Overview of Today’s Review
(At least that which can be covered in one hour)

- Inflammatory Arthropathies and Autoimmune Diseases
  - Rheumatoid Arthritis
  - Systemic Lupus Erythematosus
  - Seronegative Spondyloarthritis
- Non-Inflammatory Arthritis
- Crystalline-Induced Arthritis
  - Gout
  - CPPD

Overview of Today’s Review:
Lack of time to cover (Extra slides at end)

- Vasculitis (Covered only briefly)
- Viral and Septic Arthritis
- Scleroderma
- Inflammatory Myopathies

Case #1: Early Arthritis

- A 35 year old woman reports 6 weeks of morning stiffness in bilateral wrists, metacarpal phalangeal joints, and feet that lasts for 2 hours each morning and is worse with inactivity.
- In evaluating the arthritis, her primary care doctor notes that she has swelling in her hands and wrists, an elevated erythrocyte sedimentation rate and C-reactive protein, and X-rays of her hands that demonstrate peri-articular osteopenia but no joint space narrowing or erosions.
- Rheumatoid factor and anti-CCP antibody results are pending.
Case #1: Early Arthritis

For this patient, which of the following laboratory tests would have the best predictive value for rheumatoid arthritis?

A. Elevated erythrocyte Sedimentation Rate
B. Anti-CCP Antibodies
C. Rheumatoid Factor
D. Elevated C-Reactive Protein

Rheumatoid Arthritis

- RA is 2nd most common form of chronic arthritis (behind osteoarthritis)
- Has a prevalence of 1% in US adults
- Gender incidence 3:1 women:men
  - onset 4th-5th decade
- Marginal joint erosions distinguish RA from most other forms of arthritis

Rheumatoid Arthritis

Clinical Manifestations

- Musculoskeletal
  - Bilateral, symmetric, polyarthritis (> 5 joints) often affecting small joints of hands and feet (Wrists, MCPs, PIPs, MTPs, not DIPs)
  - Morning stiffness and gelling are common
  - 90% insidious onset over weeks to months
- Systemic signs/symptoms
  - Constitutional symptoms
    - Fatigue common
    - Weight loss can happen – less common
    - Low grade fevers (<38.3) can happen – less common

Rheumatoid Arthritis

Extra-articular Manifestations

- Rheumatoid Nodules
  - More prevalent with RF+ patients
  - Most commonly develop on extensor surfaces (arms, fingers)
- Eye
  - Keratoconjunctivitis sicca – dry eyes
  - Scleritis – painful, injected
  - Scleral ulcers
- Pulmonary
  - Effusions
  - Interstitial lung disease
  - Nodules
- Other
  - Vasculitis (medium vessel)
  - Felty’s Syndrome (leukopenia and splenomegaly)
Rheumatoid Arthritis Laboratory Testing
- Routine labs (neither sensitive, specific, nor diagnostic)
  - CBC
    * Anemia of chronic inflammation
    * Thrombocytosis
- Elevated ESR, CRP (follow disease activity)
- Rheumatoid factor
  - Negative in up to 20% of RA patients (up to 50% negative at time of diagnosis)
  - Positivity increases with disease duration
- Anti-cyclic citrullinated peptide (CCP) has 70-80% sensitivity and 90+% specificity

Factors predictive of progression from undifferentiated arthritis to RA
van Gaalen et al Arth Rheum 50: 709, 2004

<table>
<thead>
<tr>
<th>At initial evaluation</th>
<th>OR (95% CI)</th>
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<tbody>
<tr>
<td>Positive rheumatoid factor</td>
<td>1.7 (0.5-5.6)</td>
</tr>
<tr>
<td>Positive anti-CCP antibody</td>
<td>38.6 (9.9-151.0)</td>
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Imaging

Rheumatoid Arthritis
- Marginal erosions (mid-late)
- Peri-articular osteoporosis (early-onward)

