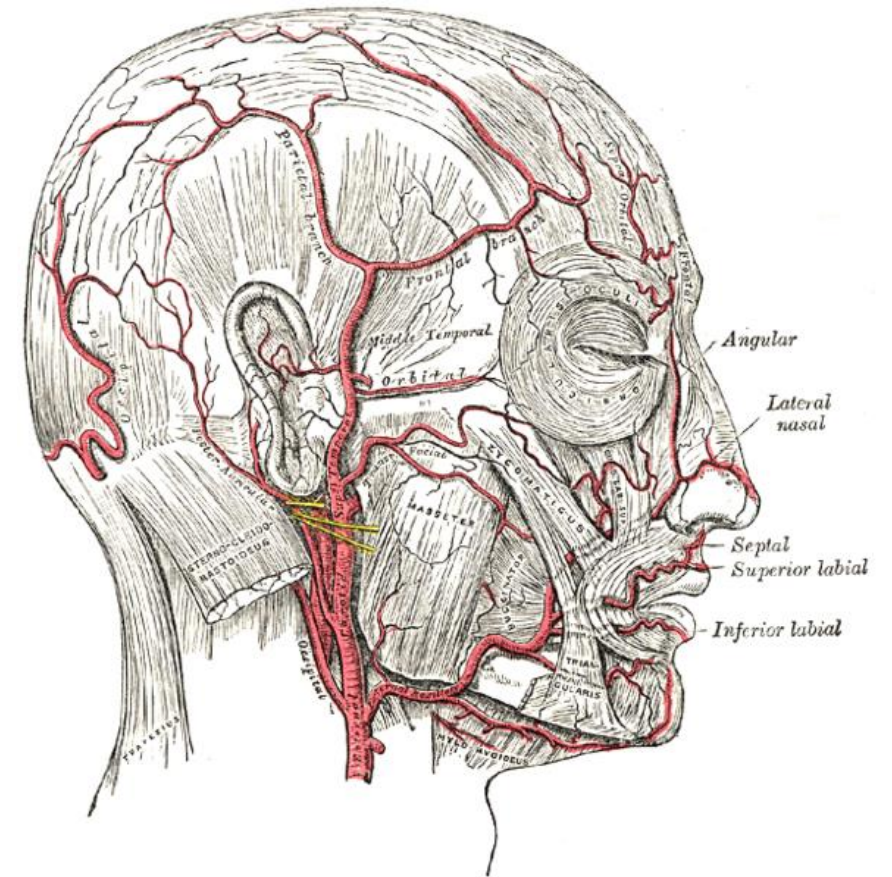
Muscle Disorders

Jason Ryan, MD, MPH



Polymyalgia Rheumatica

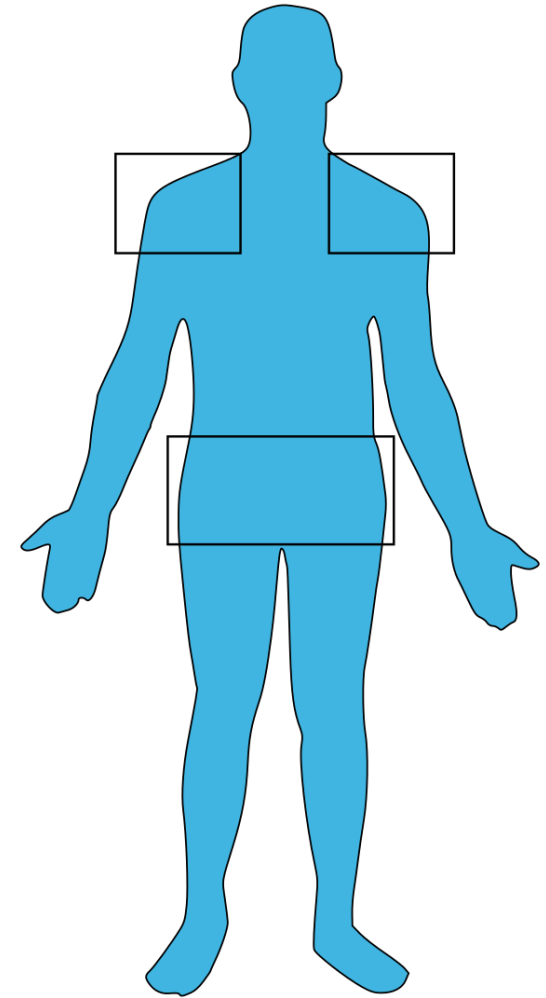
- Inflammatory disorder
- Unknown cause
- Really a joint disease – muscle tissue normal
- **Muscle pain and stiffness with normal strength**
- Strong association with **temporal arteritis**
 - PMR occurs in 50% of patients with TA



Polymyalgia Rheumatica

Clinical Features

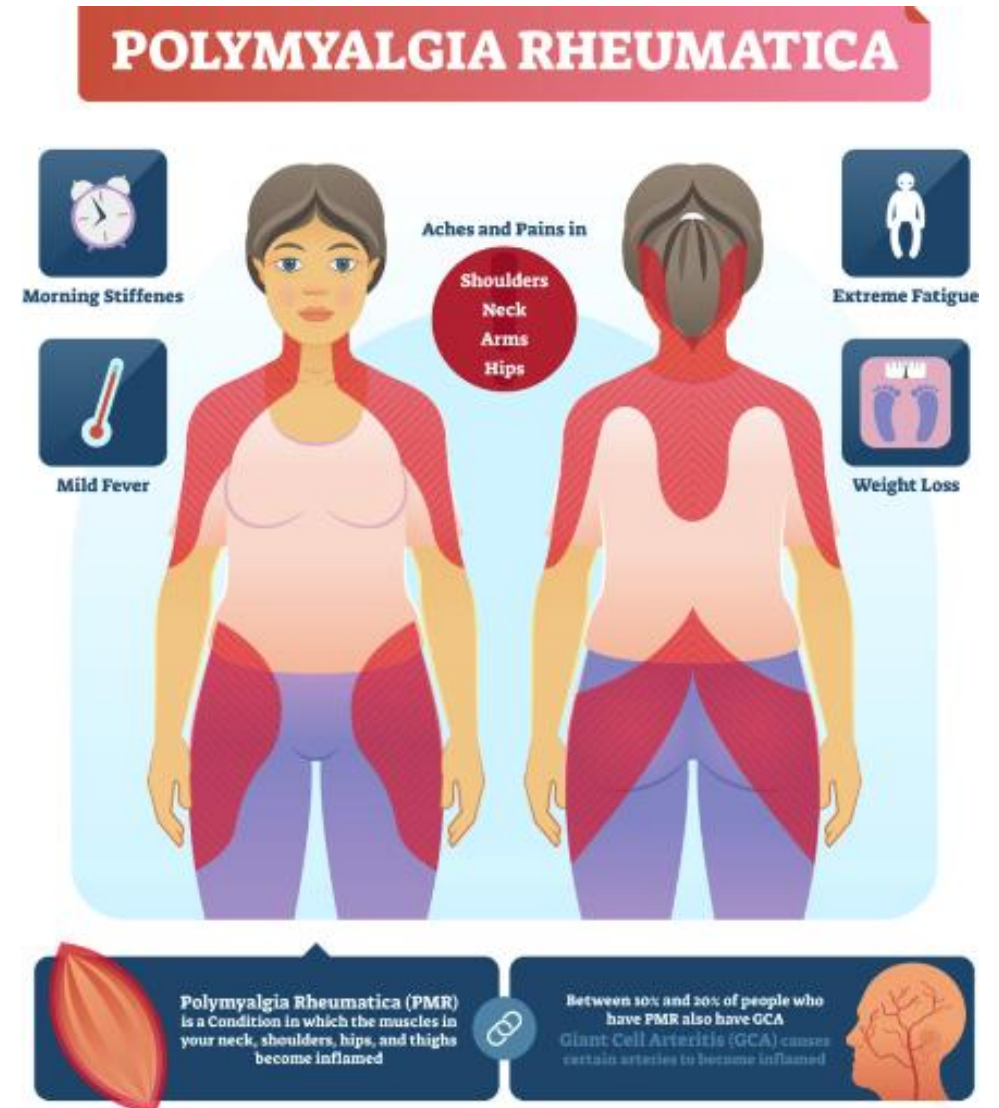
- Occurs in older patients (age > 50)
- Bilateral proximal **muscle stiffness**
 - Neck or torso
 - Shoulders/proximal arms
 - Hips/proximal thighs
 - Often difficulty dressing
- Worse in morning



