Pathophysiology I

Week 6
Seronegative Spondyloarthropathies

- Spondyloarthropathies: a group of multi-system inflammatory disorders that affect the axial skeleton, mostly the spine
- Usually begins at sites of tendon/ligament insertions
- Rheumatoid factor is negative
- Associated with HLA-B27
Seronegative Spondyloarthropathies

• Ankylosing Spondylitis
• Reactive arthritis
• Enteropathic arthritis (inflammatory bowel disease)
• Psoriatic arthritis
Ankylosing Spondylitis

- Chronic systemic inflammatory disease of axial skeleton with pain and progressive stiffness of the spine
- Begins in late adolescence or early adulthood
- More common in men
- More severe and faster progression in men
- 90% of those with AS have HLA-B27 antigen

Variable in progression. Some of that depends on medication/treatment. Definitely more common in men.
Ankylosing Spondylitis

- Inflammatory erosion where tendons and ligaments attach onto bone (Important characteristic of this disease.)
- Starts in sacroiliac joint and moves to posterior spine
- Destruction of small joints within the spine resulting in posterior fusion of spine that ascends
- Squared vertebrae as one vertebral body fuses to another with bamboo-like appearance on x-ray
- Large synovial joints can be involved, but not small peripheral joints (shouders, hips, knees yes; more distal joints no.)
Ankylosing Spondylitis

• Symptoms:
  – Low back pain, worse with rest
  – Pain in buttocks and hips, possibly thighs
  – Stiffness in morning and after rest
  – Muscle spasms
  – *loss of motion of the spine with loss of lumbar lordosis with kyphosis of thoracic spine
  – End result is a spine fused in flexion
Ankylosing Spondylitis

Severe kyphosis

Loss of lumbar lordosis

Patient before and after surgery.

http://www.espine.com/ankylosing-insets/pre-post.gif
Bamboo Spine
Ankylosing Spondylitis

Normal Spine

http://cdn.channel.aol.com/body/hv/102322

brighamrad.harvard.edu/.../X-raySpineLat.GIF
Ankylosing Spondylitis

• Complications:
  – Constriction of chest cavity with restriction of heart and lungs
    loss of lung volume, lowered O2 levels, more chance of pneumonia. Worse for overweight folks. CPAP machine to push oxygen with pressure to lungs helps.
  – Abnormal weight bearing leads to osteoarthritis of hips, knees, shoulders
    Because body mechanics have changed, more pressure wherever the weight is hanging due to the spinal fusion and changes in posture.
    Hip involvement is common and the most disabling
  – Anterior uveitis is most common extraskeletal problem (25-30% of patients)
    Uveitis is an inflammatory eye disorder - probably an autoimmune antibody process
  – Weight loss, fever
  – Fatigue
Ankylosing Spondylitis

- Diagnosed by history, physical exam of spinal range of motion and sacroiliac joints, x-rays
- Elevated ESR
- Mild anemia possible
- HLA typing is not diagnostic
- Treated with proper posture, exercise, weight maintenance
- NSAIDs and sometimes anti-rheumatic drugs
Reactive Arthropathies

- Include Reiter’s syndrome and enteropathic arthropathies
- Usually triggered by an infectious agent which could be urinary, intestinal, respiratory (Chlamydia pneumonialae, Pseudomonas, Salmonella, Shigella, Yersinia, Campylobacter, Streptococcus)
- Can occur in patients with AIDS
Reiter’s Syndrome

• Reactive arthritis along with extraarticular symptoms such as uveitis, bowel inflammation and carditis

• Patients are genetically susceptible (HLA B-27)

• Triggered by infection:
  – *Chlamydial* infection of genitourinary tract
  – *Salmonella, Shigella, Yersinia* or *Campylobacter* in GI tract

• Treat with immune suppressants
**Enteropathic Arthritis**

- Associated with inflammatory bowel disease (ulcerative colitis, Crohn’s disease)

  Don't confuse IBD with IBS - IBS is irritable bowel syndrome and is very different from IBD. IBS = alt constip and diarrhea, gas, bloating, often stress related and is a disconnect between muscles and nerves....except in TCM where it is probably Spleen Qi deficiency...but forget about that for now!

- Severity of arthritis does not necessarily correlated to severity of bowel disease

  Ulcerative colitis affects just the colon. Crohn's can be anywhere in the GI tract from mouth all the way down.

