Lecture 6A
Alterations in Bone Mass and Structure
Bone Tumors
Diseases of Skeletal Muscle

Alterations In Bone Mass And Structure

Scoliosis

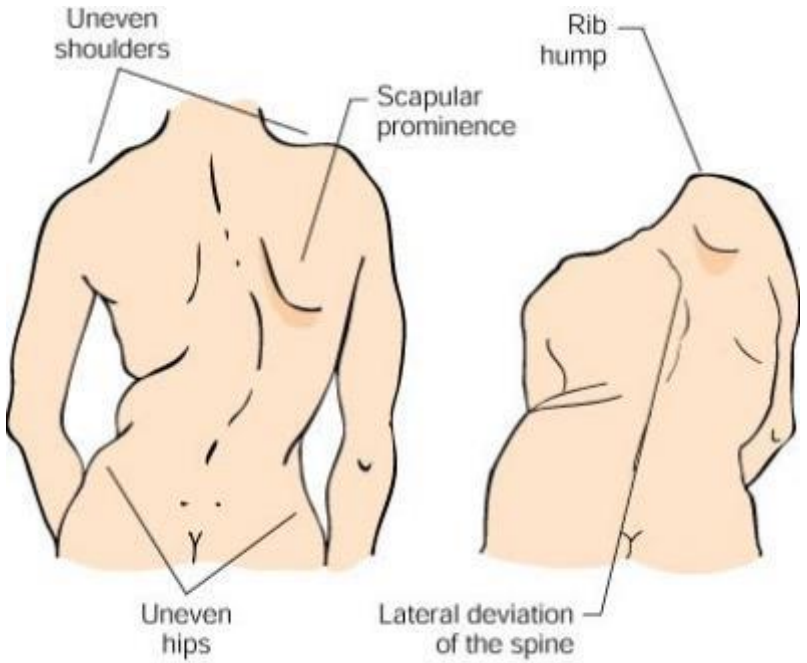
- **Lateral curvature** of spine produces an S or C-shaped spinal column. Two forms exist:
- **Nonstructural Scoliosis** does not involve deformation or vertebral rotation. When the patient bends forward the scoliotic curve disappears. May be due to neural irritation, inflammation or compensation for leg length difference.
- **Structural (Congenital) Scoliosis** involves bony deformity and vertebral rotation. Hips, shoulders and scapulae are uneven in position. Usually develops between age 10 and 15 years. Females are much more likely to require treatment.
- **Etiology**
  - May be congenital; usually idiopathic; annual incidence is about 1% in the general population
  - Risk is higher in children of women with scoliosis.

Alterations In Bone Mass And Structure

Structural Scoliosis Treatment

- Exercises, braces and frequent reevaluation
- Surgery (spinal realignment and fusion) for curvatures of 40 to 50 degrees or higher, followed by bracing and PT

Structural Scoliosis



Alterations In Bone Mass And Structure

Osteoporosis

- The most common metabolic bone disease
  - Rate of bone resorption exceeds rate of bone formation
  - Decrease in bone density, width, and mass
  - Leads to fragile bones
  - Cancellous bone is lost faster than cortical bone.
  - Affects 50% of women over 60 (post-menopausal); 20% of men over 60 (Estrogen facilitates bone remodeling.)
  - Other risk factors: small frame, Asian or Caucasian race, early menopause, thyroid hormone supplementation, corticosteroid drug therapy, dietary deficiency of calcium or Vitamin D, inactivity, smoking, alcoholism
- **Diagnosis** is by DXA (dual energy x-ray absorptiometry) to determine **bone mineral density (BMD)**.

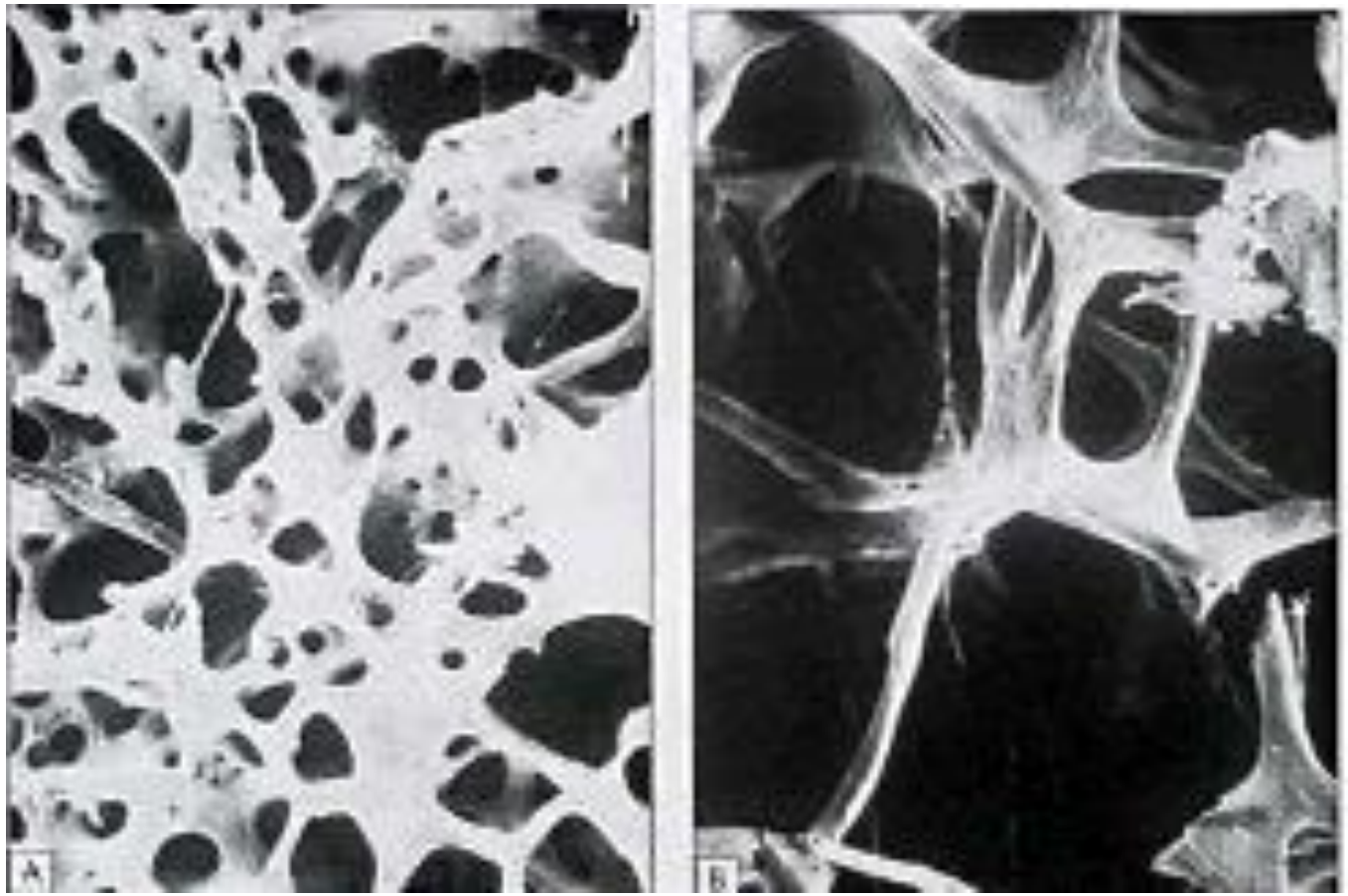
Alterations In Bone Mass And Structure

Osteoporosis

- **Clinical Manifestations**
  - Femoral head fracture (hip fracture)
  - Vertebral compression fractures
  - Colles fracture (distal radius)
  - Kyphosis (dowager's hump)
  - BMD (bone mineral density) T score of -2.5 or greater. (2.5 standard deviations below normal)
- Radiology shows radiolucent bones, wedge-shaped thoracic vertebrae, biconcave lumbar vertebrae
- **Treatment**
  - Dietary supplements
  - HRT (hormone replacement therapy) in postmenopausal women
  - Bisphosphonates to block osteoclast activity (Fosamax etc.)
  - Weight-bearing exercise

Alterations In Bone Mass And Structure

Normal **Osteoporosis**



Alterations In Bone Mass And Structure

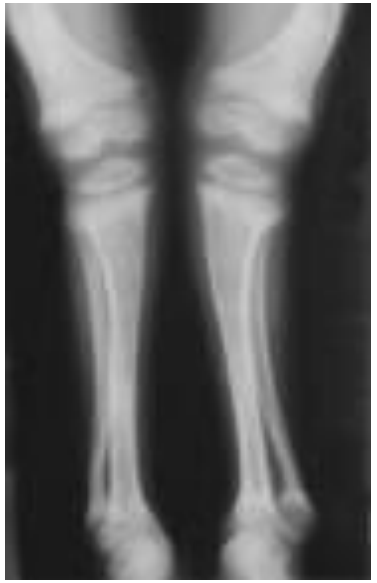
Rickets and Osteomalacia

- Due to deficits in mineralization of newly formed osteoid (organic bone matrix) with resulting soft (osteopenic) bone
- **Osteomalacia occurs in adults**. It is related to decreased intake or malabsorption of Vitamin D or defective Vitamin D metabolism (lack of sunlight) or renal disease (Kidneys are involved in Vitamin D production.) Bowing and "pseudofractures" occur in weight-bearing bones.
- **Ricketts occurs in children,** usually due to vitamin D deficiency. Epiphyseal cartilage doesn't calcify and continues to enlarge; results:
  - Kyphosis
  - **Genu varum** (bowlegs)
  - **Genu valgum** (knock knees)
  - Growth retardation
  - Delayed eruption of teeth
  - Enlargement of costochondral junction of the ribs
  - Decreased muscle tone
- **Treatment**-dietary supplements: vitamin D, calcium, phosphorous; sunlight

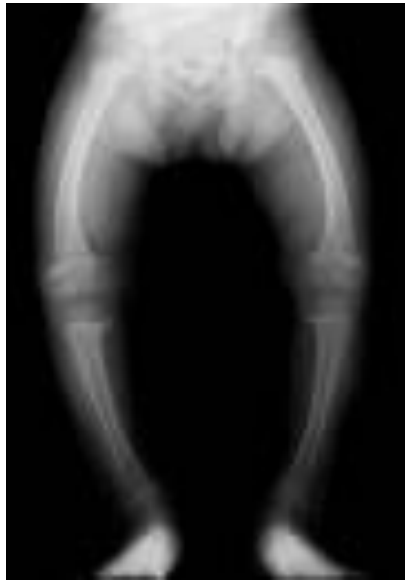
Alterations In Bone Mass And Structure

Rickets

Genu valgum



Genu varum



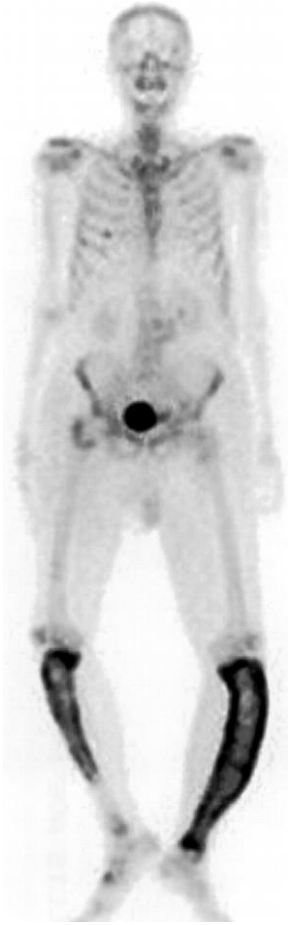
Alterations In Bone Mass And Structure

Paget Disease – Osteitis Deformans

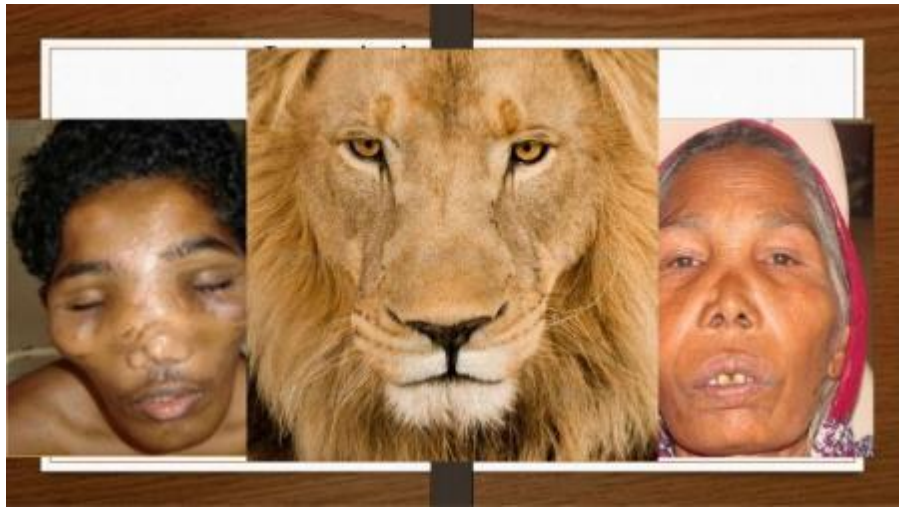
- Slowly progressive metabolic bone disease, unknown etiology; diagnosed after age 40 years.
- Three phases
  - **Lytic phase:** excessive bone resorption by osteoclasts; painful
  - **Mixed phase:** osteoclasts activity is balanced by osteoblast activity. The bone tissue (Pagetic bone) formed is abnormal, disorganized and weak. Fractures occur.
  - **Sclerotic phase:** osteoblast activity outpaces osteoclast activity causing overgrowth of abnormal bone tissue.
- **Bone** deformities are most-common in the skull, lumbar vertebrae, pelvis and femur.
- Involvement of the skull causes a lion-like appearance (leontiasis ossea). Cranial nerve compression may cause vertigo, blindness, deafness, facial paralysis, headache, etc. Surgery may be required.
- **Treatment** with **bisphosphonates to inhibit osteoclasts**

Alterations In Bone Mass And Structure

Pagetic bone appears darker on x-rays.