Polymyalgia Rheumatica

Clinical Features

- Muscle pain (myalgias) especially in shoulder
- Does not cause muscle damage
 - Strength testing normal
 - Normal creatinine kinase level
- Sometimes malaise, fever, fatigue



Polymyalgia Rheumatica

Diagnosis and treatment

- **Clinical diagnosis** based on characteristic clinical features
 - Elevated acute phase reactants: **↑ CRP, ↑ ESR**
 - Muscle biopsy not indicated
- Responds well to low-dose **glucocorticoids**
 - Often prednisone 15 to 25 mg/day
 - Usually complete resolution of symptoms
- Differential diagnosis: rheumatoid arthritis
 - Onset usually before age 50
 - Often small joints of hands and feet
 - Only partial response to low-dose glucocorticoids
 - Positive RF and anti-CCP



Fibromyalgia

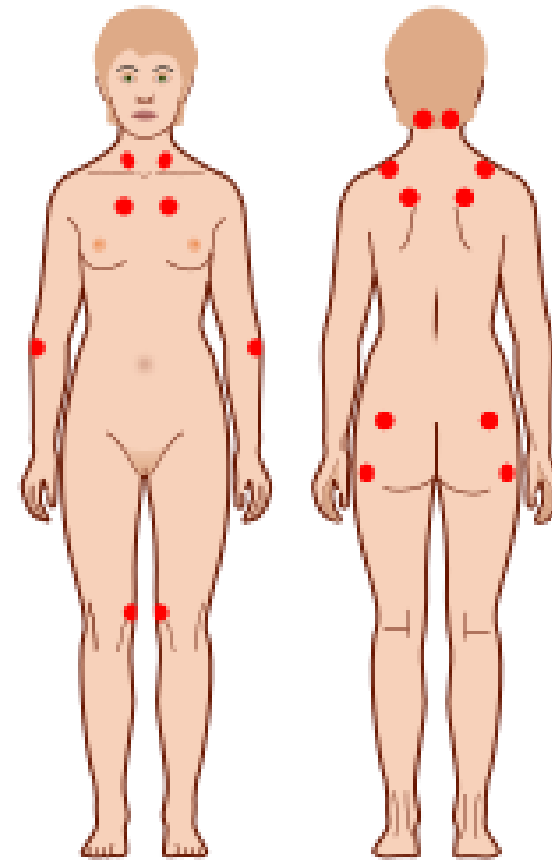
- **Chronic pain disorder**
- Widespread musculoskeletal pain
- Unknown cause
- Common in women 20 to 55 years old
- Depression/anxiety in 30 to 50% of patients
- Diagnosed clinically
- Muscle biopsy: normal
- Laboratory testing: normal



Fibromyalgia

Clinical features and diagnosis

- Chronic, widespread pain
- Point tenderness on exam
 - Often in specific anatomic locations
- Labs normal: CK, ESR, TSH
- 2010 ACR diagnostic criteria
 - Widespread pain
 - Symptoms present for at least three months
 - No other disorder that explains symptoms



Fibromyalgia

Treatment

- **Patient education**
 - Reassurance that fibromyalgia is a real illness
 - Emphasis that fibromyalgia is not life-threatening
- Treat co-morbidities: depression, anxiety, sleep
- **Exercise**
- Amitriptyline (TCA)
- Others drugs



Inflammatory Myopathies

- Autoimmune muscle disorders
- Classic subtypes: polymyositis and dermatomyositis
- Diagnosis: muscle biopsy
- Treatment: immunosuppression
 - Usually corticosteroids (prednisone) initially
 - Long term treatment with steroid sparing drugs

Inflammatory Myopathies

Clinical Features

- Myalgias
- Slow onset symmetric muscle weakness
- Hallmark: **proximal muscle weakness**
 - Muscles closest to midline
 - Difficulty rising from a chair
 - Difficulty climbing stairs
 - Difficulty combing hair
 - Fine hand movements intact
- Distal weakness occurs later in disease



Inflammatory Myopathies

Clinical Features

- Abnormal strength testing on exam
 - Contrast with PMR
- Dysphagia may occur



Inflammatory Myopathies

Lab testing

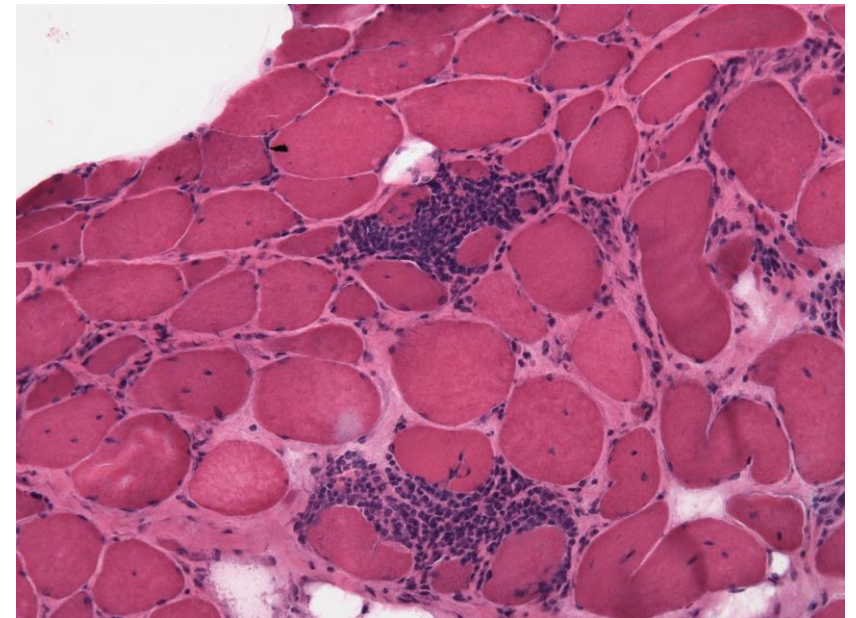
- Elevated creatinine kinase (CK)
- ESR can be elevated (sometimes normal)
- **Anti-nuclear antibodies (ANA)**
 - Not specific for myopathies
 - Positive in 80-90% of patients
- **Anti-Jo1 antibodies**
 - Antibody to RNA synthetase enzymes
 - Most common myositis antibody
- Other antibodies (anti-Mi2, anti-SRP)



Polymyositis

- Slow onset proximal muscle weakness
- No skin involvement
- Elevated CK and autoantibodies
- ESR normal or mildly elevated
- Muscle MRI: inflammation or edema
- Diagnosis: **muscle biopsy**
 - Endomysial inflammation with CD8+ T-lymphocytes
 - Endomysium = tissue surrounding each muscle fiber