  Treat Enteropathic Arthritis by treating the underlying bowel disease.
Psoriatic Arthritis

- Seronegative arthritis
- Occurs in 5-7% of psoriasis patients
- Can present like a spondyloarthropathy or like rheumatoid arthritis
- Exact etiology unknown
- Diagnosis requires presence of skin or nail changes of psoriasis
- Usually progresses slowly
- Can have elevation in uric acid (as in gout)
- Treatment is similar to rheumatoid arthritis

more on that later...
Psoriasis

hyperkeratotic plaques. Can be seen in extensor surfaces as seen here, but can be anywhere.

Also flakey, dry pitting in the nails.

www.lib.uiowa.edu/.../dermnet/psoriasis_02ar.jpg
Psoriatic Arthritis

The bones are rough above. Should be nice and smooth. Those spikey things coming off of the distal phalanges are not how they should look!
Osteoarthritis

• A.K.A. degenerative joint disease (DJD)
• The leading cause of disability in the elderly
• Can be primary or secondary (due to joint defects, trauma, metabolic disorders or inflammatory diseases)
• Can be local or generalized
Osteoarthritis

• Characterized by:
  – Loss of cartilage
  – Synovitis *inflammation of the synovium*

• Results from inflammation caused by the cartilage trying to repair itself

• Symptoms:
  – Joint pain
  – Stiffness
  – Limited range of motion
  – Possible instability and deformity
Osteoarthritis

• Men are affected at an earlier age but by middle age, more women are affected

• OA of the DIP joint in the hand is hereditary

• Obesity is a risk factor for knee OA and weight loss reduces the risk of symptoms
Pathogenesis of OA

- Articular cartilage and synovial fluid provide a smooth surface and low friction during joint movement
- Forces are transmitted down to the subchondral bone which absorbs energy
- Cartilage components: chondrocytes, extracellular matrix (water, proteoglycans, collagen and ground substance)
- Proteoglycans provide stiffness and elasticity
- Ground substance is a highly hydrated gel
Pathogenesis of OA

• Articular cartilage undergoes constant turnover—chondrocytes replace worn-out matrix

• Early in disease, cartilage has more water and less proteoglycans

• Weakening of collagen due to decreased synthesis and increased breakdown

• Release of cytokines that degrade cartilage

• Chondrocytes reorganized

• Edema of matrix due to inflammation response
Pathogenesis of OA

• Smooth articular surface becomes rough
• Cracks form in cartilage and gradually widen and can extend to subchondral bone
• Areas of cartilage can completely erode away
• Subchondral bone becomes thickened
• Pieces of bone and cartilage form loose bodies
• New bone formation is sclerotic and less shock-absorbing
• Osteophytes: abnormal bony outgrowths
Clinical Manifestations of OA

- Pain
- Crepitus/grinding
- Limited range of motion & instability
- Joint feels hard and enlarged
- Most affected joints: hips, knees, lumbar & cervical vertebrae, PIP/DIP hand joints, 1st MTPs of feet
- Can be mono or polyarticular
- Secondary joints may be affected due to shift in forces while trying to protect affected joints
Osteoarthritis

http://www.4-arthritis-info.com/images/Osteoarthritis_image.jpg
Osteoarthritis

• Diagnosed by history and physical exam findings, x-ray, exclusion of other diseases by labs

• Labs typically normal, ESR may be slightly elevated, but not as high as in untreated RA

Elderly patients will probably have an elevated ESR (elevated sedimentation rate)
Knee Osteoarthritis

Figure 1

Figure 2

Narrowing of medial usually happens fri since our mechanic weight to the medi

Gotta Xray pt sta
Treatment of Osteoarthritis

- Rehab to strengthen opposing muscle groups that cushion weight bearing
  Offloads some of the weight and evens out the force. Especially important for knees.
- Resting affected joint
- Splints
- Heat and cold
- Weight reduction
- Proper body mechanics
  Especially for lumbar spine and neck.
- Oral acetaminophen is initial treatment, NSAIDs
- Intraarticular corticosteroid injections
- Viscosupplementation by injection
  Especially for knees. Synthetic synovial fluid injected to replace the joint fluid. Puts off joint replacements, but then you
- Surgery: debridement, loose body removal, replacement
Tylenol is currently preferred in the stomach.
Knee and Hip Replacements

http://www.boiseorthoclinic.com/BOC%20Images/JointAfter.jpg

upload.wikimedia.org/wikipedia/commons/thumb/...
Gout

- Deposition of monosodium urate or uric acid crystals in joints
- Pseudogout (chondrocalcinosis) is the deposition of calcium pyrophosphate dihydrate crystals
- Gout can be acute or recurrent
- Primary gout (90% of cases) mostly occurs in men, peaking in 4th-6th decades, is hereditary
- Secondary gout results from another primary disorder like cancer. bummer.
Gout