Leontiasis Ossea



Bone Tumors: Benign, Cartilage-Forming

Osteochondroma

- Most common bone tumor
- Cartilage-forming benign tumors occur at **bone surface**.
- Hereditary; usually presents before age 30
- Usually asymptomatic unless putting pressure on surrounding soft tissue
- Affects **metaphyses** (epiphysis/diaphysis junction) of long bones, shoulder area, pelvis

Chondroma (aka Endochondroma)

- Cartilage-forming benign tumors; occur in **medullary cavity or subperiosteal layers of bone**
- Possibly from remnants of epiphyseal cartilage
- **Small bones of hands and feet** most often affected
- Usually presents between age 30 and 40 years

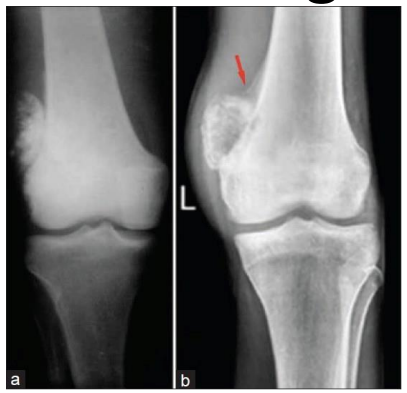
Bone Tumors: Benign

- **Osteoma**
  - Small, benign bone-forming tumors on surface of **skull bones** in children and young adults ages 4-25 years; males 3 times more often than females; especially common in the paranasal sinuses.
- **Osteoid osteoma**
  - Painful (especially nocturnal pain), benign, bone-forming tumor
  - Small lesions most often in the **cortex** of the tibia, fibula and vertebrae
  - Presents between 10-20 years of age
- **Giant cell tumor (aka osteoclastoma)**
  - Usually benign, but aggressive vascularized tumors originating in osteoclasts
  - Tumor cells destroy bone tissue.
  - May transform to malignancy (5-10% of cases)
  - Cells (giant osteoclasts) can metastasize without malignant transformation.
  - Usually in adults 20-40 years of age, more common in women.
  - **Distal femur and proximal tibia** are most often affected (50-65% of cases).

Bone Tumors: Malignant

Osteosarcoma

- Extremely malignant bone-forming tumor, the most common primary malignancy in bone tissue
- Develops in **metaphyseal** region of **long bones**; also in axial flat bones and scapulae
- Most commonly occurs between the age of 10 and 30; a second peak (10%) in the elderly
- **Rapid destruction** of bone cortex occurs increasing fractures.
- **Metastasis to lungs** common
- Joint function near tumor may be lost

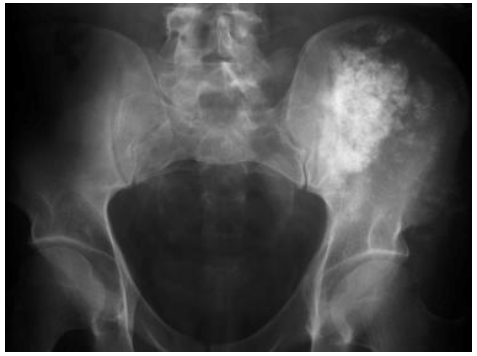


- **Treatment**-surgery to remove, radiation, chemo; amputation may be needed; 5-year survival rate is 77% if diagnosed before metastasis; 65%, if not.

Bone Tumors: Malignant

Chondrosarcoma

- Malignant cartilage-forming tumor
- **Develops slowly** so pain is not a prominent feature.
- Occurs most often in adults age 30-60 years.
- Eventually metastasizes to **lung**
- Most common in the **pelvic and shoulder girdles, lumbar vertebrae, ribs and proximal ends of femur and humerus**
- **Treatment**-amputation; does not respond well to radiation or chemo; 5-year survival rate is 90% down to 29%, depending on grade/stage. Dedifferentiated tumor cell types have the worst prognosis.

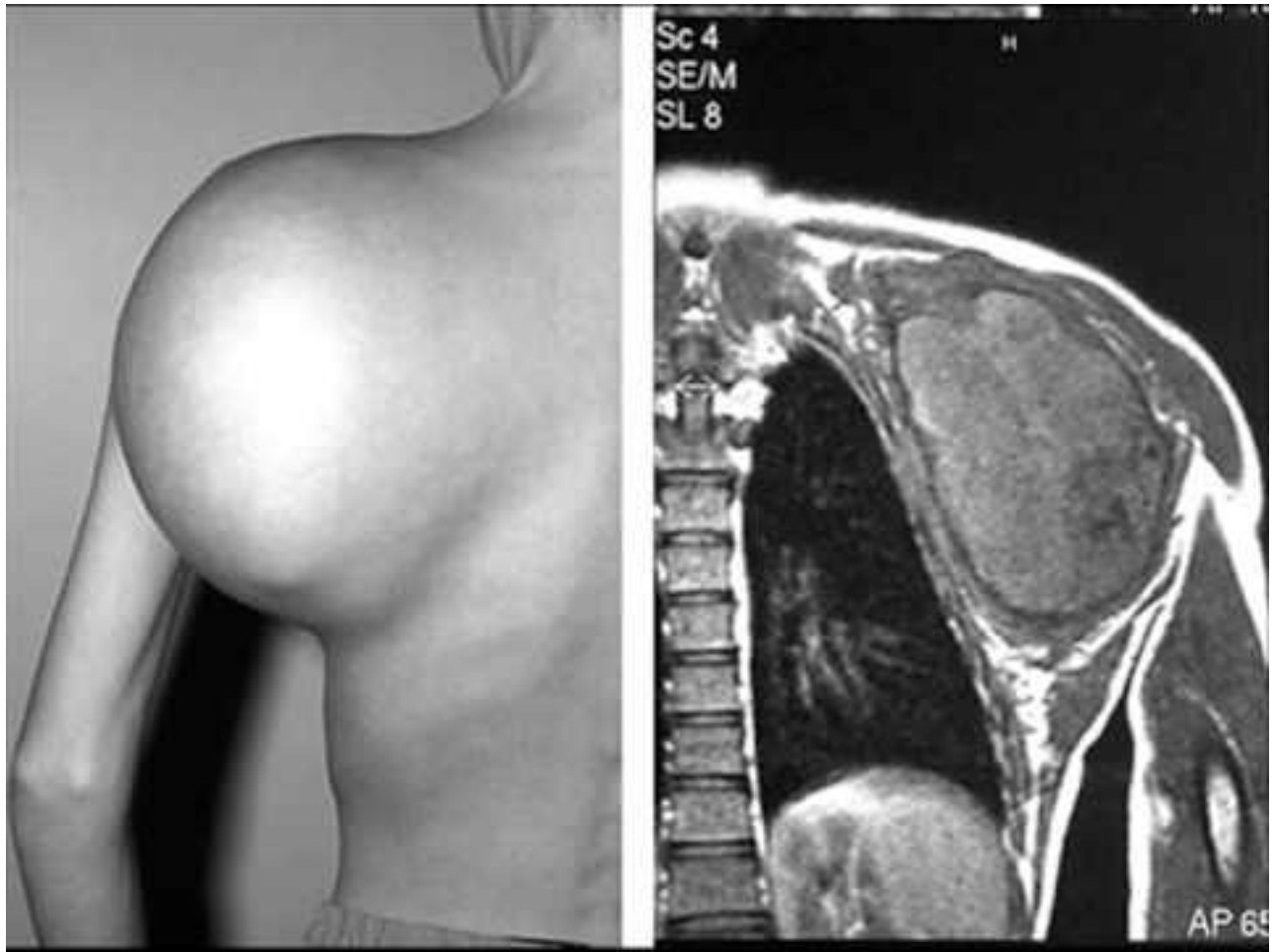


Bone Tumors: Malignant

- **Ewing sarcoma**
  - 90% of cases are due to translocation and fusion gene formation.
  - Most often in **diaphyses of long bones, pelvis or scapulae of children and young adults** 5-25 years of age; severe pain
  - Densely packed small cells with round nuclei in **medullary canal**; may penetrate cortex to form **soft tissue mass at bone surface.**
  - **Metastasizes early** to lungs and other bones; teens age 15-19 have a worse 5-year survival rate (56%) than children (70% are cured if there is no metastasis.).
  - **Treatment**-radiation, surgery
- **Multiple myeloma**
  - Malignant proliferation of a **single clone of plasma cells** – covered earlier
  - Most common in thoracic and lumbar vertebrae, also skull and ribs

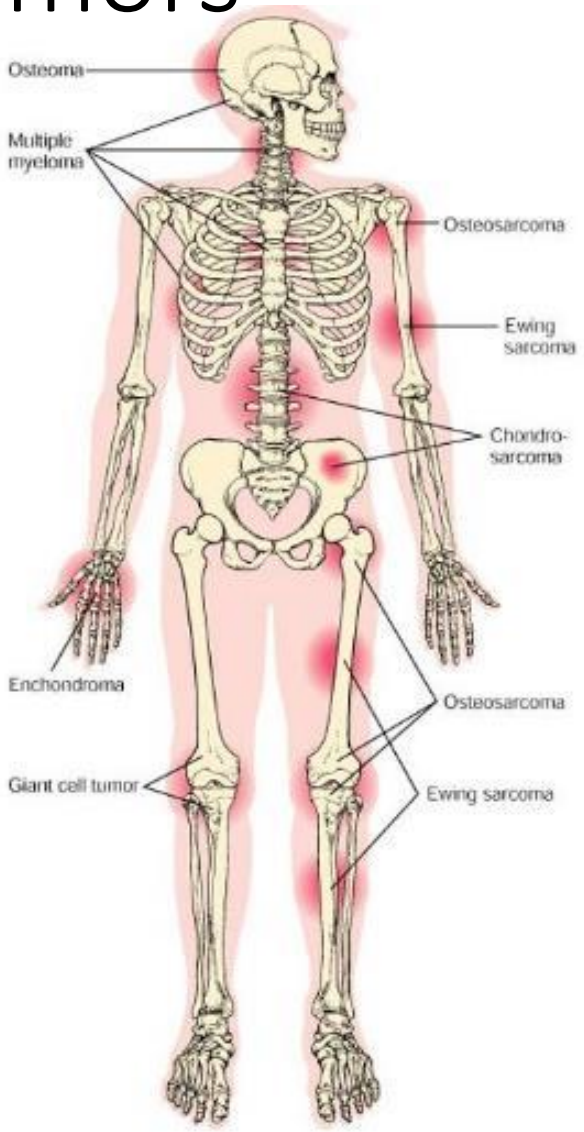
Bone Tumors: Malignant

Ewing Sarcoma



Bone Tumors

Most Common Bone Tumor Sites



From Damjanov I: Pathology for the health-related professions, ed 2, Philadelphia, 2000, Saunders, p 453.

Diseases Of Skeletal Muscle

Duchenne Muscular Dystrophy-DMD

- Most common, most severe form of muscular dystrophy, a progressive degeneration of muscle tissue; affects both skeletal and cardiac muscle fibers.
- **X-linked** trait; 1 in 3500 male births
- Due to **frameshift** mutation in the **dystrophin gene**
- Normal **dystrophin** is one of a group of structural proteins that anchor the cytoskeleton of the muscle cell to the extracellular matrix through the plasma membrane.
- In DMD the sarcolemma loses integrity and allows extracellular fluid to leak in.
- Inflammatory activation of proteases leads to necrosis of muscle tissue.
- Muscle is replaced by fat and fibrous tissue.
- **Enlarged calf muscles**, frequent falling by age 5 or 6; confinement to a wheelchair by age 12. **Cardiomyopathy** develops in the early teens.
- Survival to age 20 is rare. Death is due to **cardiac failure or pulmonary infection.**
- **Treatment**-education, preservation of physical function, prevention of contractures; corticosteroids may help but include a risk for osteoporosis

Diseases Of Skeletal Muscle

Becker Muscular Dystrophy

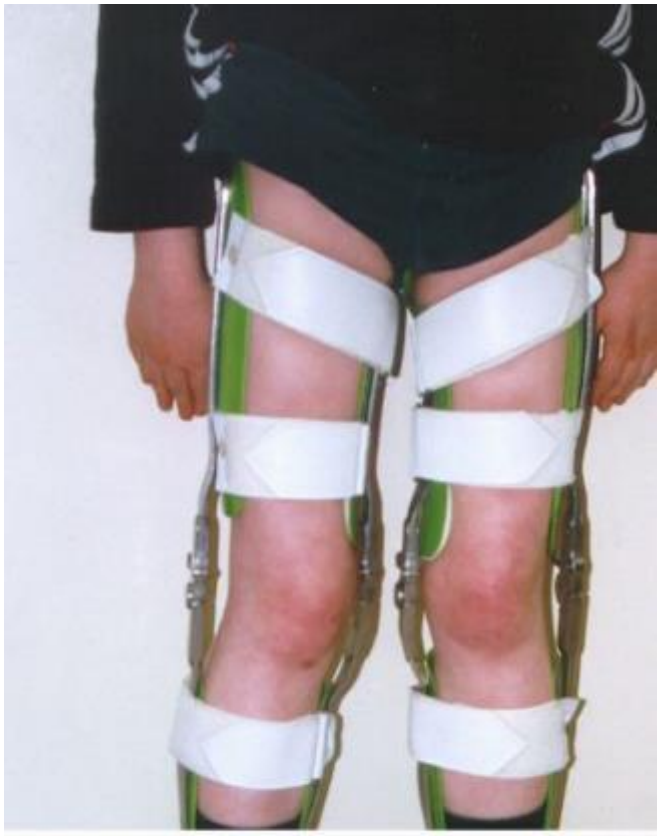
- Milder, rarer form than DMD; inherited partial deletion of dystrophin gene on the X chromosome
- Production of reduced amount of abnormal dystrophin protein – slower muscle degeneration
- Calf muscle hypertrophy and cardiomyopathy are common, but onset is later (5 -15 years)
- Confinement to a wheelchair by age 30