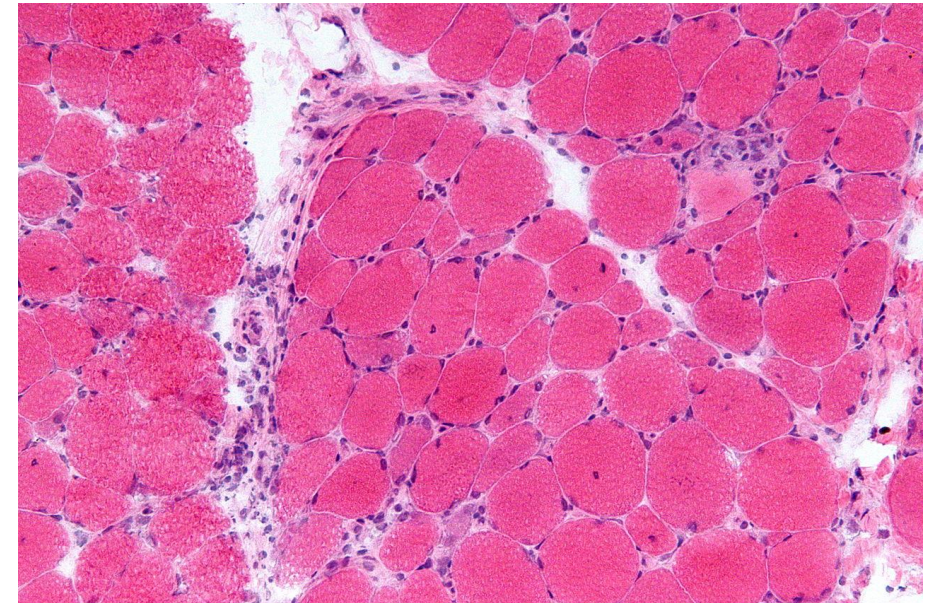
Polymyositis



Dermatomyositis

- Similar clinical features to polymyositis
- **Skin changes present**
- Diagnosis: **muscle biopsy**
 - Perimysial inflammation with CD4+ T-lymphocytes
 - Perimysium = connective tissue surrounding fascicles
 - Inflammation surrounding bundles of fibers
 - “Perifascicular atrophy”

Dermatomyositis



Dermatomyositis

Classic skin findings

- **Heliotrope rash**
 - Purple discoloration of upper eyelid
- **Gottron papules**
 - Symmetric red, scaly papules on hand/finger joints
- Both pathognomonic for dermatomyositis



Dermatomyositis

Other skin findings

- Malar rash (similar to SLE)
- “Shawl and V signs”
 - Red-brown discoloration of skin
 - Occurs in sun-exposed area
 - Upper back (like a shawl)
 - Neck/upper chest sparing skin below chin (V sign)
- Mechanic’s hands
 - Cracks/fissures on palms with increased pigmentation

Shawl Sign



Low Back Pain

Jason Ryan, MD, MPH



Low Back Pain

- Common presentation in primary care
- Large differential diagnosis
- Over 85% of patients have **“non-specific” low back pain**
 - No identifiable specific underlying condition
 - Extended workup will not identify a specific cause
- Only ~10% have a specific cause
- Less than 1% have a dangerous cause

Dangerous Causes	Specific Causes
Metastatic cancer Spinal abscess Vertebral osteomyelitis	Vertebral compression fracture Spinal stenosis Radiculopathy

Low Back Pain

Subtypes

- Acute: < 4 weeks
 - Most common type
 - Usually resolves
 - May progress to subacute or chronic
- Subacute: 4 to 12 weeks
- Chronic: > 12 weeks
- Mechanical (common)
 - Disease of spine, disks or surrounding tissues
- Non-mechanical
 - Cancer, infection, rheumatic disease



Low Back Pain

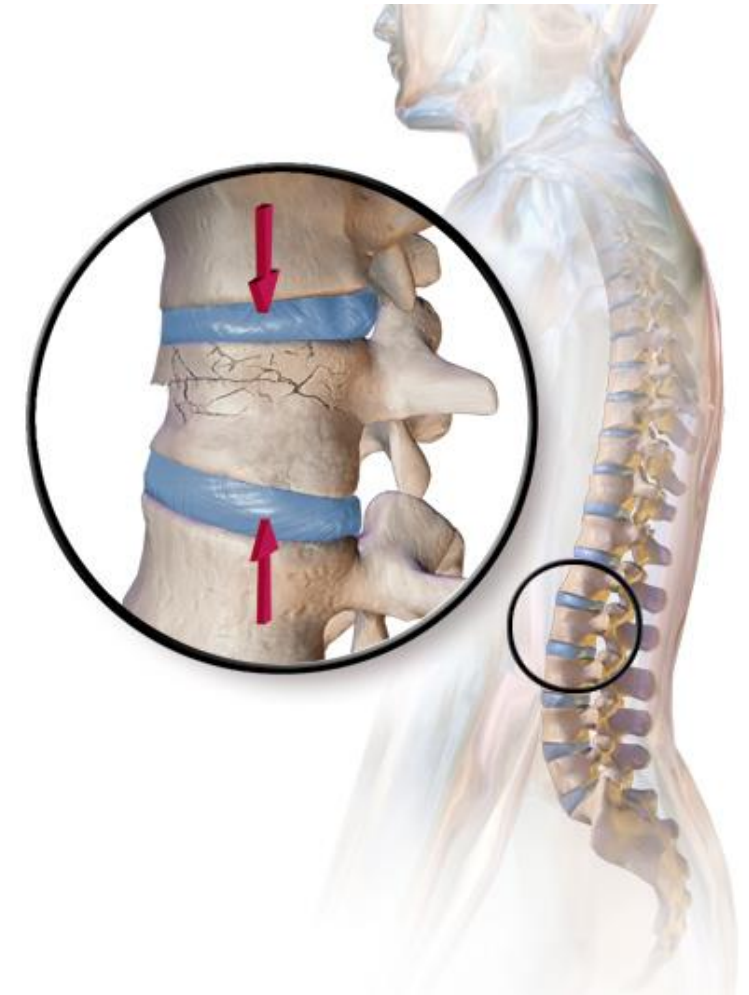
Workup

- **History**
 - Constitutional symptoms (weight loss, fever, sweats)
 - History of malignancy
 - Neurologic symptoms (weakness, numbness, bowel/bladder symptoms)
 - History of injection drug use
- **Physical examination**
 - Neurologic exam
 - Straight leg raise test
 - Palpation for vertebral tenderness

Vertebral Tenderness

- Tenderness with palpation of vertebrae
 - Contrast with *paraspinal* tenderness (lumbosacral strain)
- **Spinal infection**
 - Sensitive but not specific sign
 - May indicate abscess or vertebral osteomyelitis
- **Vertebral metastases**
- **Compression fractures**

Vertebral Compression Fracture



Low Back Pain

Workup

- **Lab testing**
 - Rarely necessary
 - ESR or CRP screening for infection/malignancy/AS
- **Imaging**
 - Not indicated for most patients
 - Only used in patients with specific indications
 - Should be done in patients with “red flags”

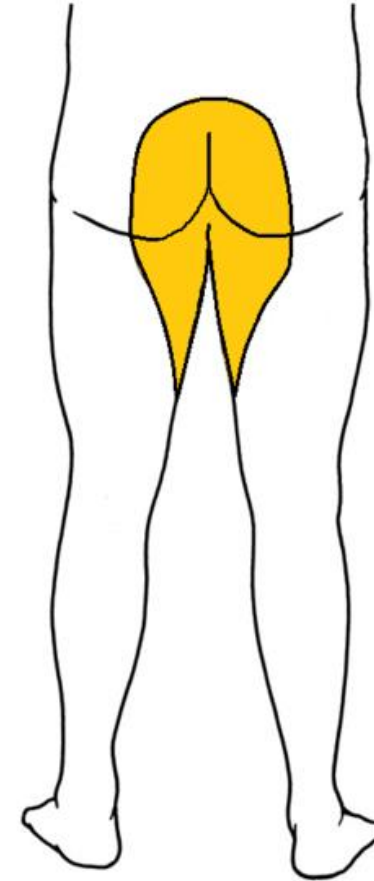


Low Back Pain

Red flags

- **Possible cauda equina syndrome**
 - Progressive motor or sensory loss
 - New urinary retention or overflow incontinence
 - New fecal incontinence
 - Saddle anesthesia
- **History of cancer**
 - Current or recent cancer
 - High risk for cancer