Osteoarthritis
- Sclerosis
- Osteophytes
- Joint space narrowing

Rheumatoid Arthritis
Her rheumatoid factor, CBC, complete metabolic panel, and hepatitis serologies come back normal but her anti-CCP antibodies are high-titer positive. She has 8 tender and 7 swollen joints. Your next most appropriate step in managing this patient is to:

A. Prednisone monotherapy and return in 4 weeks to assess clinical response
B. Start naproxen and low dose prednisone and return in 12 weeks to assess clinical response
C. Start methotrexate therapy and low dose prednisone and return in 4 weeks to assess clinical response
D. Start methotrexate and low dose prednisone therapy and return in 2-3 months for routine lab safety monitoring
Brief Summary of RA Management Goals

- Initiate appropriate DMARD therapy as soon at time of diagnosis.

- Perform routine clinical disease activity assessment
  - Several disease activity scores to choose from
  - Most use combination of joint counts, visual analog assessments of disease activity +/- inflammatory markers

- Advance therapy (increasing dose or adding second agent/biologic) to achieve low disease activity or better

Commonly used medications Monitoring and toxicity

- Methotrexate (cornerstone of RA DMARD therapy)
  - Early initiation of DMARD therapy now standard of care
  - Dosed one day per week, 7.5mg-20mg total
  - Toxicity
    - Hepatotoxicity – transaminitis, hepatic fibrosis and cirrhosis
    - Myelosuppression – especially lymphocytes
    - Hypersensitivity pneumonitis and interstitial lung disease
    - Mucosal irritation – Use concurrent folate supplements
    - Monitor CBC, LFTs q 4 weeks until achieve stable dose then q 4-8 weeks as long as take medication

- Glucocorticoids (e.g. prednisone)
  - Dosed daily, maintenance 5 – 15 mg/day
  - Toxicity
    - Hyperglycemia
    - Cushingoid changes – truncal obesity, "moon facies"
    - Adrenal insufficiency – must consider during acute stress
    - Osteoporosis – initiate bisphosphonates, Ca, Vitamin D Rx

Commonly used medications Monitoring and toxicity

- Anti-Tumor Necrosis Factor Agents:
  - Standard of care for patients with DMARD refractory disease
  - Class Toxicity
    - Reactivation of latent tuberculosis
      - 50% of patients within 12 weeks of initiating treatment
      - 50% of reactivation manifests with extra-pulmonary TB
      - Screen with PPD, treat latent infection with INH prior to RX
    - Increased rate of soft tissue infections
    - Contraindicated in Class III-IV CHF
    - Question of increased risk of malignancy

- Hydroxychloroquine
  - Dosed daily
  - Most common toxicity – retinal damage (generally after long use)
  - Monitor – baseline retinal exam then q 6-12 months
Case #2

A 66 yo Caucasian woman with ischemic heart disease and congestive heart failure notes development of arthritis in her wrists, knees and ankles that is worse in the morning and associated with occasional chest pain of a possible pleuritic quality. She denies skin lesions or oral ulcers. She has no family history of rheumatic conditions. Past medical history also includes hypertension and diabetes. Her medications include: aspirin, carvedilol, hydralazine, benazepril, and metformin. Her physical examination is consistent with mild synovitis in her hands and wrists and x-rays show small pleural effusions but are otherwise negative.

Case #2

She is found to have a negative RF and an ANA that is 1:320 in a diffuse pattern. Her chemistry panel is otherwise unremarkable and a urine dipstick in the office is only positive for 1+ proteinuria. What is the LEAST appropriate next step?