Facioscapulohumeral Muscular Dystrophy

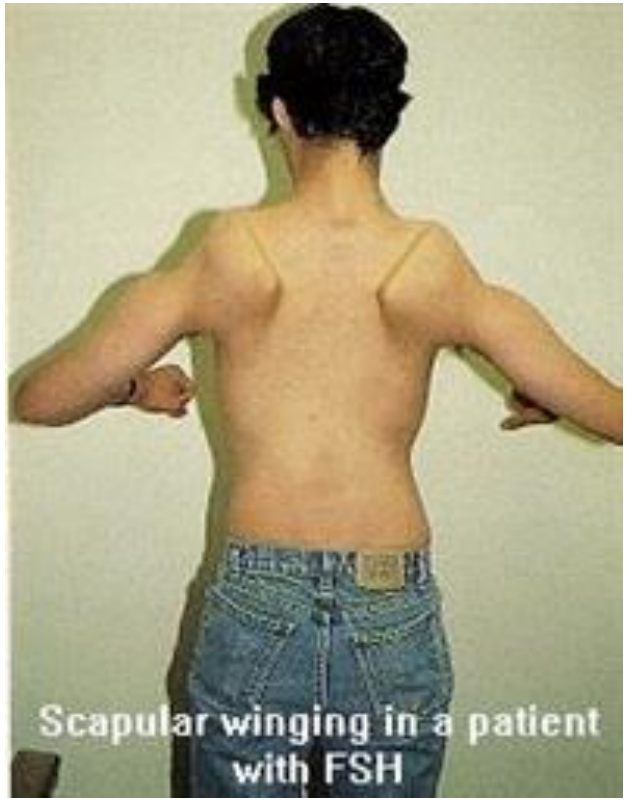
- Rare; autosomal dominant disorder; defect on chromosome #4 in a region of triplet repeats that is normally highly methylated and thus not expressed. The defect reduces the number of repeats and the level of methylation. An abnormal gene product is synthesized.
- Muscles of the face are affected first, then the shoulder girdle and upper arm. Muscles of the lower arm and the lower extremity are sometimes involved. Cardiac muscle is not affected.
- Scapulae extend outward into a wing-like position.
- Most live to a normal age.

Diseases Of Skeletal Muscle

Duchenne Muscular Dystrophy



Facioscapulohumeral Muscular Dystrophy



Diseases Of Skeletal Muscle

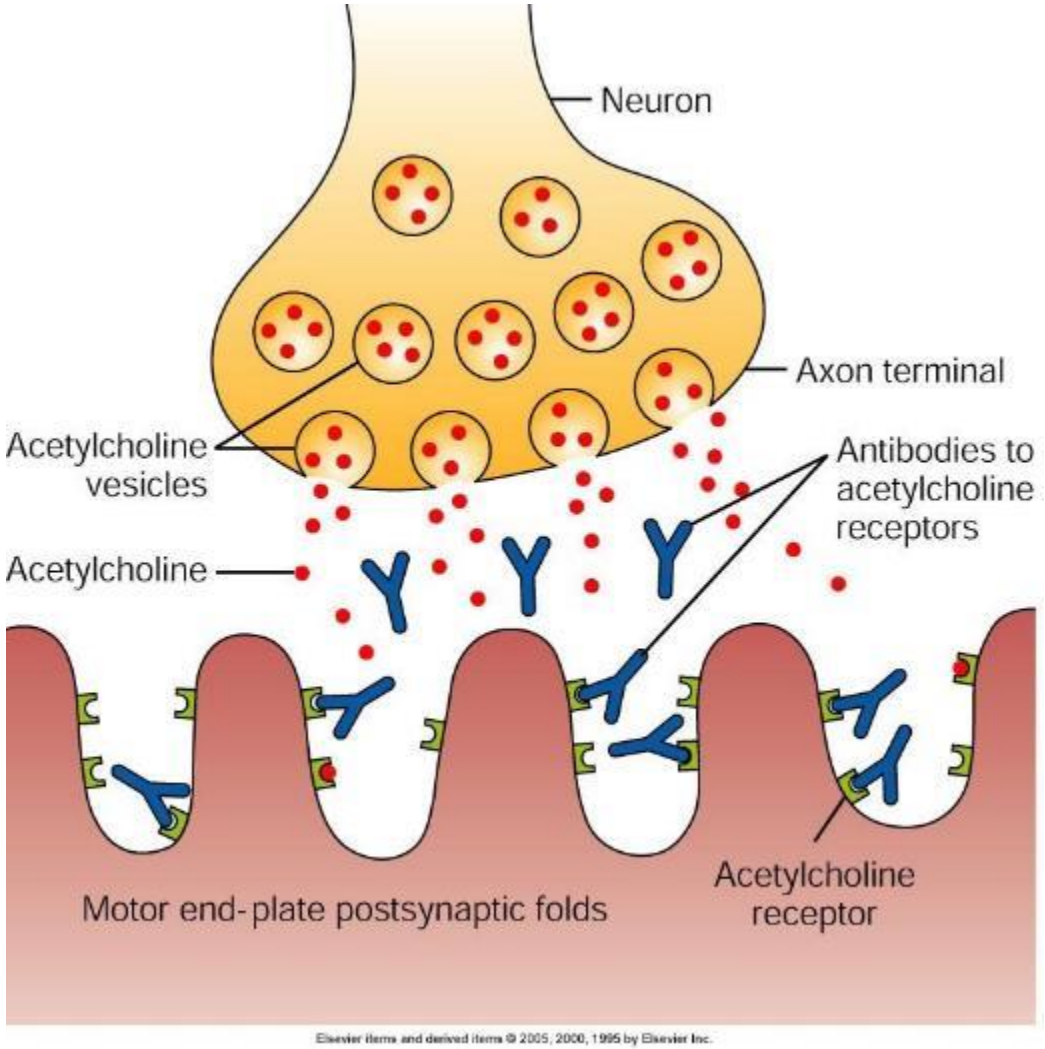
Myasthenia Gravis

- Chronic **autoimmune** disease; women most often affected
- Profound, widespread muscle weakness and fatigue
- Most often the **levator palpebrae superioris muscle** (upper eye lid muscle) and the **external eye muscles** are affected first, producing **ptosis and double vision**.
- **Anti-ACH receptor antibodies** destroy or block ACH receptors at the motor end plate on skeletal muscle fibers (**Type II Hypersensitivity**)
- Certain MHC allelic combinations increase the risk of MG.
- **Treatment:**
  - **Anticholinesterase agents** (neostigmine) to prevent enzymatic breakdown of ACH in the synaptic cleft
  - Also **corticosteroids**, cytotoxic agents, plasmapheresis, mechanical ventilation

Diseases Of Skeletal Muscle

Myasthenia Gravis

Anti-ACH receptor antibodies bind to ACH receptors.



Lecture 6B
Rheumatic Disorders
Local Disorders of Joint Function
Systemic Disorders of Joint Function
Secondary Joint Dysfunction

Rheumatic Disorders

Diagnosis

- Rheumatic disorders are diseases involving joints, autoimmunity, or both. Both **local and systemic** rheumatic disorders exist.
- In systemic rheumatic disorders blood testing often reveals
  - Auto-antibodies
  - Elevated sedimentation rate (ESR)
  - Elevated C-reactive protein (CRP)
- **Arthrocentesis** is the extraction and analysis of synovial fluid for the presence of infectious agents, crystals, blood, and WBCs.
- Synovial fluid is classified as non-inflammatory, inflammatory, or septic based on the number of white blood cells per uL (mm^3).

Non-inflammatory:	**<2000**
Inflammatory:	**>2000**
Septic:	**>100,000**

Rheumatic Disorders

Treatment

- NSAIDS-review mechanism of action given earlier in the course.
- Corticosteroids-review mechanism of action
- Immunosuppressives=**DMARDs** (Disease Modifying Anti-Inflammatory Drugs)
- DMARDs are preferable to corticosteroids because the long-term use of corticosteroids leads to **Cushing syndrome**.
  - **Methotrexate** is the most commonly used DMARD. It blocks the synthesis of DNA nucleosides (purines and pyrimidines) from **folic acid.**
- Inhibitors of inflammatory cytokines: monoclonal antibodies directed against **tumor necrosis factor (TNF)** and receptor blockers for **interleukin-1 (IL-1)**
- Injection of corticosteroids or **hyaluronic acid**, a ubiquitous polymer of disaccharides, into the joint cavity
- Hyaluronic acid is a major component of synovial fluid (It acts as a lubricant.) and cartilage (It forms an aqueous coating around chondrocytes).
- Physical therapy
- Surgery to relieved pressure on nerves.

Local Disorders of Joint Function

- Infectious (Septic) Arthritis
- Osteoarthritis (OA) aka Degenerative Joint Disease (DJD)

Local Disorders of Joint Function

Infectious (Septic) Arthritis

- **Etiology**
  - Pathogens invade the synovial membrane to cause a **closed-space infection.**
- **Diagnosis**
  - Made by recovery of bacteria from the synovial fluid or blood. The most common offenders are *Staphlococcus aureus* and *Haemophilus influenza.*
  - Purulent exudate forms if the infection is bacterial.
  - May lead to destruction of cartilage or **ankylosis** (fixation) of the joint
  - May occur in association with joint prosthesis surgery.
- **Clinical Manifestations**
  - Warm, very swollen joint (usually a single joint, but may be multiple joints) along with low-grade fever, chills, leukocytosis

Local Disorders of Joint Function

Infectious (Septic) Arthritis

- **Treatment**
  - Antibiotic therapy for 4-6 weeks is required
  - Drainage of fluid from the affected joint is often required to facilitate bacterial clearance, decrease pain, and prevent loss of function

Osteoarthritis

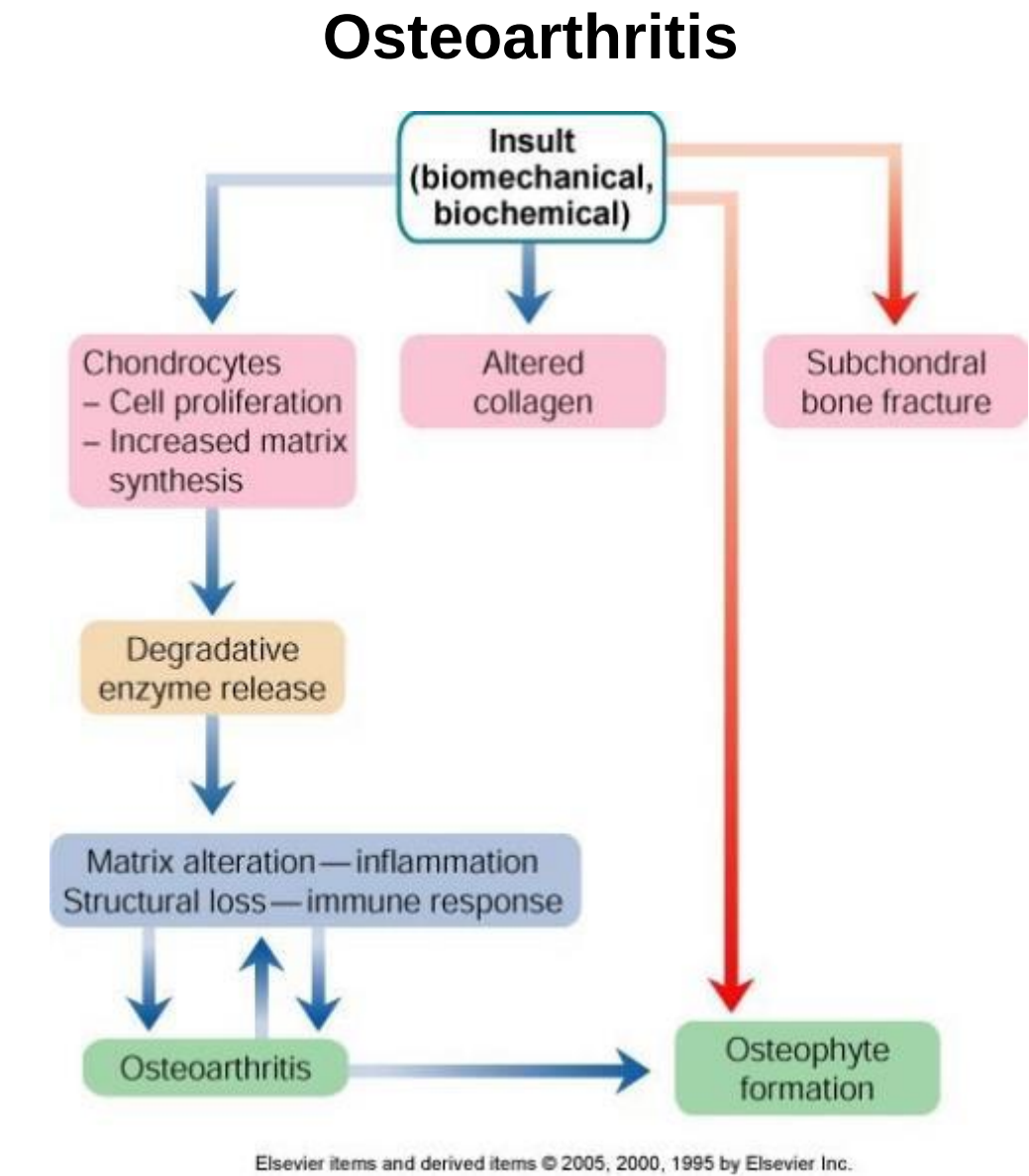
- Progressive, degenerative disease of synovial joints (especially **weight bearing** joints). It is NOT systemic.
- The most common form of arthritis worldwide
- **Etiology and Pathogenesis**
  - Progressive loss of articular cartilage and formation of thick **subchondral bone** with **new bone** (bone spurs) at joint margins
  - Initial injury causes release of **enzymes from chondrocytes** that breakdown the cartilage matrix exposing subchondral bone.