Saddle Anesthesia



Low Back Pain

Red flags

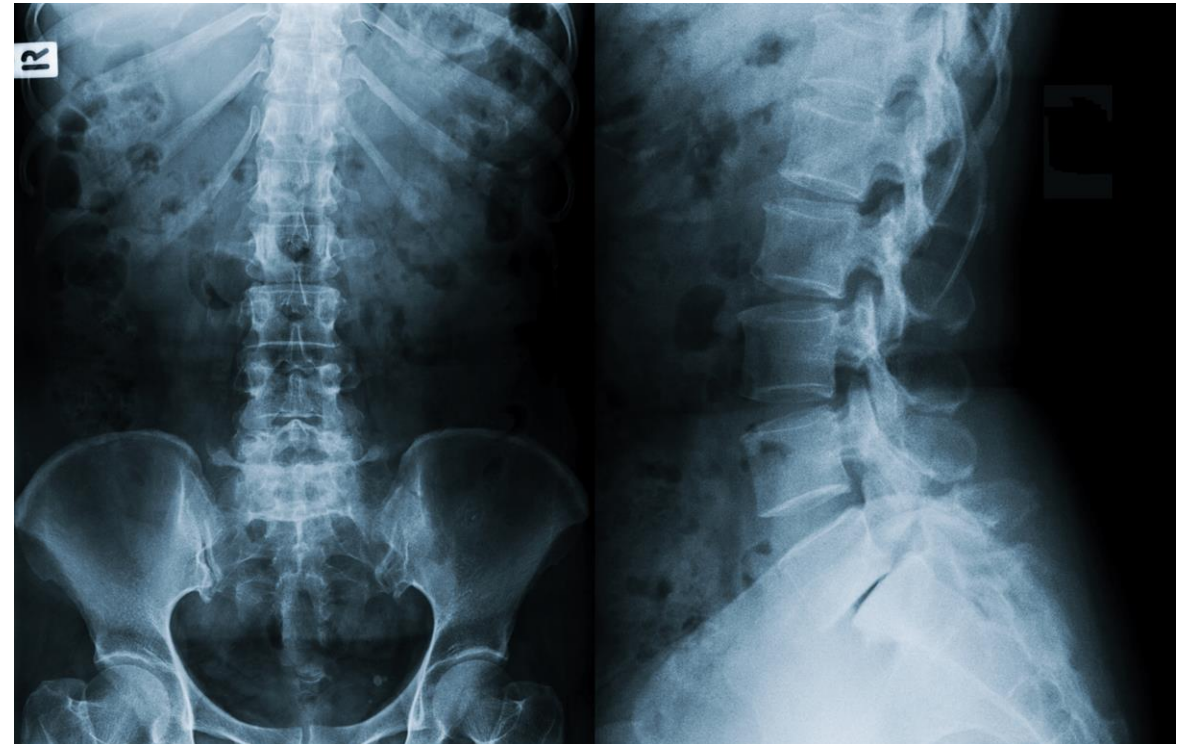
- **Risk of infection**
 - **Fever**
 - Immunosuppression
 - Hemodialysis
 - Recent bacteremia
 - Injection drug use
 - Recent spinal procedure past 12 months
- **Risk of vertebral compression fracture**
 - Advanced age
 - Prolonged glucocorticoids
 - Trauma
 - Should have X-ray



Low Back Pain

Imaging

- **Spinal X-ray**
 - Often an initial test +/- ESR-CRP
 - Screen for malignancy or infection
 - Identification of **compression fractures**
- **MRI**
 - Most sensitive/specific test
- **CT**
 - Usually for patients who cannot have MRI



Low Back Pain

Treatment for non-specific cases

- Most patients improve with time
- Moderate activity
- Heat or massage
- NSAIDs
- Other treatments in select cases
 - Physical therapy
 - Exercise therapy
 - Acupuncture
 - Muscle relaxants/opioids

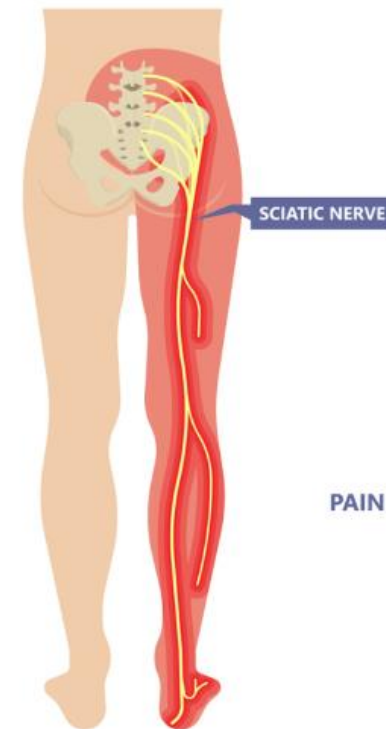


Lumbosacral Strain

- Usually due to **trauma or overuse**
- Pain worse with movement, relieved by rest
- Restricted range of motion on exam
- **Paraspinal muscle tenderness**
- Normal neurologic exam
- Imaging not indicated
- Same treatment as non-specific low back pain

Radiculopathy

- Radiculopathy = compression of spinal nerve root
- Lumbar radiculopathy = radiculopathy lumbar spine
- Also called sciatica
- Low back pain radiating one down leg
- Many causes
- **Herniated disc**
- Spondylolisthesis
- Spinal stenosis