• Pathogenesis: elevated uric acid levels
• Uric acid results from purine metabolism—overproduction, increased breakdown, or decreased urinary excretion
• Primary gout is most likely due to an enzyme deficiency that causes a combination of overproduction and inadequate elimination
• Secondary gout often results from increased cell turnover (tumor lysis during treatment)
Gout

• Attacks occur when crystals precipitate into the joint and cause inflammation

• Often happen in peripheral joints where temperatures are cooler (classic site is great toe)

• Repeated attacks cause chronic arthritis and formation of tophi-large hard nodules
  – Chronic tophaceous gout-often polyarticular

  Usually only affect one joint...

  Temps cooler, crystals come out of the fluids.

  Mostly on fingers and toes – uric acid crystals. Comes with time.
Gout

- Attacks usually monoarticular
- 1st MTP, tarsal joints, insteps, ankles, heels, knees, wrists, fingers, elbows
- Often at night, severe pain
- Triggers: excessive exercise, medications, food, alcohol, diet
- Redness, swelling
- Lasts days to weeks

Over time causes joint destruction and chronic arthritis.

Classic one is in the big toe. 1st MTP in the periphery.

All in the periphery. Toe hurts so bad that even the sheet resting on it hurts.

Meds: diuretics, especially.

Gout comes in "attacks" often depending on intake. Eliminating meat (protein from other sources), diet, alcohol intake.
Gout

- Diagnosed by history, physical
- Hyperuricemia (but many people have this and do not have gout)
- Synovial fluid analysis is gold standard test
- Measure 24 hour urine urate excretion
- Treat with NSAIDs, uric acid lowering medications like colchicine and allopurinol

Problem: gout can affect the kidney and so do the high does anti-inflammatories. Can also take oral steroids which help a lot. Colchicine taken during a gout attack every 2 hours, can fix over the course a day or so. Allopurinol is a daily treatment for people with chronic regular attacks.
Acute Gout and Crystals

Really needs a pedicure! -->

Vegetarian! -->

Acute gout with erythema (redness) of the great toe joint.

Synovial fluid analysis - Monosodium urate crystals, the cause of gout, as seen under a microscope.

Gout won't have a distinct border for the redness and may not even have swelling. With infection you will see a distinct border.

www.myfootshop.com/.../ortho/gout_labeled.jpg
Juvenile Rheumatoid Arthritis (JRA)

• Juvenile form occurs younger than age 16
• 10% will have systemic symptoms: high fever, rash, lymphadenopathy, hepatosplenomegaly, leukocytosis, anemia
  – Infection, heart disease, adrenal insufficiency can be fatal
• 50% have pauciarticular arthritis (no more than 4 joints affected)
• 40% have polyarticular disease (5 or more joints affected)
Juvenile Arthropathies

• SLE is similar in children, the extent of renal involvement determines the prognosis

• Juvenile dermatomyositis causes similar symptoms as in adults, along with generalized vasculitis and calcifications over pressure points

• Other spondyloarthropathies can also occur in children, more common with HLA-B27 subtypes
Rheumatic Disease of Elderly

- Older patients do not cope as well and may be harder to diagnose due to increased production of autoantibodies.
- Seronegative RA in elderly is usually relatively mild.
- SLE may be more often drug-induced.
- OA is most common.
- Gout may be induced by diuretic medications used for hypertension.
- Pseudogout more common in elderly.
- Bursitis, tendinitis are very common localized inflammatory conditions.
Rheumatic Diseases of Elderly

- Polymyalgia Rheumatica (PMR)
  - Inflammatory condition causing aching and morning stiffness in neck, shoulders and pelvis
  - Women at higher risk
  - Usually occurs after age 60
  - Onset can be abrupt
  - Diagnosis: pain/stiffness > 1 month, elevated ESR
  - Symptoms resolve with prednisone, dose is tapered over 1 ½ - 2 years
  - Some may have giant cell arteritis, treatment important to avoid blindness

- Giant cell arteritis can cause temporal arteritis (infarcts in temple leading to the eye, causing blindness).