Local Disorders of Joint Function

Osteoarthritis

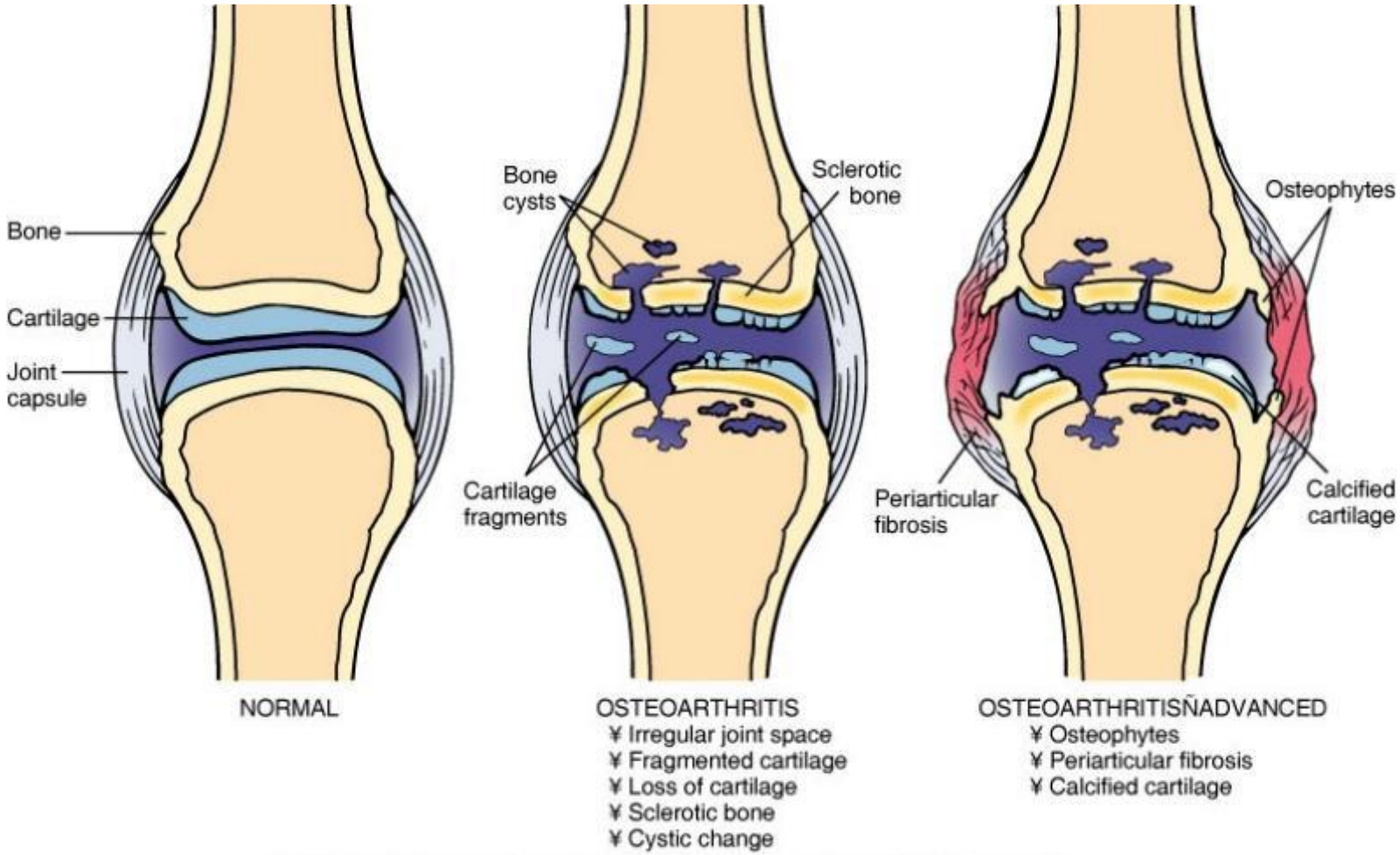
- Subchondral bone undergoes sclerosis with cyst formation and fracture, and **osteophytes** (bone spurs) form at the joint periphery.
- Cartilage fragments may break off into joint cavities and form **“loose bodies”.**
- The **synovium** becomes inflamed and secretes an increased amount of synovial fluid leading to distension of the cavity and fibrosis of periarticular connective tissue.
- More prevalent with increasing age, obesity, joint trauma, joint sepsis, congenital hip dysplasia or leg length differences, Paget’s disease, diabetes, affected family members, and in postmenopausal women.

Local Disorders of Joint Function



Local Disorders of Joint Function

Osteoarthritis



From Damjanov I: Pathology for the health-related professions, ed 2, Philadelphia, 2000, Saunders, p 455.

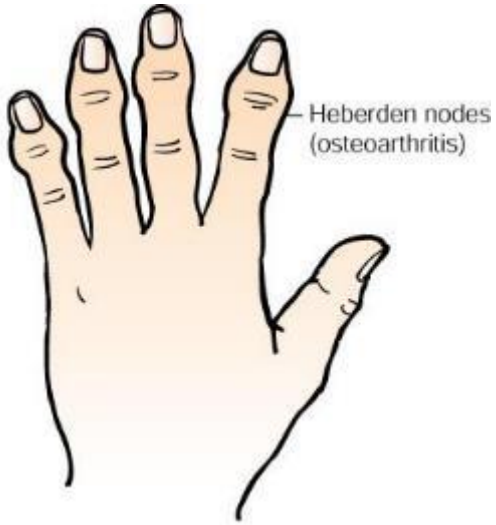
Local Disorders of Joint Function

Osteoarthritis

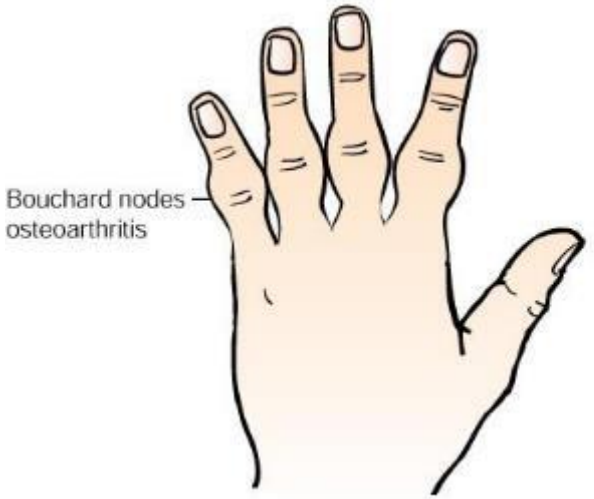
- **Clinical Manifestations**
  - Bony enlargement of joints
  - Crepitus (noisy joints due to osteophytes), morning stiffness/pain for less than 30 minutes; pain occurs with movement but not at rest.
  - Normally in **isolated** joints, rather than symmetric, most commonly knees, hips, intervertebral, and interphalangeal joints
  - **OA is termed "non-inflammatory" based on typical arthrocentesis results.**
  - Radiologic abnormalities are normally consistent with clinical symptoms – bone spurs, asymmetric joint cavity, subchondral bone sclerosis
  - Formation of **Heberden (DIP)** and **Bouchard (PIP)** nodes in hand joints
  - **Genu valgus** or **genu varus** in knees
  - OA is the most common cause of joint replacement surgery.

Local Disorders of Joint Function

Osteoarthritis of DIP (distal interphalangeal)
Joint=Heberden node

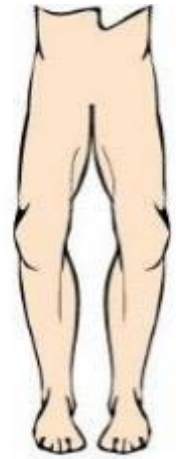


Osteoarthritis of PIP (proximal interphalangeal)
Joint=Bouchard node



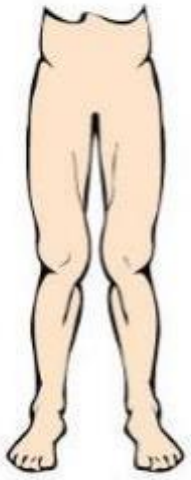
Local Disorders of Joint Function

Osteoarthritis of the Knees (bow legs) Genu varus



Genu varus

Osteoarthritis of the Knees (knock knees) Genu valgus



Genu valgus

Systemic Disorders of Joint Function (Immune Related)

- Rheumatoid Arthritis
- Systemic Lupus Erythematosus (SLE)
- Scleroderma
- Ankylosing Spondylitis (AS)

Systemic Disorders of Joint Function

Rheumatoid Arthritis

- Systemic, progressive, degenerative, inflammatory disease of the joints
- **Etiology and Pathogenesis**
  - Women more than men, 40-60 years old, all races, affects 1-2% of US population
  - Triggers may be infectious, environmental, psychological, or trauma-related
  - It is believed to be an **autoimmune** response in genetically predisposed individuals.
  - The **DR4 MHC gene (aka HLA-DR4)** has been found in 60-70% of adult RA patients.
  - Several genes are likely involved.
  - B cells produce **anti-IgM antibodies (rheumatoid factor=RF)** against IgG antibodies.
  - Immune complexes accumulate in joint cavities. Complement is activated. (**Type III hypersensitivity)**
  - Products of autoimmune inflammation stimulate edema, neovascularization and proliferation (tumor-like) of the synovium, and subchondral bone loss.
  - **Hypertrophied synovium** invades surrounding tissues.

Systemic Disorders of Joint Function

Rheumatoid Arthritis

- Granulation tissue forms over articular cartilages and leads to **pannus** formation.
  - Pannus is vascular scar tissue containing immune cells and fibroblasts.
  - Pannus enzymes and free radicals erode and destroy articular cartilage and lead to subchondral bone erosion, bone cysts and bone fissures.

- **Diagnosis**
  - The American Rheumatology Association has **seven criteria** for the diagnosis of rheumatoid arthritis. Diagnosis requires that **four** of the seven criteria be present.
  - Criteria #1 through #4 must be present for 6 weeks in order to "count" toward diagnosis.
  - See the table on the next slide.
  - **Note:** Unlike OA, the morning stiffness/pain of RA is prolonged, and affected joints are usually symmetrical (both L and R joints affected). Pain occurs both at rest and with movement. Unlike OA, which causes sclerotic (thick) bone tissue formation, RA causes bone tissue erosion.