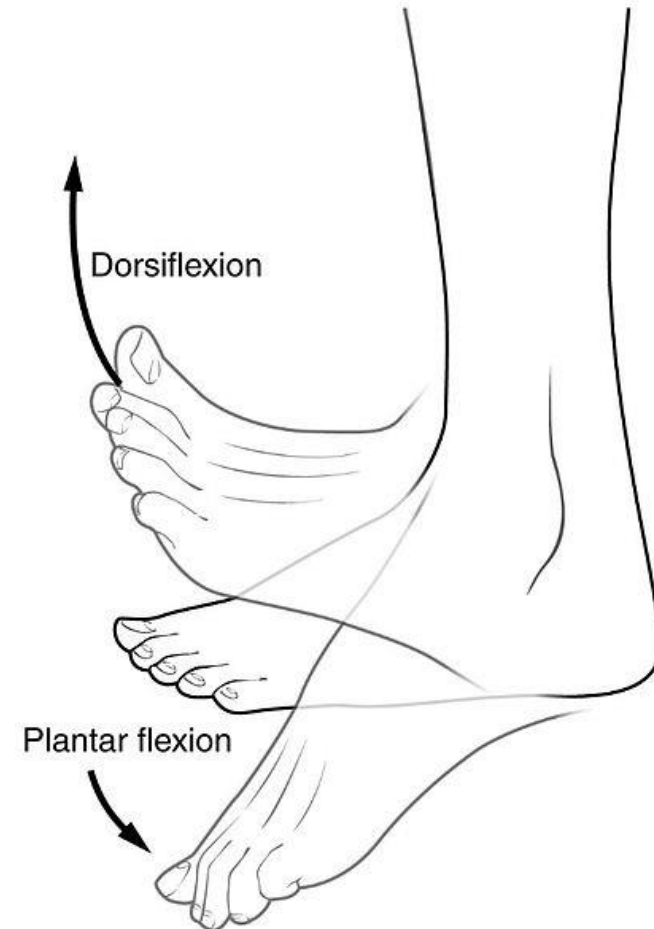


SCIATICA

PAIN THAT RADIATES ALONG THE PATH OF THE
SCIATIC NERVE

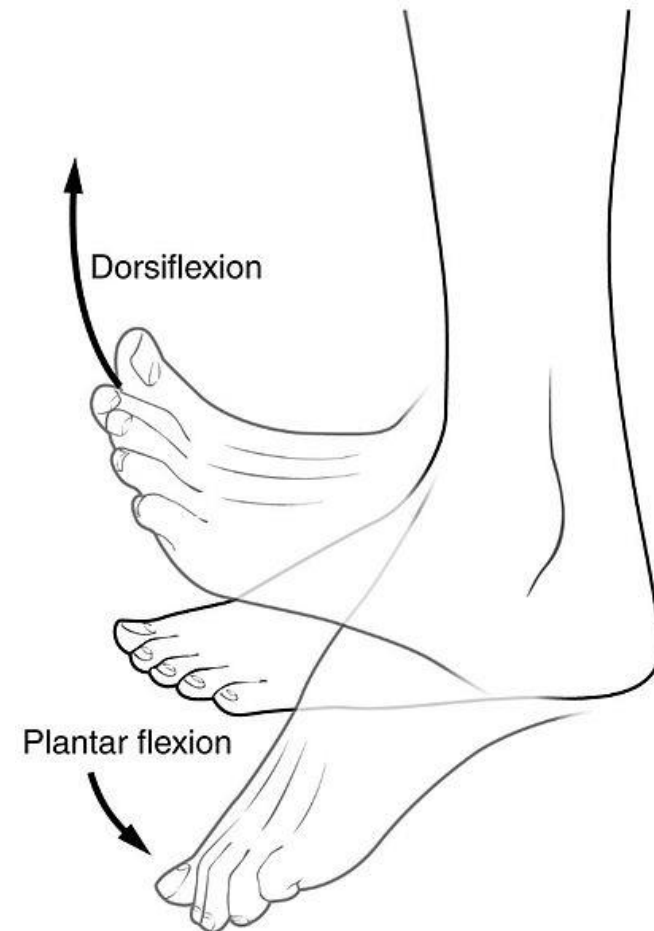
Radiculopathy Syndromes

- **Nerve root L5:** most common
 - Herniated disc at L4/L5 vertebrae
 - Back pain down lateral leg
 - Weak **foot dorsiflexion**, toe extension
 - Difficult walking on heels
 - Common Peroneal Nerve



Radiculopathy Syndromes

- **S1 nerve root:** 2nd most common
 - L5/S1 disc
 - Pain down back of leg
 - Weakness **plantar flexion**
 - Difficulty standing on toes
 - **Ankle reflex lost**
 - Tibial nerve

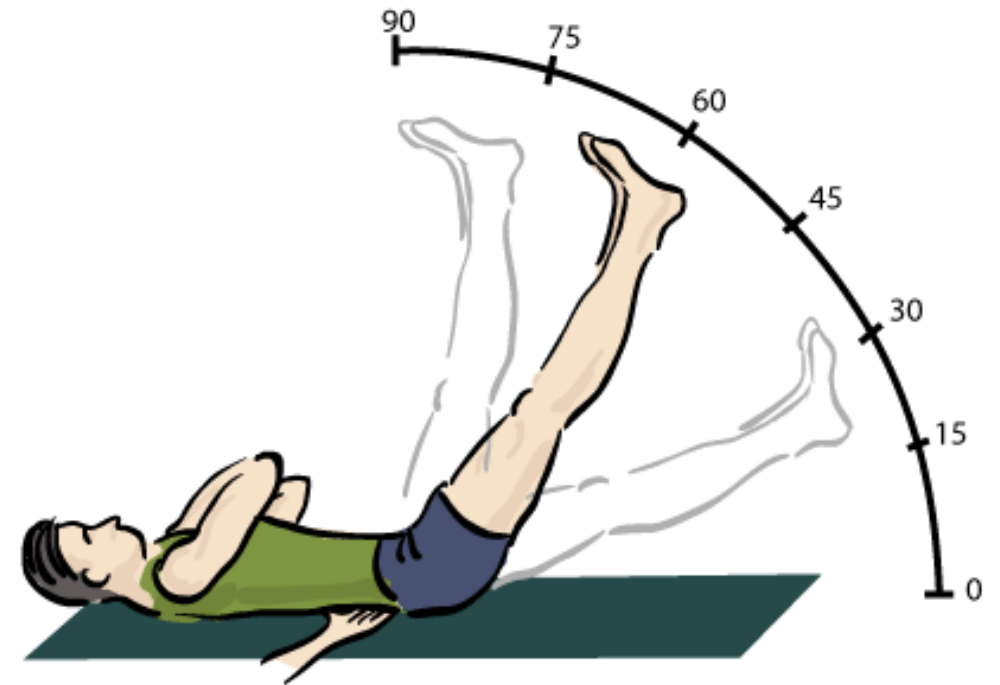


Radiculopathy Syndromes

- **L2/L3/L4 nerve roots**
 - Higher nerve roots → thigh/knee symptoms
 - Pain to anterior thigh and knee
 - Weakness: hip flexion, knee extension
 - Reduced knee (patellar) reflex
 - Femoral nerve

Straight Leg Raise Test

- Bedside maneuver for **lumbar radiculopathy**
- Examiner raises extended leg on symptomatic side
- Stretches sciatic nerve and nerve roots
- Lasègue's sign: worsening pain



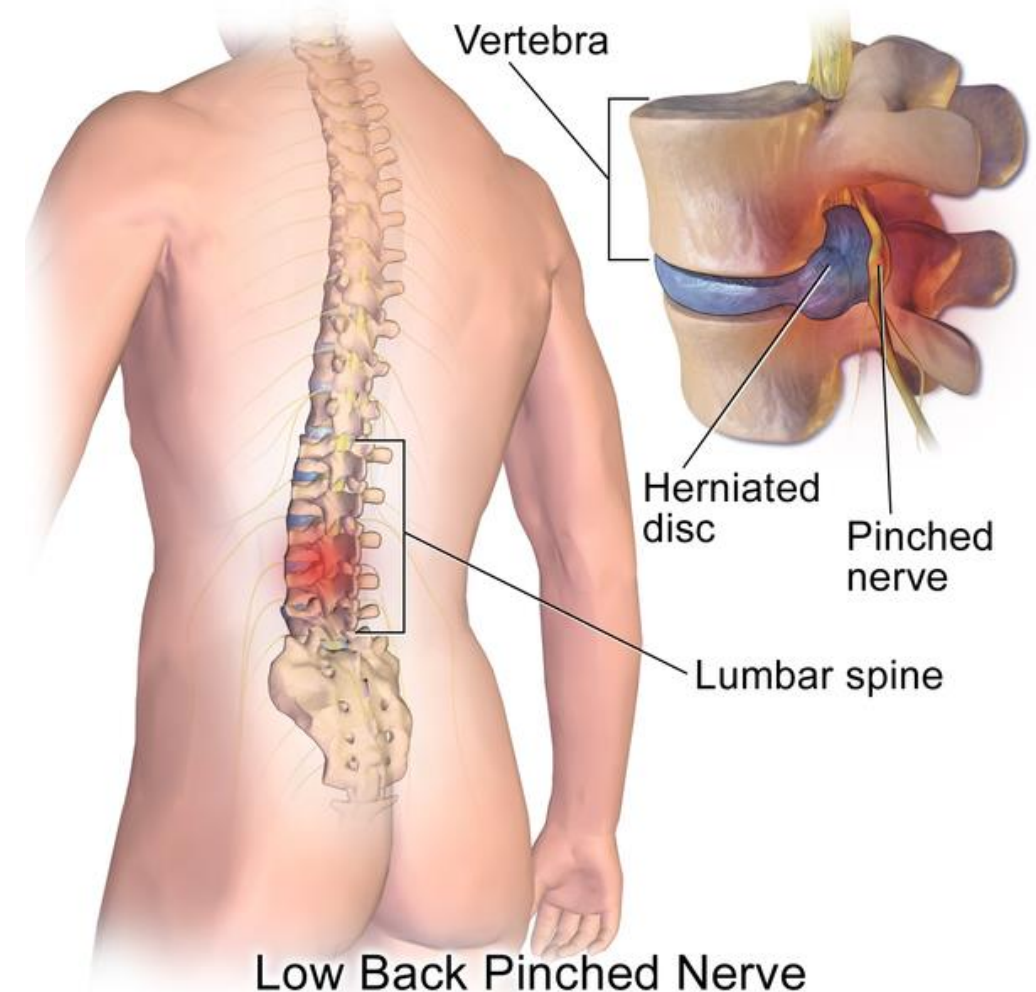
Acute Lumbosacral Radiculopathy

Workup and treatment

- Usually a **clinical diagnosis**
- **Usually not an indication for imaging**
 - High suspicion for cauda equina, malignancy, infection or fracture
 - Patients who do not respond to initial conservative treatment
 - Patients with severe/intractable pain or severe weakness
- Mild/moderate symptoms and no red flags: **NSAIDs or acetaminophen**
- Activity modification: avoid activities that cause pain
- If symptoms persist → neuroimaging
- Surgery and other advanced treatments based on specific cause