PMR affects muscle/blood vessel/fascia, not so much bones actually.
Chapter 61

ALTERATIONS IN SKIN FUNCTION AND INTEGRITY
Skin

- Skin diseases may be caused by:
  - Sunlight
  - Insects
  - Infection
  - Chemicals
  - Physical agents
  - Systemic disease

- Appearance can be influenced by skin tone, scratching, infection or treatment so can be hard to diagnose.
Skin Terms

• See Figure 61-1
• Flat lesions: macule, patch
  - like a birthmark.
  - Can't feel the flat ones.
• Solid palpable lesions: papule, plaque, nodule, tumor, wheal
  - small, in skin
  - remember psoriasis
  - firm bump under
  - like a hive
• Elevated fluid-filled lesions: vesicle, bulla, pustule
  - vesicle and bullae are filled w/ clear fluids
  - pustules are full of...well, pus.

--hive
Skin Terms

- **Rash**: a temporary eruption of the skin
- **Lesion**: a traumatic or pathologic loss of normal tissue continuity, structure, or function of other types.
- **Described by size and features**: blanching, erythema, hemorrhagic or purpuric, pigmentation
- **Lichenification**: thickened and rough skin due to repeat scratching
- **Excoriation**: raw, broken skin
Lichenification and Purpura

Henoch-Schönlein Purpura

Elderly people looking for a rest with much purple border

missinglink.ucsf.edu/.../Lichenification-101.jpg

www.nlm.nih.gov/.../ency/fullsize/19834.jpg
Skin Terms

• Blister: a vesicle, fluid-filled papule caused by disruption of the layers of skin
  – Due to friction or bullous skin disorders
• Callus: hyperkeratotic plaque due to chronic pressure or friction that causes hyperplasia of dead keratinized cells
• Corn: small, well-circumscribed areas of hyperkeratosis
Skin Terms

• Pruritus: itching
  – Occurs with many skin disorders as well as chronic kidney disease, biliary disease
  – Can be triggered by warmth, touch, vibration
  – Histamine, bradykinin, substance P, bile salts, prostaglandins
  – Scratching is a reflex response but usually does not relieve itching
Skin Terms

- Xerosis: dry skin
- Dehydration of the stratum corneum
- Decreased moisture and sebaceous gland secretions in elderly increase dryness
- Often pruritic, rough, scaly, cracked, wrinkled
Dark Skin Variations

• Darker skin is the result of more melanin pigment in skin
• Protects against skin cancer and wrinkles
• More prone to color variation: hypopigmentaion (vitiligo) or hyperpigmentation (keloids)
Effects of UV Radiation

- UV accounts for 5% of solar radiation
- UVB rays responsible for most skin effects
- UVA rays pass through glass, not as potent but can still cause same effects as UVB
- Melanocytes increase their melanin content in response to UV rays

And that's why you get a tan. And when something is producing more and more you are more at risk for cancer. And that's why those tanners tend toward skin cancer.
Effects of UV Radiation

• Sunburn: excessive exposure of the dermal and epidermal layers
  – Severe burns may require hospitalization and can cause weakness, chills, fever, malaise, pain, blistering

• Drug-induced photosensitivity: produce an exaggerated response to UV
  – Antibiotics: sulfa, tetracycline
  – Antihistamines: benadryl
  – Antipsychotics, diuretics, hypoglycemics, NSAIDs
Effects of UV Radiation

• Sunscreen: absorbents work in UVB range, reflectants work on all rays (PABA)  
  <--better! PABA is a reflectant.

• Apply 30 minutes before exposure and reapply every 2 hours  
  <--minimum..but should probably be more frequent esp if swimming, sweating, mudwrestling.

• Most skin cancers are correlated with childhood sunburns (number and severity)  
  <--oh crap. multiple severe sunburns are the high risk

• SPF: sun protection factor
  – The amount of UV rays needed to produce a mild sunburn in protected vs unprotected skin  
  – Very little increase in protection over SPF 15  
  Past 15 you don't get much more protection. Just the best deal.
Effects of UV Radiation

• Prolonged sun exposure with sunscreens can still increase risk of skin cancers

• Also important:
  – Clothing that is sun protective
  – Hats with wide brims
  – Eyeglasses that block UV
  – Sunscreen with minimal SPF of 15
  – Shade in midday

• It is possible to burn on a cloudy day, in water and sitting under an umbrella on sand
Review

• Seronegative spondyloarthropathies
  — HLA-B27

• Characteristics of ankylosing spondylitis (spine changes/appearance), Reiters, psoriatic arthritis, enteropathic arthritis including potential causes, complications, begin at tendon/ligament insertions

• OA: all, especially what joints, symptoms and pathogenesis
Review

- Gout: what joints, lab tests, pathogenesis, tophi
- Differences in juvenile and elderly forms of rheumatic diseases
- Know skin terms
- Classes of medications that can cause photosensitivity
- Skin protection with SPF of at least 15 as well as clothing, etc.