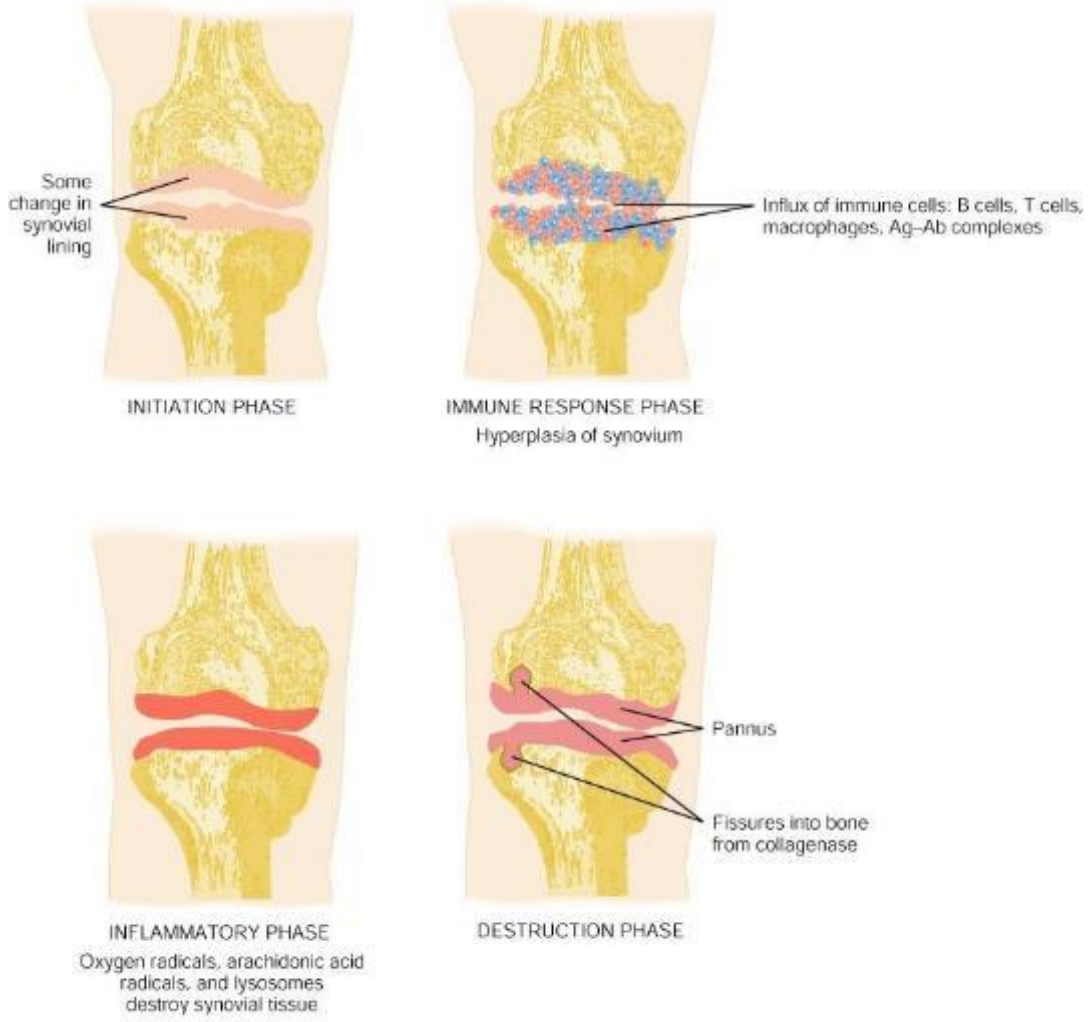
Systemic Disorders of Joint Function

American Rheumatology Association: Seven Criteria for the Diagnosis of RA

1.	**Morning stiffness in and around the joints lasting at least 1 hour before maximal improvement.**
2.	**Soft tissue swelling of 3 or more joint areas including: PIP, MCP, wrist, elbow, knee, ankle, and MTP joints.** **NOTE: DIP joints are usually unaffected.**
3.	**Swelling of at least one wrist, MCP, or PIP joint**
4.	**Simultaneous symmetric swelling in joints listed in #2**
5.	**Subcutaneous rheumatoid nodules**
6.	**Presence of rheumatoid factor (RF) in the serum**
7.	**Radiographic erosions and /or periarticular osteopenia (decreased bone density) in hand and/or wrist joints**

Systemic Disorders of Joint Function

Rheumatoid Arthritis



From Black JM, Hawks JH, Keene AM, Medical-surgical nursing, clinical management for positive outcomes, ed 6, Philadelphia, 2001, Saunders.

Systemic Disorders of Joint Function

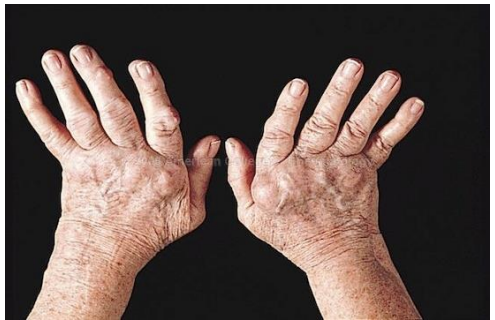
Rheumatoid Arthritis

- **Clinical Manifestations**
  - Malaise, fatigue, diffuse musculoskeletal pain
  - Joint effects are widespread and severe.
  - RA may also have cardiac, pulmonary, and ophthalmological manifestations.
    - Cardiac: pericarditis, myocarditis, mitral valve disease, heart block
    - Pulmonary: pleuritis, pleural effusions, pulmonary nodules, pulmonary fibrosis
    - Ophthalmological: episcleritis, scleritis, Sjogren syndrome (dry eyes and mouth)
  - It is imperative that a **definitive diagnosis** be made to distinguish RA from OA, Lyme disease, SLE, or gout.

Systemic Disorders of Joint Function

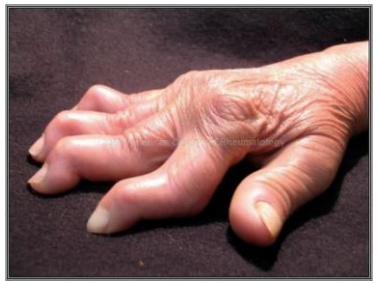
Rheumatoid Arthritis

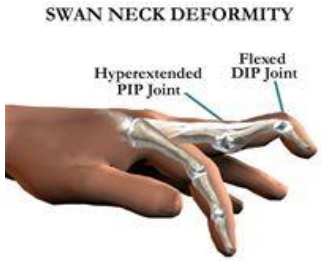
- **Lab Features**
  - **85%** of RA patients have rheumatoid factor (RF) in their serum.
  - Sedimentation rate and C-reactive protein are often elevated in the serum.
  - WBC count in synovial fluid is usually in the "inflammatory" range with high levels of monocytes and lymphocytes.
- **Radiography** may reveal structural damage.
- **Characteristic changes in the hands and wrist:**
  1. **Ulnar drift (aka ulnar deviation)**-RA in the MCP (metacarpophalangeal) joints causes digits to deviate toward the ulna (ulnar side).



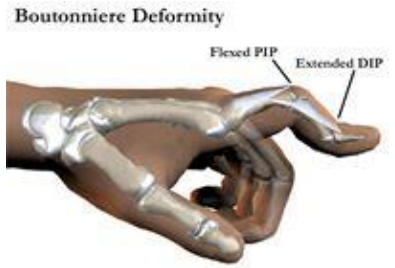
Systemic Disorders of Joint Function

2. **Swan-neck deformity**-hyperextension of the PIP joints with flexion of the MCP and DIP joints due to contractures of muscles and tendons





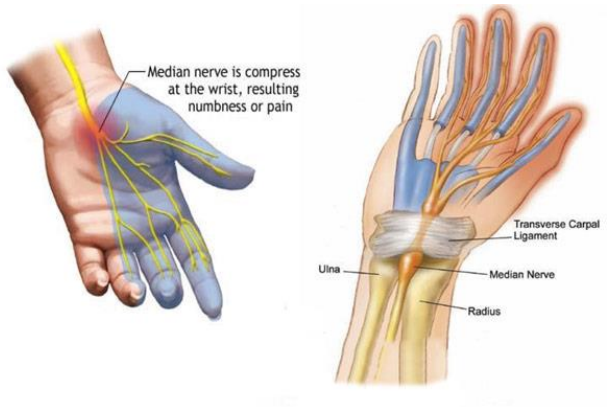
3. **Boutonniere deformity**; flexion of the PIP joints and hyperextension of the DIP joints due to rupture of the extensor tendons over the fingers.



NOTE: DIP joints are not inflammed, but they are flexed/extended due to inflammed and swollen MCP and/or PIP joints.

Systemic Disorders of Joint Function

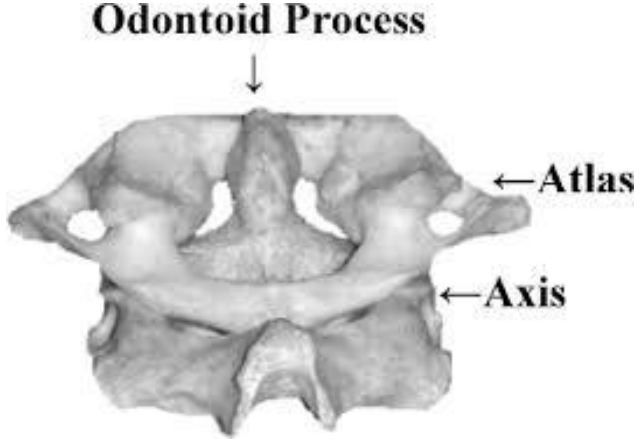
4. Loss of the ability to extend the fingers
5. Proliferation of the synovium in the wrist may cause compression of the median nerve leading to **carpal tunnel syndrome.**



- **Changes to joints other than those in the hand and wrist:**
  1. Flexion contractures and swelling of the **elbow** are common in later stages.
  2. **Shoulder** involvement may occur causing limited movement and pain at palpation of the coracoid process. Dislocation, subluxation, and joint capsule rupture may occur in time.

Systemic Disorders of Joint Function

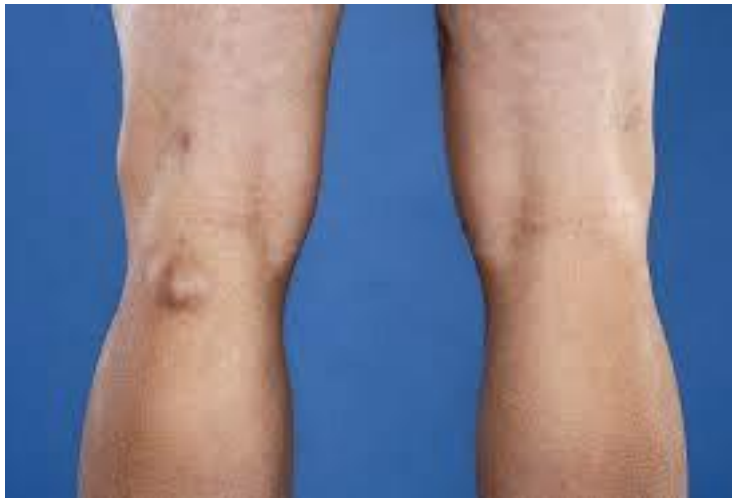
3. Involvement of the **cervical vertebrae** is common. Subluxation of the **atlantoaxial joint** may lead to enlargement of the cervical spinal cord. Laxity in the cervical region may cause compression of the **vertebral arteries** which supply blood to the brain.

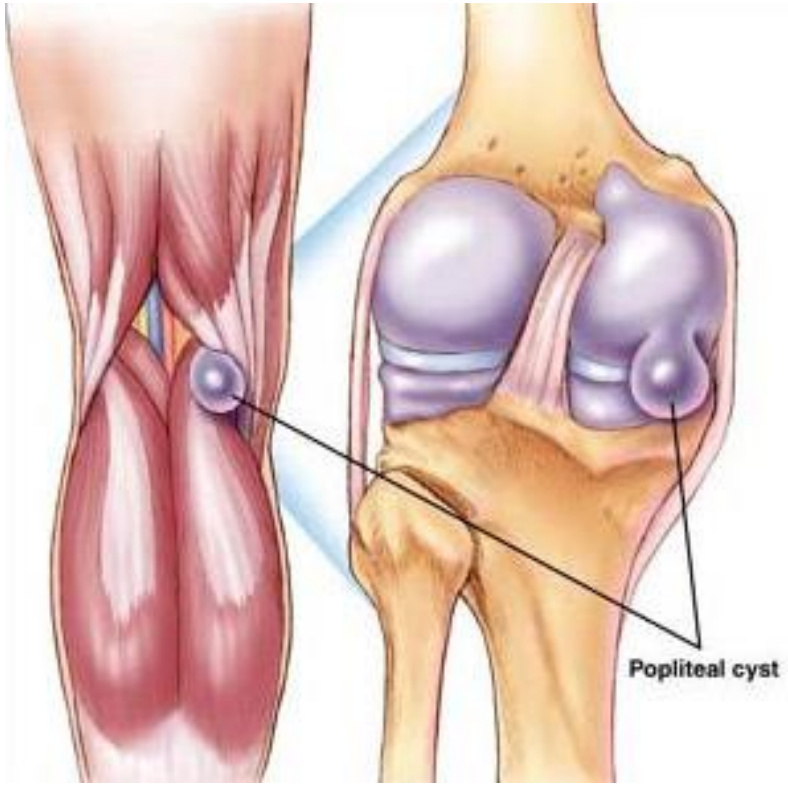


3. RA may affect the hips causing gait disturbances.

Systemic Disorders of Joint Function

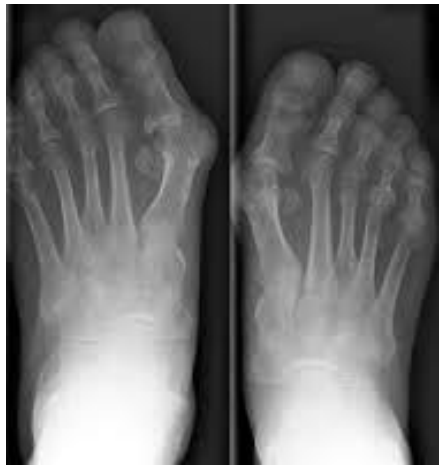
5. **Knee** involvement is usually extensive. Effusion, quadriceps atrophy, contractures, and synovitis of the semimembranosus bursae (**Baker's cyst aka popliteal cyst**) may be noted.