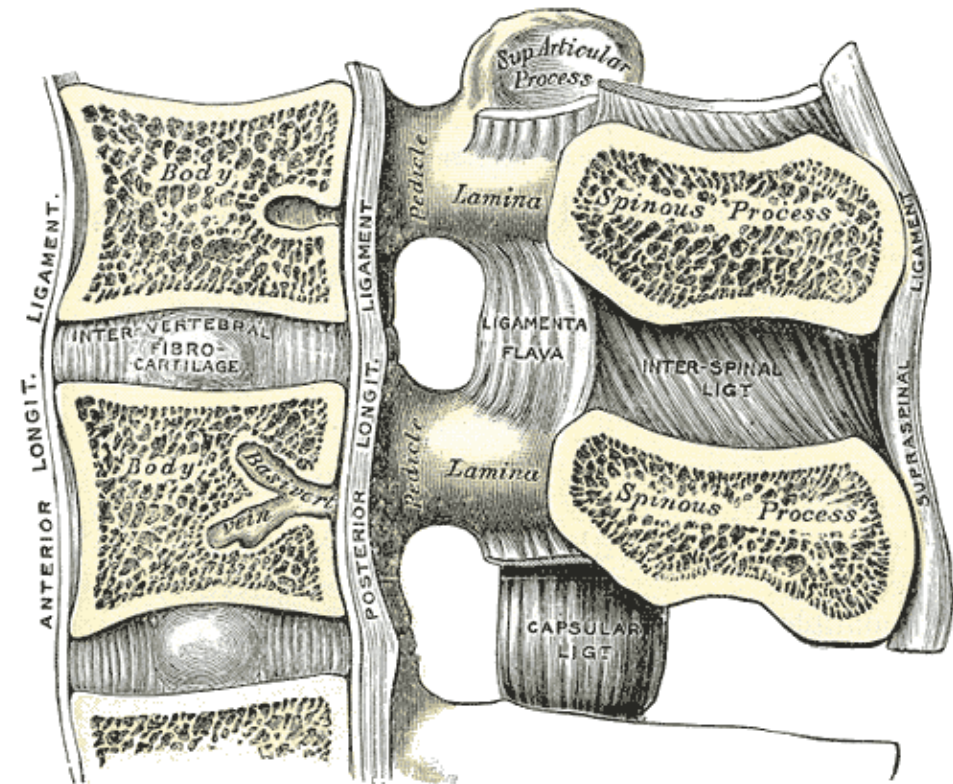
Herniated Disc

- Most common cause of radiculopathy
- Degeneration of **annulus fibrosus**
 - Surrounds soft core of disc
- Bulging/extrusion of **nucleus pulposus**
- Unilateral nerve root compression
- Presents as acute lumbosacral radiculopathy
- Diagnosis by MRI if necessary
- Surgical therapy available in select cases



Herniated Disc

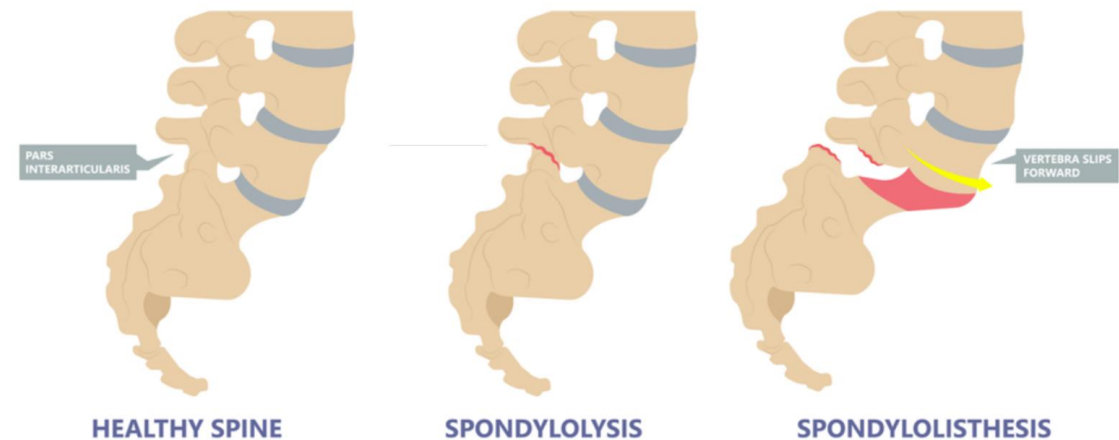
- Often occurs posteriorly
- Two ligaments contain disc in spine
 - Anterior and posterior longitudinal ligaments
- **Posterior longitudinal ligament**
 - Sits within spinal canal
 - Covers posterior surface of vertebrae
 - Weaker containment than anterior ligament



Spondylolisthesis

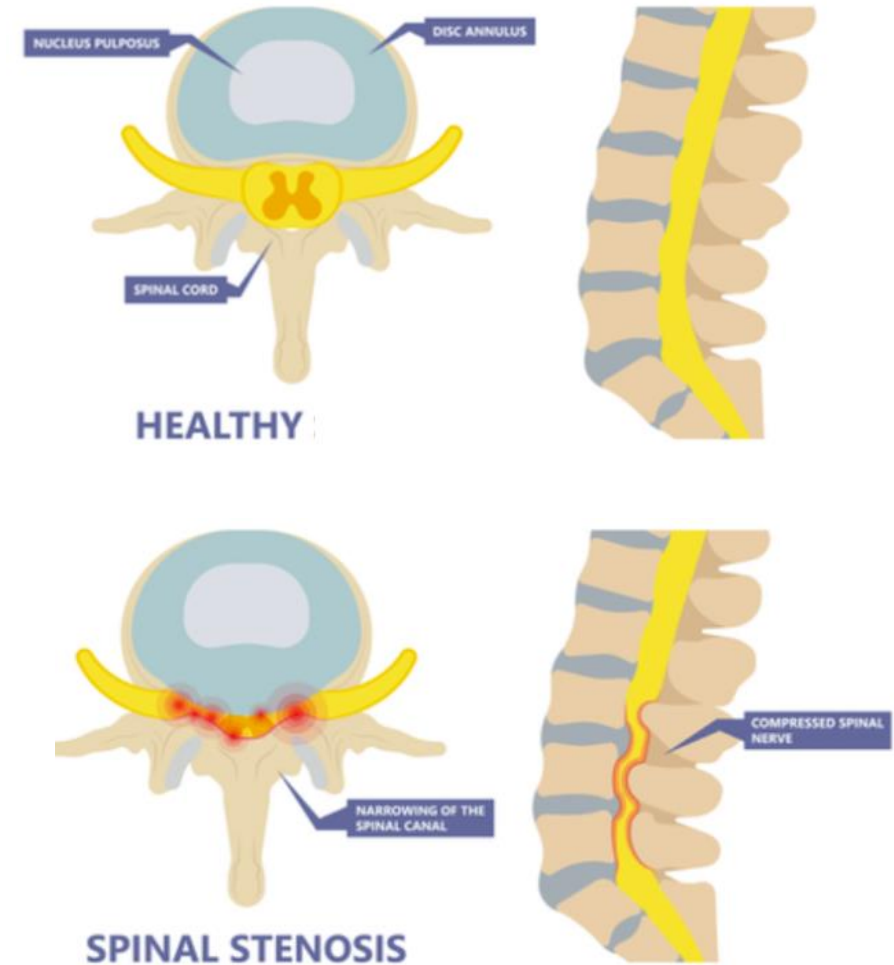
Terminology

- **Spondylosis:** age-related change of vertebra/spine
- **Spondylolysis**
 - Fracture of pars interarticularis
 - Determined by imaging
 - Usually due to aging/degeneration
- **Spondylolisthesis**
 - Forward slippage of a vertebral body
 - Occurs in patients with spondylolysis
 - May lead to lumbar radiculopathy
 - Can occur in children from fracture and overuse