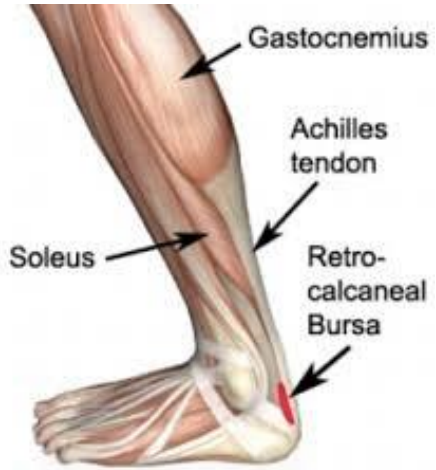


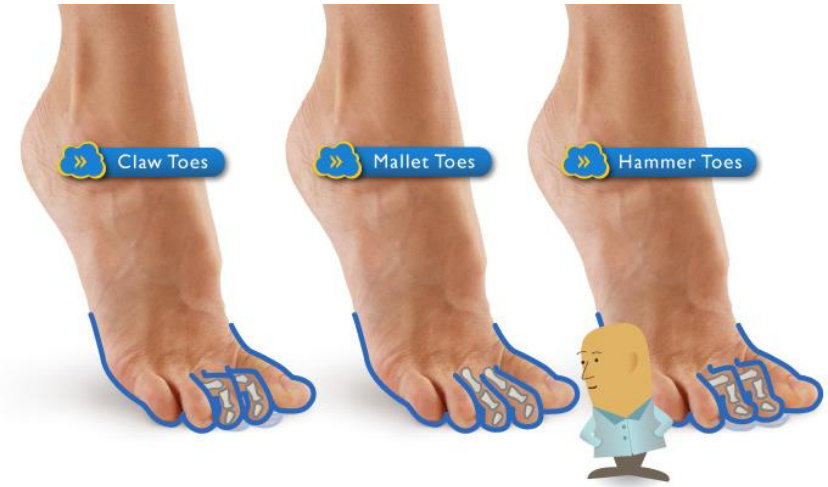


Systemic Disorders of Joint Function

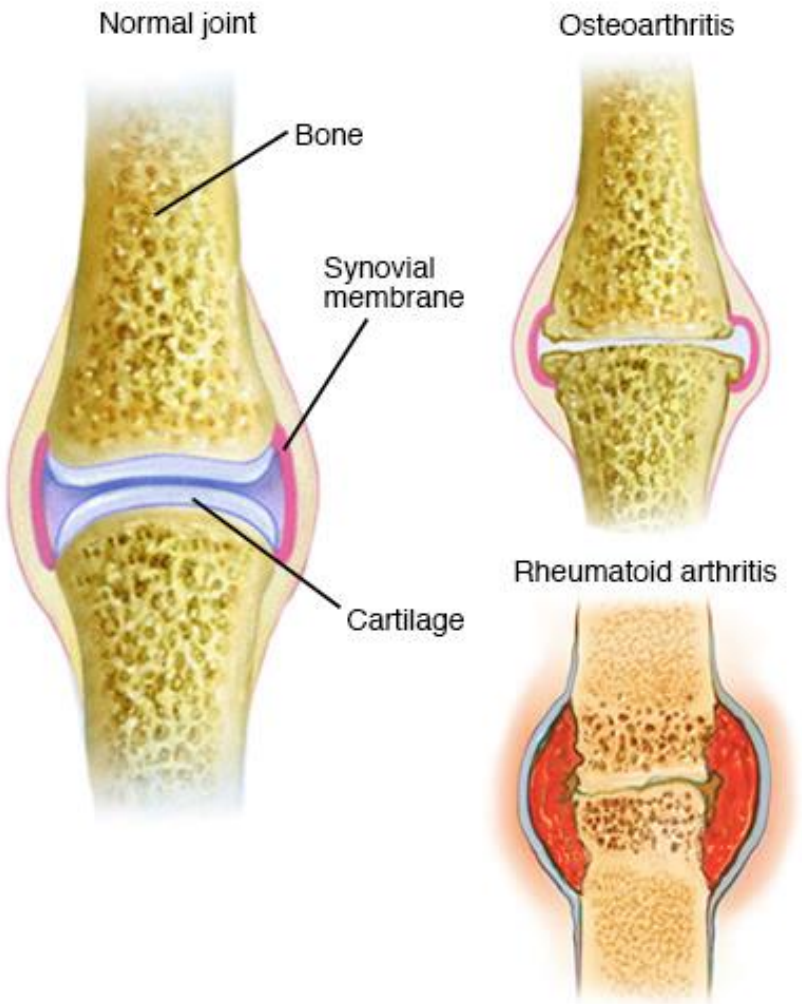
6. Features of the foot include claw toes (DIP, PIP flexion), mallet toes (DIP flexion), hammer toes (PIP flexion, DIP extension), lateral deviation of digits 1-4, and inflammation of the retrocalcaneal bursae.







OA vs RA



Systemic Disorders of Joint Function

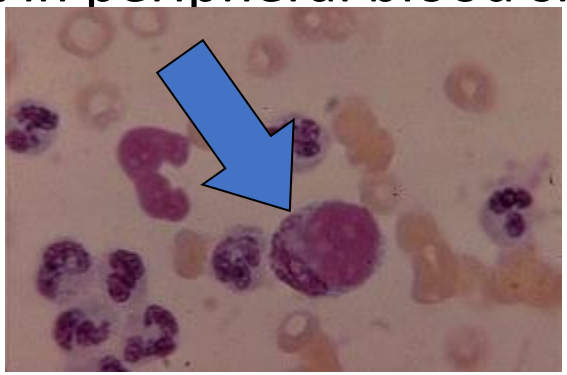
Serum Lupus Erythematosus

- Chronic multi-system inflammatory autoimmune disorder; periods of exacerbation and remission; introduced earlier in the course (integumentary system disorders)
- **Etiology and Pathogenesis**
  - It occurs more often in the US among African-Americans than among Caucasians and yet is uncommon in Africa.
  - It is more common among women with peak incidence between 15 and 40, suggesting **hormone** involvement.
  - Sunlight, thermal burns, and other physical stressors may trigger development.
  - B lymphocytes become overactive leading to excessive antibody production.
  - Antibodies are produced against a myriad of self-molecules located in the **nucleus** of cells (including RNA and DNA).

Systemic Disorders of Joint Function

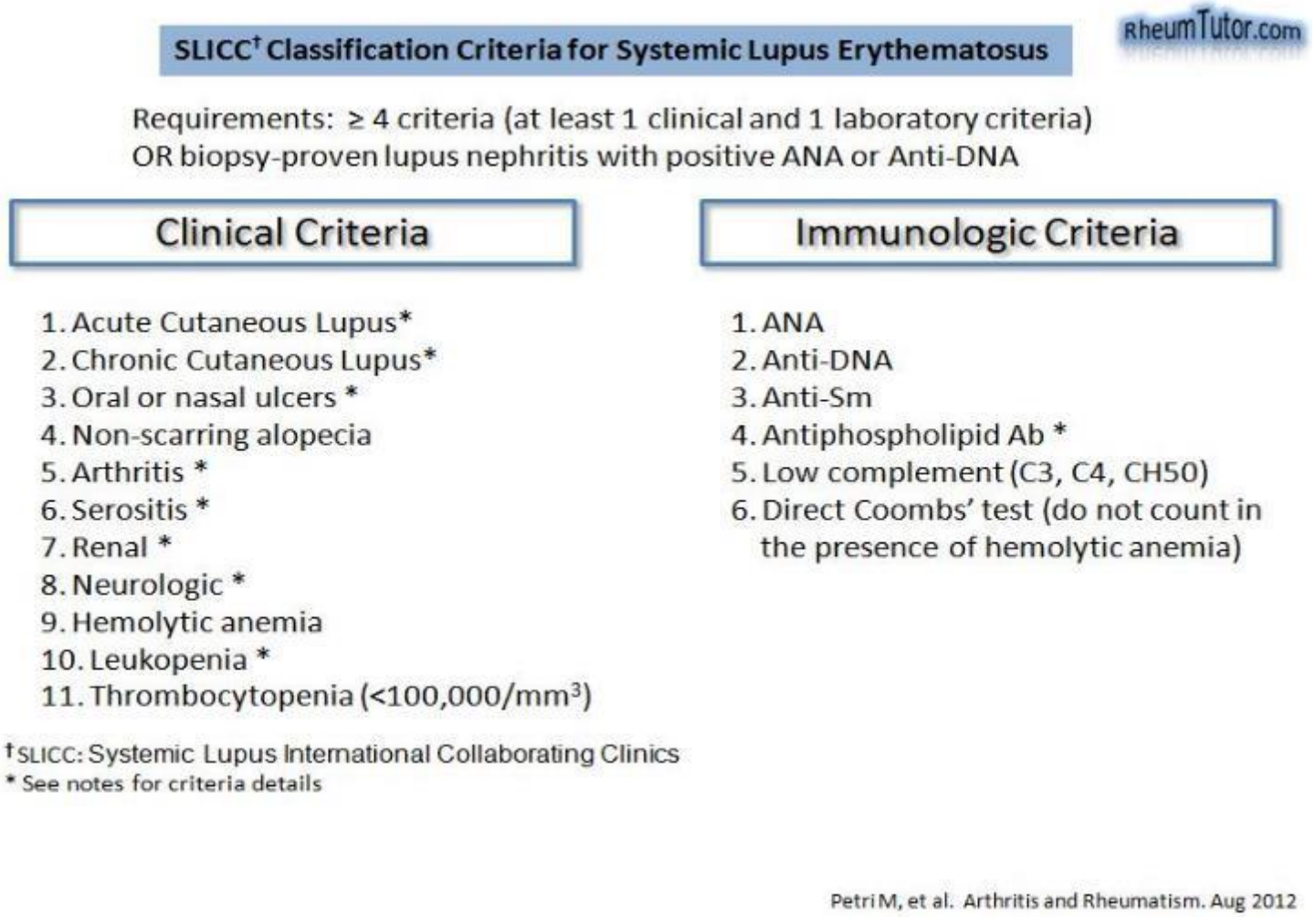
Serum Lupus Erythematosus

- **Anti-nuclear antibodies (ANAs)** are found in the blood of more than 95% of SLE patients.
- Antigen-antibody complexes form and enter the basement membranes of capillaries in the kidneys, heart, skin, brain, and joints **(Type III hypersensitivity)**
- Complement is activated and inflammation is triggered leading to tissue destruction.
- **LE cells (neutrophils that have phagocytosed the damaged nuclei of another cell)** are usually present in peripheral blood smears.



- **Musculoskeletal Effects**
  - Arthralgia and synovitis are common.
  - Deformities may occur, especially in hands and feet.
- **Diagnosis (SLICC Criteria 2012—See next slide.)**

Systemic Disorders of Joint Function



Petri M, et al. Arthritis and Rheumatism. Aug 2012

- NOTE: Anti-Sm=Smith's antibodies. They are directed against proteins in the core of small nuclear ribonucleotide proteins (sn-RNPs).

Systemic Disorders of Joint Function

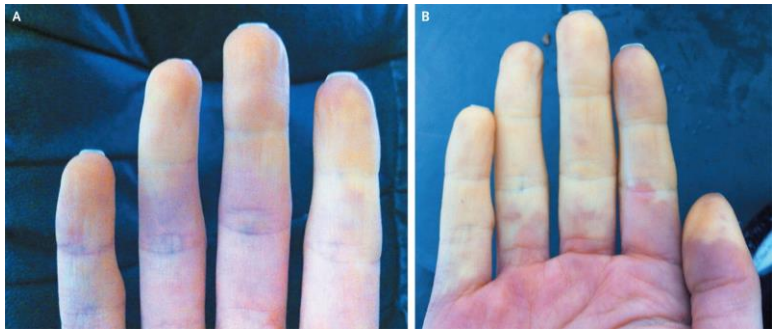
Systemic Scleroderma ("Thick Skin")

- Multi-system inflammatory disease associated with abnormal deposits of collagen in connective tissue and fibrosis
- Affects skin, blood vessels, synovium, skeletal muscle, and internal organ microvasculature
- Women more frequently than men
- **Etiology is unknown.**
- **Clinical Manifestations:**
  - Initially: **Raynaud's phenomenon**-damage to blood vessels causes the digits of the hand to blanche or turn blue in response to cold. Arthritis develops in the hands.
  - Later: **thickening of the skin**, bilateral hand and foot edema; skin edema is replaced by tight, thick skin; folds are lost and skin appears shiny. Thickening of the skin may spread to arms, face, and trunk. Typical changes in facial appearance occur.

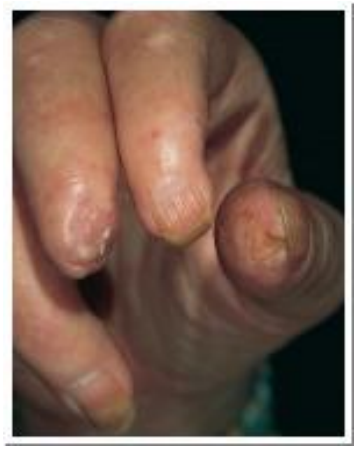
Systemic Disorders of Joint Function

Systemic Scleroderma

Raynaud's Phenomenon



Sclerodactyly



Typically the lips and eyelids recede, the nose becomes less rounded.