Spinal Stenosis

- Narrowing of spinal canal
- Usually age-related
- Intervertebral discs shrink → narrows foramen
- Classic imaging findings:
 - Facet joint arthritis → **bone spurs/osteophytes**
 - **Ligamentum flavum hypertrophy**
 - Disc bulging and spondylolisthesis
- Leads to nerve root compression
- Standing (straight spine) narrows lumbar canal



Neurogenic Claudication

Pseudoclaudication

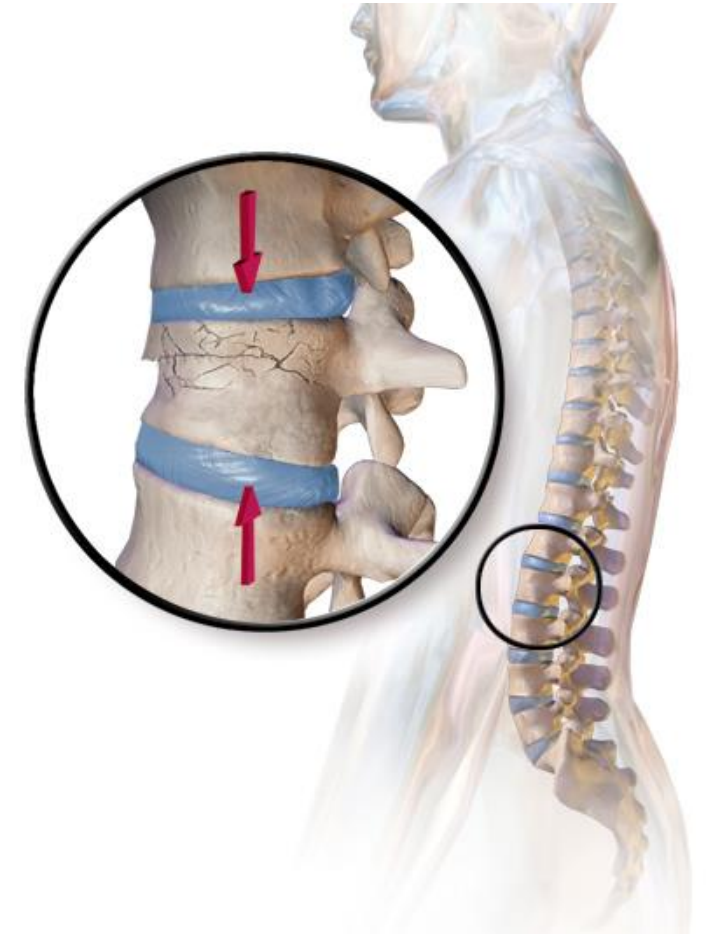
- Classic clinical feature of spinal stenosis
- Leg pain with walking in spinal stenosis
- Can mimic vascular claudication
- **Often persists with rest when standing**
- **Improves with stooped/flexed posture**
- No pain with sitting
- Diagnosis: symptoms + imaging findings
- Most patients treated conservatively
- Surgical treatments available



Vertebral Compression Fractures

- Fracture of vertebral body due to weight-bearing
- Classic fragility fracture of **osteoporosis**
- Occur mid thoracic (T7-T8) or thoracolumbar (T12-L1)
- Cause back pain and impaired mobility
- Tenderness to palpation of spine
- Diagnosis: X-ray
- Most patients treated conservatively
- Treatment for osteoporosis indicated
- Surgical treatments available (vertebroplasty/kyphoplasty)

Vertebral Compression Fracture



Spinal Cord Compression

- Trauma, malignancy or abscess
- Gradually worsening back pain
- Classically worse when lying in bed at night
- Symmetric lower extremity weakness
- Acute: diminished/absent deep tendon reflexes
- Chronic: **hyperreflexia with positive Babinski**
- Possible cord compression requires urgent MRI



Public Domain

Neoplastic Epidural Spinal Cord Compression

ESCC

- Caused by **cancer metastasis**
 - Most commonly prostate, lung, and breast
- Major clinical feature: **back pain**
 - Severe back pain at level of lesion
 - Progressively worsens over time
 - Worse at night
- Advanced cases may have motor or sensory loss
 - Arms or legs depending on level of lesion



Neoplastic Epidural Spinal Cord Compression

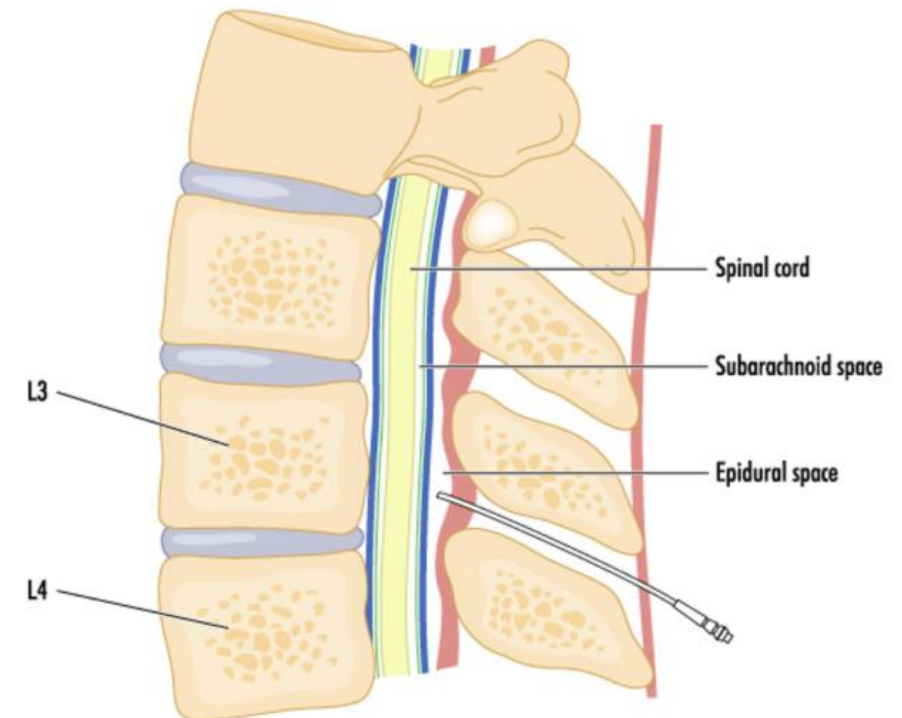
ESCC

- Most commonly in **thoracic spine**
- Diagnosis: imaging
- Initial treatment with **glucocorticoids**
 - Used for patients with neurologic deficits
 - Anti-edema effect may improve neurologic function
- Definitive treatment based on tumor type
 - Chemotherapy
 - Radiation
 - Neurosurgery



Epidural Abscess

- Abscess in **epidural space** via several mechanisms
 - Hematogenous spread
 - Direct extension from infected tissue (e.g. vertebra)
 - Direct inoculation from spinal procedure
- Risk factors
 - Injection drug use
 - Dental abscesses
 - Infected catheters
 - Endocarditis
 - Spinal interventions especially epidural catheter placement