Systemic Disorders of Joint Function

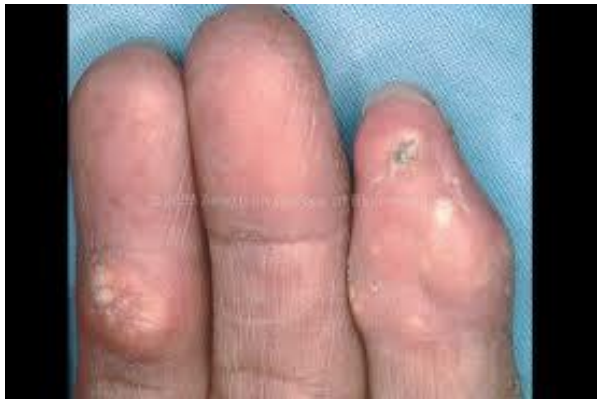
Scleroderma

- Joint and tendon involvement may follow next.
  - **Polyarthritis** of small hand joints is common
  - **Polyarthralgia** (joint pain) in both small and large joints is common
  - Leads to disuse atrophy of skeletal muscles in affected regions
- **Changes in blood vessel walls** cause occlusion of blood flow that affects many organs: lungs, kidneys, GI tract etc.
- **CREST Syndrome** may occur**.** It is associated with pulmonary hypertension and malabsorption in the GI tract, often resulting in death.
  - **Calcinosis-**white, calcium-containing “bumps” that form under the skin of the fingers and other locations
  - **Raynaud phenomenon-see above**
  - **Esophageal dysmotility**-smooth muscle atrophy in the inferior esophagus causes dysphagia (difficult, painful swallowing)
  - **Sclerodactyly-**thickened, tight skin on fingers and/or toes
  - **Telangiectasia** (on face, lips, and fingers)

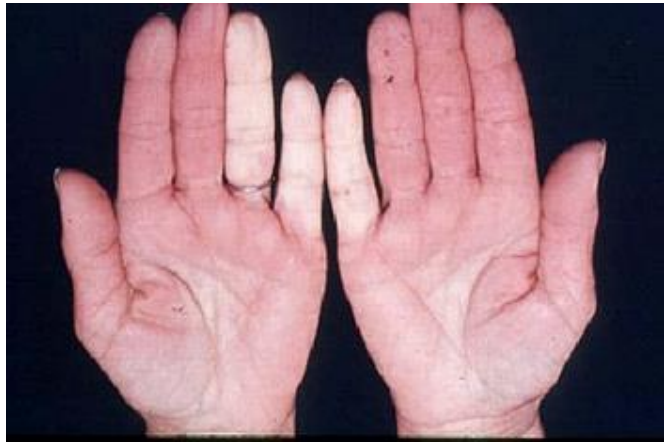
Systemic Disorders of Joint Function

CREST Syndrome of Scleroderma

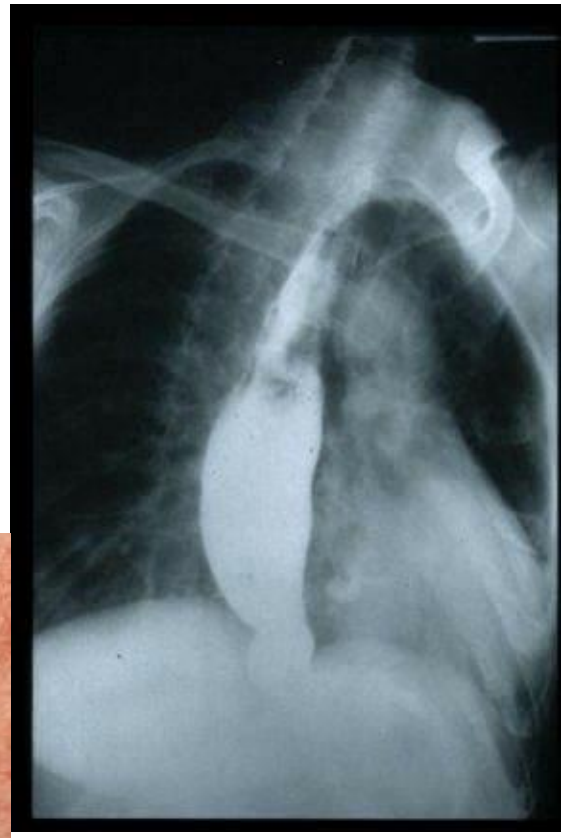
Calcinosis



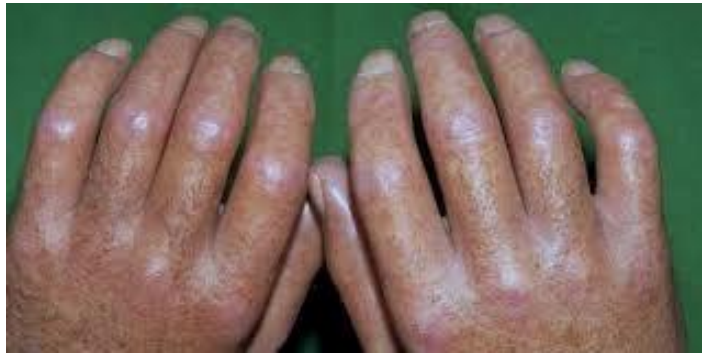
Raynaud's



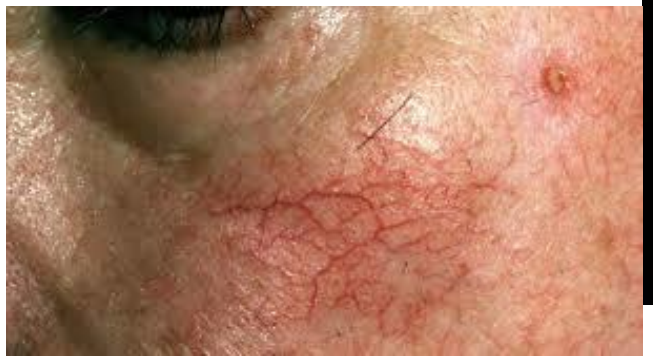
Esophageal Dysmotility



Sclerodactyly



Telangiectasia



Systemic Disorders of Joint Function

Ankylosing Spondylitis

- Fusion (**ankylosis**) of inflamed vertebrae (**spondylitis**) and sacroiliac joints
- **Etiology and Pathogenesis**
  - Arthritis may spread, often to the entire axial skeleton, and sometimes to peripheral joints.
  - Occurs in males more often than females.
  - Begins in teens or 20s.
  - Strong genetic component-**HLA-B27 gene (aka MHC B27 gene)** is present in 95% of cases
  - Antigen presenting cells (APCs) with certain HLA markers may interact with bacterial or environmental factors causing them to cross-react with self-antigens in joint tissues.
  - NOTE: The abbreviation **HLA** stands for **human leukocyte antigen**. The most studied HLA genes are those that code for the MHC I and MHC II self antigen proteins. There are six MHC genes: **HLA-A, HLA-B, HLA-C, HLA-DP, HLA-DQ, and HLA-DR.**

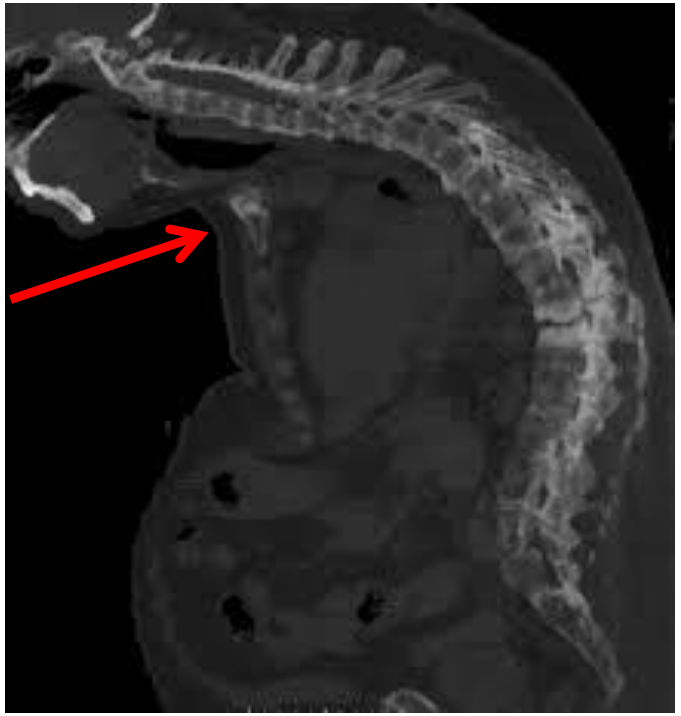
Systemic Disorders of Joint Function

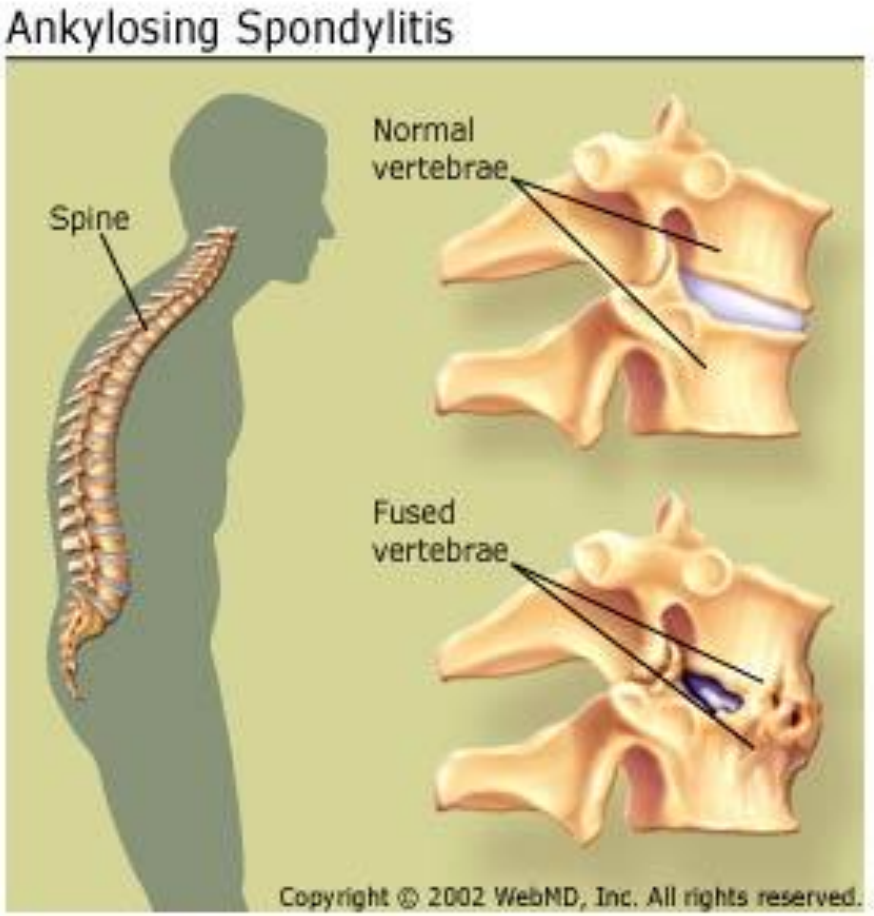
Ankylosing Spondylitis

- **Clinical Manifestations**
  - Low back pain and morning stiffness for more than 3 months.
  - Increased back muscle tone and **loss of lumbar curvature with spinal flexion**; extra stress on the hips and knees leading to joint deformities.
  - Tidal volume (volume of a breath) may be diminished due to compression of the thoracic cavity.
  - Swelling of knees, ankles, and toes may occur with **enthesitis** (inflammation at ligament and tendon attachment sites on bones) especially of the plantar fascia (arch of the foot) and the Achilles tendon.

Systemic Disorders of Joint Function

Ankylosing Spondylitis





Systemic Disorders of Joint Function (Post-Infective)

- Reiter Syndrome (Reactive Arthritis)
- Acute Rheumatic Fever
- Lyme Disease

Systemic Disorders of Joint Function (Post-Infective)

Reiter Syndrome

- **Etiology and Pathogenesis**
  - Genetically susceptible (**HLA-B27 antigen**) individuals are infected with certain bacteria
    - *Chlamydia trachomatis* (usually sexually transmitted) in the **urogenital tract**
    - *Salmonella, Shigella, Yersinia, or Campylobacter* in the **digestive tract**
  - Bacterial antigens persist and immune cells aimed at those antigens cross react with self-antigens to cause inflammation.
  - More common in men than in women
- **Lab Tests**
  - Blood testing may reveal elevated C-reactive protein and sedimentation rate, mild anemia, transient leukocytosis and thrombocytosis.
  - **RF (rheumatoid factor) test** is usually negative.

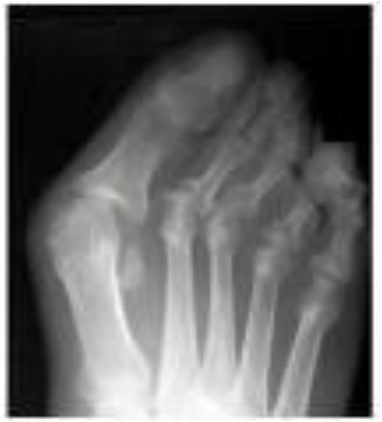
Systemic Disorders of Joint Function (Post-Infective)

- **Clinical Manifestations**
  - **Arthritis** appears 2-6 weeks after the onset of infection
    - Usually in the knees and ankles at onset
  - **Enthesitis**-inflammation at sites where ligaments or tendons attach to bone; especially the **Achilles tendon**
  - **Dactylitis-** swelling of the entire digit (“sausage digit”)
  - **Urinary tract inflammation:** urethritis (urethra), prostatitis (prostate gland) and cystitis (urinary bladder) are not uncommon.
  - **Inflammation of eye structures**: noninfective conjunctivitis (most common), iritis (iris), uveitis (choroid layer), scleritis (sclera), and corneal ulceration characterize eye involvement.
  - **Cutaneous lesions**
    - Small painless ulcers on the urethral meatus.
    - Hyperkeratotic skin lesions (**keratoderma blennorrhagicum**) may occur on the palms and soles.
    - Hyperkeratosis beneath the nails may also occur.
  - **Plantar fasciitis**

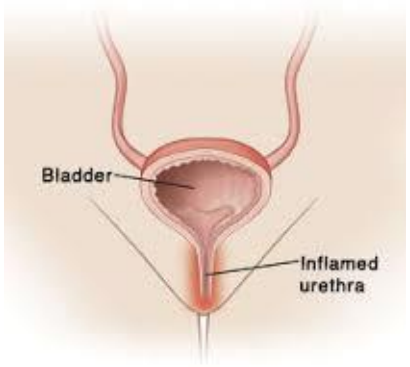
Systemic Disorders of Joint Function (Post-Infective)