Epidural Abscess

Clinical features

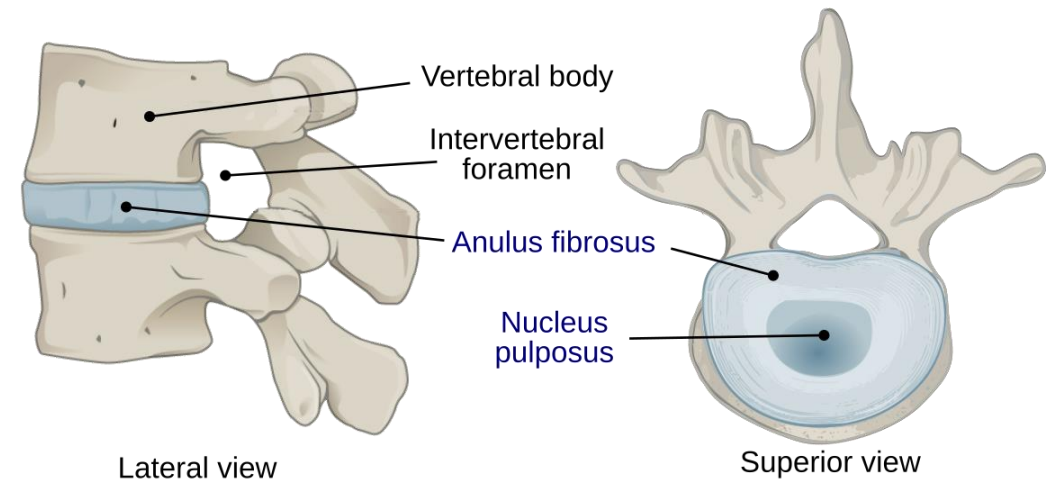
- Fever
- Back pain
- Neurologic deficits
- ↑ ESR or CRP
- Diagnosis: blood culture and MRI
- Treatment: **antibiotics and surgical decompression**
 - Most common pathogen: Staph aureus
 - Empiric therapy usually vancomycin + 3rd/4th cephalosporin



Oh, K., Inoue, T., Saito, T. *et al.* Spinal epidural abscess caused by *Pasteurella multocida* mimicking aortic dissection: a case report. *BMC Infect Dis* **19**, 448 (2019).

Vertebral Osteomyelitis and Discitis

- Infection of vertebrae or disc
- Most commonly due to hematogenous spread
- Less commonly from contiguous spread
 - Example: infected pressure ulcer → sacrum
- Back pain worse at night
- Tenderness of spine
- Fever
- ↑ ESR or CRP
- Usually no neuro defects
 - Unless complicated by epidural abscess



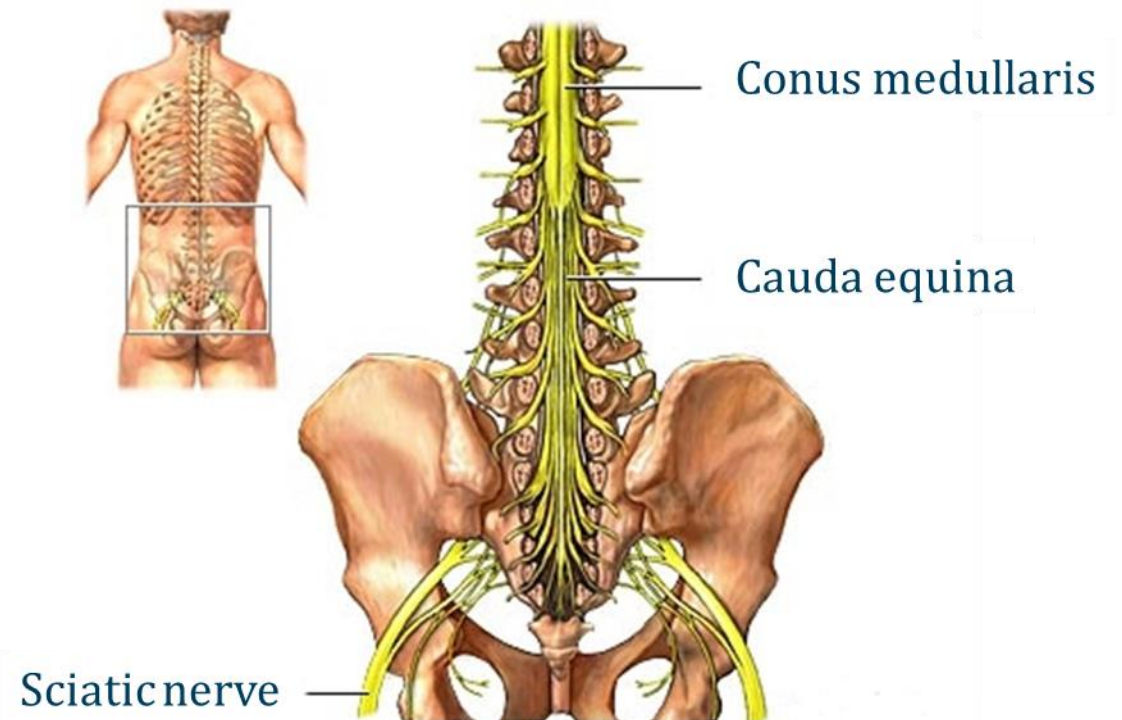
Vertebral Osteomyelitis and Discitis

Diagnosis and treatment

- Suspected based on clinical features
 - Fever, back pain, tenderness on exam
- Diagnosis: MRI and cultures
 - Blood cultures +/- tissue biopsy
- Treatment: antibiotics
 - Most common pathogen: Staph aureus
 - Empiric therapy with Vancomycin + 3rd/4th cephalosporin
 - Therapy tailored to culture results when available

Cauda Equina/Conus Medullaris Syndromes

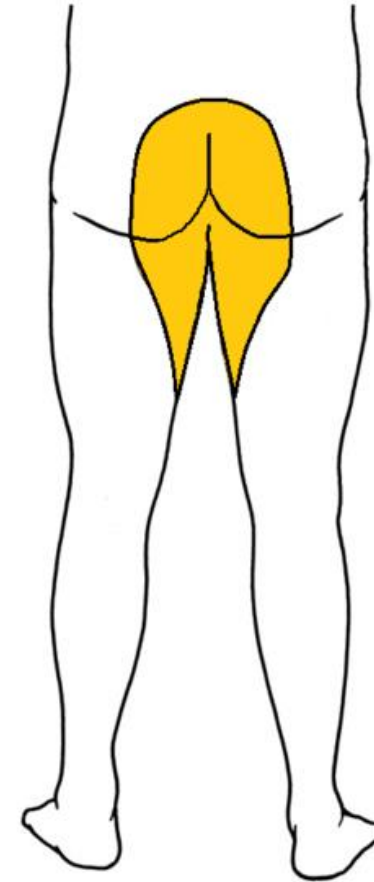
- Spinal cord ends about L2 (conus medullaris)
- Spinal nerves continue inferiorly (cauda equina)
- Cauda equina contains 18 nerve roots:
 - Motor and sensory to lower extremity
 - Pelvic floor/sphincter innervation
- Many potential causes of compression
 - Massive disk rupture, trauma, tumor
 - Neural tube defects in children
- Clinical features often overlap
- Both are neurosurgical emergencies



Cauda Equina Syndrome

- Lesion from L2 to sacrum
- Often caused by herniated disc with **gradual onset**
- Low back pain radiating to one or both legs
- Lower extremity weakness to flaccid paralysis
- Lower motor neuron deficits with **hyporeflexia**
- Bowel and bladder dysfunction
 - Either retention or incontinence
- Saddle anesthesia
- Sexual dysfunction in men may occur

Saddle Anesthesia



Conus Medullaris Syndrome

- Lesion at L1-L2 level
- More often due to trauma with **sudden onset**
- Anesthesia more localized around anus
- Less severe motor weakness
- Sexual dysfunction in men more common
- Upper motor neuron deficits with **hyperreflexia**