Reiter Syndrome

Arthritis



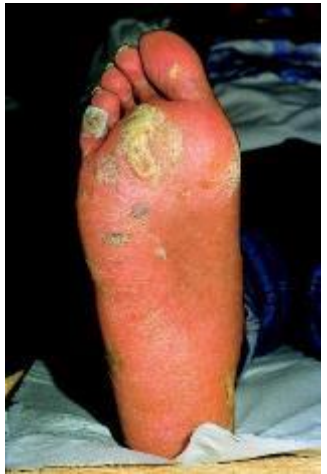
Urethritis

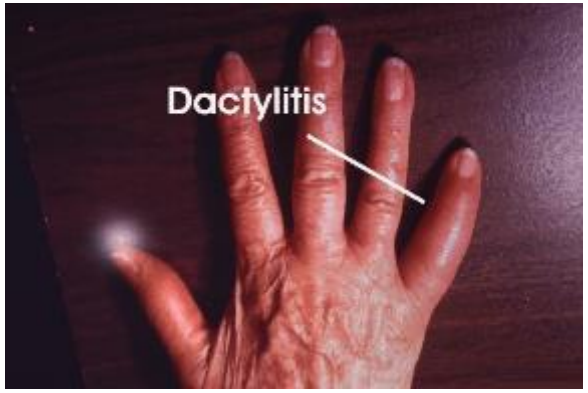


Conjunctivitis

Hyperkeratosis:

Keratoderma blennorrhagicum





Systemic Disorders of Joint Function (Post-Infective)

Acute Rheumatic Fever

- Inflammatory disorder that follows a **beta-hemolytic group A streptococcal pharyngeal infection (strep throat)**
- **Etiology**
  - Possibly antigen cross-reactivity: Immune cells directed against strep antigens cross-react with proteins in target structures (joints, heart, skin, nervous system)
- **Clinical Manifestations** dependent on age of individual; peak incidence in children and young adults, 5-20 years old
  - **Children**
    - **Polyarthritis** with severe pain – synovial effusion, inflammation, erythema in knees, ankles, elbows and shoulders; may include hips, wrists and small joints in hands and feet
    - **Carditis is common.**
    - 20% have a **rash** on proximal extremities and trunk
  - **Adults:** Polyarthritis, but **carditis is rare.**

Systemic Disorders of Joint Function (Post-Infective)

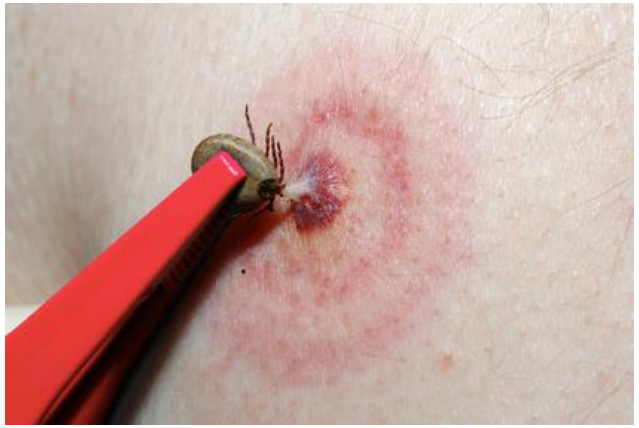
Lyme Disease

- Complex disease caused by a spirochete (***Borrelia burgdorferi***) carried by deer ticks and other **tick** species
- Lesion (tick bite) may expand and become quite red. It is warm to the touch but not painful. Bite area assumes a typical "bullseye" appearance.
- Tick bite may be accompanied by severe headache, stiff neck, fever, chills, myalgia, arthralgia, malaise, and fatigue.
- **Etiology**
  - Theoretically, persistent antigenic fragments of dead or inactivated bacteria trigger an inflammatory response.

Systemic Disorders of Joint Function (Post-Infective)

Lyme Disease

- **Clinical Manifestations:**
  - **Stage I**: single or multiple papules with surrounding rash that clears in between the bite and periphery to form a **"bullseye" pattern**; may be accompanied by flu-like symptoms
  - **Stage II**: occurs weeks or months later if the patient remains untreated; meningitis; peripheral neuropathy; cranial nerve palsies, and possible cardiac involvement
  - **Stage III**: months or even years after infection: oligoarthritis, muscle weakness
- **Treatment:** antibiotics



Secondary Joint Dysfunction

- Psoriatic Arthritis (PA)-already covered
  - Psoriasis
- Enteropathic Arthritis-Patho II topic
  - Inflammatory Bowel Disease
    - Crohn's Disease
    - Ulcerative Colitis
- Neuropathic (Charcot Joint)-covered later in this course
  - Diabetes mellitus
  - Syphilis in the spinal cord
  - Syringomelia (spinal cord disease)
- Hemophilic Arthropathy-already covered
  - Hemophilia A or B
- **Gout-covered here**

Secondary Joint Dysfunction

Gout

- Disturbance of **uric acid** metabolism. Uric acid (urate) is a product of purine (adenine and guanine, the bases found in nucleic acids) metabolism and is usually kept at normal levels by excretion in the urine. When purines are catabolized they are converted to either **xanthine or hypoxanthine**, and both of those molecules are converted to uric acid in a reaction catalyzed by **xanthine oxidase**.
- Deposit of monosodium urate salts in articular, periarticular and subcutaneous tissue occur when serum uric acid is high.
- Most common in middle-aged men and postmenopausal women
- **Clinical Manifestations (Four Phases)**
  1. **Asymptomatic hyperuricemia-elevated** serum urate; no symptoms
  2. **Acute gouty arthritis**
     - Joints are warm, red, and tender. The MTP (metatarsal phalangeal) joint of the **great toe** is most often involved. The first attack is often sudden with intense pain that wakes the patient from a sound sleep.
     - Urate crystals are found in synovial fluid.

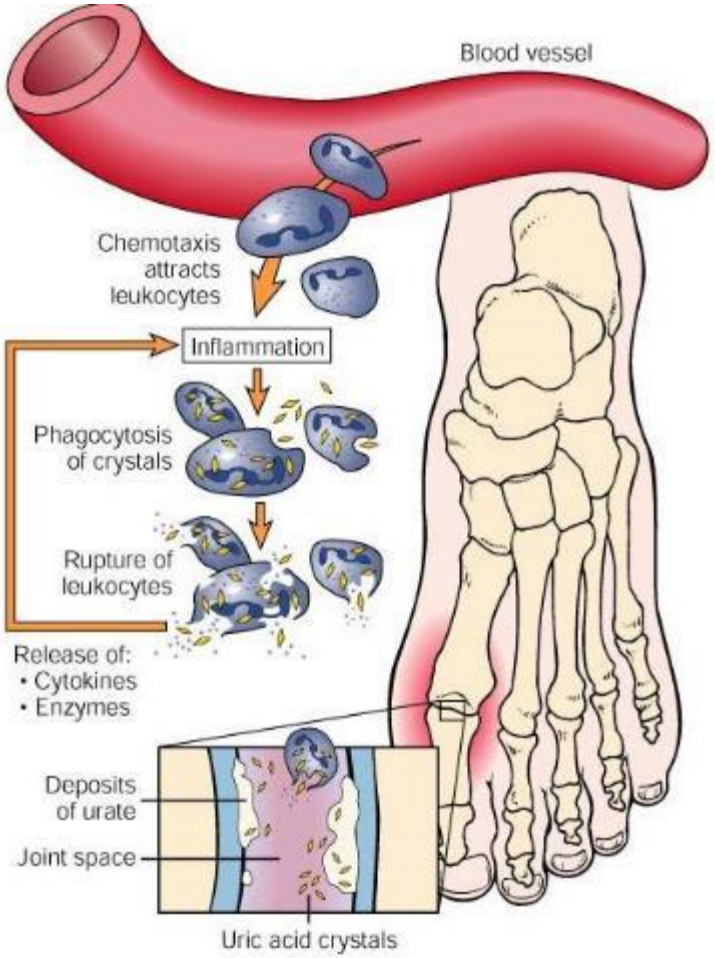
Secondary Joint Dysfunction

3. **Intercritical gout**
    - The period between attacks
    - Urate crystals can still be aspirated from joint cavities.
4. **Chronic tophaceous gout**
    - **Tophi (large urate crystal deposits)** begin to appear about **10 years** after onset of gout.
    - They occur under the skin, in the synovium, subchondral bone, olecranon bursae, infrapatellar and Achilles tendons causing joint deformity.
    - Tophi also occur in the aorta, heart valves, ear cartilage, cornea, sclera, and kidneys.

- **Treatment**
    - **Allopurinol,** an inhibitor of the enzyme, **xanthine oxidase,** is a medication that reduces serum urate.
    - A diet containing fewer purines. Alcoholic beverages, red meat, certain fish and shell fish are major sources of purines.

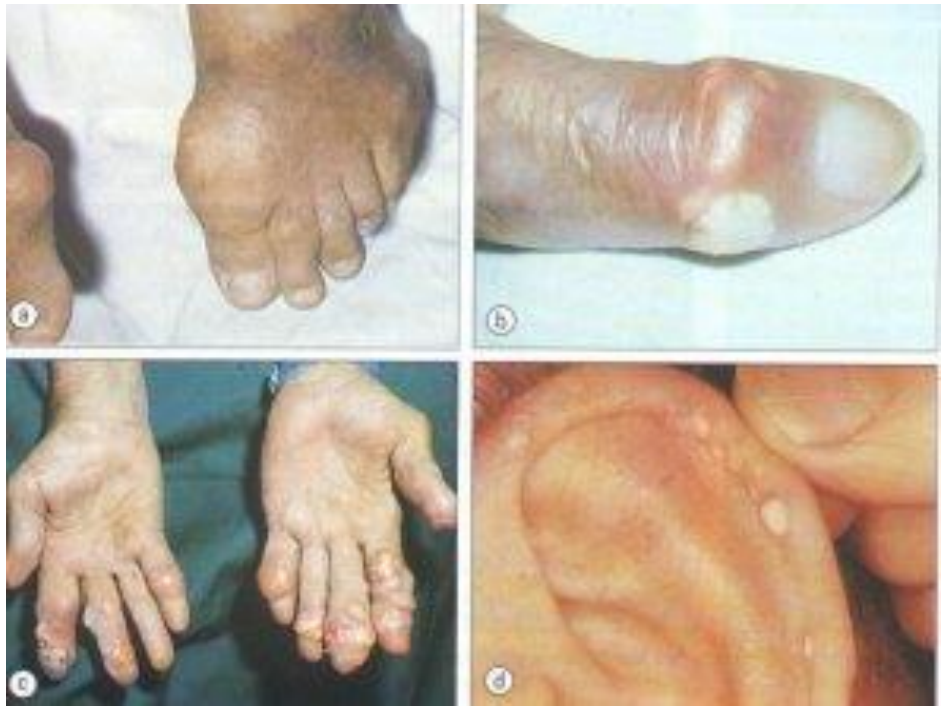
Secondary Joint Dysfunction

Gout



From Damjanov I: Pathology for the health-related professions, ed 2, Philadelphia, 2000, Saunders, p 459.

Tophi



RF-Negative Polyarthritis

Adult Onset Still Disease

- Rare systemic inflammatory disease that includes **RF-negative polyarthritis;** etiology unknown.
- **Clinical Manifestations:**
  - Persistent **high fever** for at least one week
  - **No gender preference**
  - Distinctive **salmon-colored rash** on the trunk and extremities while febrile
  - Possible sore throat
  - Polyarthritis (**more than 5 joints** affected) usually in PIP and MCP joints, also wrist, knees, hips, and shoulders for at least two weeks
  - Fusion of CM (carpometacarpal) and IC (intercarpal) joints is seen.
  - Visceral involvement: hepatic insufficiency, respiratory failure, cardiac tamponade, CHF, splenomegaly
- **Lab features**
  - Anemia, leukocytosis, elevated sedimentation rate, thrombocytosis, elevated liver enzymes
  - RF-negative

RF-Negative Polyarthritis

Juvenile Rheumatoid Arthritis (JRA) aka Juvenile Idiopathic Arthritis (JIA)

- Chronic, inflammatory childhood disease
- Early diagnosis is important to prevent growth retardation.
- Usually RF-negative
- **Clinical Manifestations (3 possible onsets)**

1. Systemic Onset (Still Disease)

- The average onset is 1-6 years; occurs in 2-17% of JRA patients (least common form); **no gender preference**
- **Spiking high fevers, salmon-colored rash**
- Anemia, leukocytosis, and thrombocytosis occur.
- Pericardial and pleural effusions are common.
- Lymphadenopathy and hepatosplenomegaly are common.
- Polyarthritis occurs in weeks to months and may persist at a severe level

2. Polyarticular Onset

- Involves 5 or more joints **including hip joints**, occurs in 10-28% of JRA patients
- Peak occurrence between 8-16 years.
- **Females** more often than **males by 3:1 ratio**
- Lacks the severe symptoms of the systemic onset
- Malaise, growth retardation, weight loss, low grade fever, adenopathy, anemia, organomegaly may occur.

RF-Negative Polyarthritis

3. **Pauciarticular (Oligoarthritis) Onset**
   - Involves **4 or fewer joints, hip joints not involved**
   - **Females** more often than males
   - Peak incidence is before age 3.
   - About 50% of cases are this type (the most common form of JRA)

QUIZ 6AB

- COMPLETE QUIZ 6AB.
- THEN GO ON TO MODULE 6CD PPT.