A. Check a urinalysis with micro, CBC, C3, C4
B. Check anti-ds DNA, Smith, and other ANA sub-serologies
C. Substitute another agent for hydralazine
D. Perform a kidney biopsy to rule out early lupus associated proteinuria

Drug Induced SLE

- Well Characterized with the following drugs:
  - Hydralazine, Procainamide, Quinidine, Isoniazide
  - Minocycline can have somewhat different LE presentation

- Clinically
  - Patients are often > 50 (bias given medications involved?)
  - ANA is a diffuse or homogenous pattern
  - Sub-serologies are usually negative
  - Experience arthritis, serositis, cutaneous disease
  - Infrequent visceral involvement

- Disease improves with cessation of the agent
  - ANA may be persistently positive
ANA is not only a test for SLE

- Abnormal ANA does not equal SLE
  
  - 99.9% Sensitive for SLE

- Poor Specificity
  
  + Other autoimmune diseases (scleroderma, sjogren's, thyroid disease), medications, neoplasms, etc... associated with positive ANA

- Pearl: The test does have a high sensitivity and high negative predictive value:
  
  + A negative ANA by immunofluorescence rules out most SLE

Using the ANA in the appropriate Clinical Context

- When considering a diagnosis of SLE in a patient with a positive ANA, consider the clinical context
  
  - Women:men 9:1, particularly African American pts
  
  - Usually post-pubertal onset, affecting 3rd-5th decade

  - ACR "Diagnostic” SLE criteria: Not intended for use in diagnosis, but can help guide general thinking of clinical context

SLE: ACR Classification Criteria:

4 of 11 Criteria without better explanation (Not diagnostic)

- Malar Rash
- Discoid Rash
- Photosensitivity
- Oral Ulcers
- Arthritis
- Serositis
- Renal Disorder

SLE Criteria Cont.

- Hematologic Disorder
- Immunologic Disorder
- ANA
- Neurologic Disorder
Malar Rash

- Fixed malar distribution of erythema, flat or raised

Discoid Rash

- Erythematous raised patches with keratotic scaling and follicular plugging; some atrophic scarring in chronic lesions

Photosensitivity

- Skin rash as an unusual reaction to sunlight, by patient history or physical examination

Oral Ulcers

- Oral or nasopharyngeal ulcers, usually painless, observed by a physician
**Arthritis**
- Non-erosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling, or effusion

**Other SLE Criteria**
- Serositis
  - Pleuritis (convincing history of pleuritic pain or rub heard by a physician or evidence of pleural effusion)
  - Pericarditis (documented by EKG, rub, or evidence of pleural effusion)
- Renal Disorder
  - Persistent proteinuria >0.5g/day (or >3+)
  - Cellular casts of any type

**Hematologic Abnormalities**
- Hemolytic anemia (usually coomb’s positive)
- Leukopenia (WBC < 4,000 on at least 2 occasions)
- Lymphopenia (<1500 on 2 or more occasions)
- Thrombocytopenia (PLT<100,000 on 2 or more occasions)

**Immunologic Disorder**
- Anti-dsDNA
- Anti-Smith
- Positive findings of anti-phospholipid Abs
  - Abnormal level of either IgG or IgM CLIP Abs
  - Positive test for Lupus Anticoagulant (RVVT)
  - False positive RPR/VDRL > 6months neg. FTA
Positive ANA

- An abnormal titer of ANA in the absence of drugs known to be associated with "drug-induced lupus syndrome"

Neurologic Disorder

- Classically defined only as:
  - Seizures (in the absence of other causes)
  - Psychosis (in the absence of other causes)

SLE Management:

A 40 year old woman with a six year history of lupus (ANA+, anti-dsDNA+, diffuse proliferative glomerulonephritis) managed with prednisone hydroxychloroquine and mycophenolate mofetil develops fever, worsening respiratory failure, and infiltrates on chest CT. Your next best step is to:

A. Start prednisone therapy immediately
B. Check her anti-dsDNA titer
C. Arrange for an open lung biopsy
D. Start antibiotics, pan culture, and arrange for bronchoscopy

SLE: Management

- Less important to know specific therapies for treating SLE
  - Mycophenolate mofetil (Cellcept, Myfortic) now standard of care for most cases of lupus nephritis (at least non-inferior to cyclophosphamide)
  - Hydroxychloroquine also standard first line therapy (withdrawal can precipitate flares)

- SLE patients are doubly susceptible to infectious complications
  - 1. from SLE, itself
  - 2. from the use of immunosuppressive therapies (mycophenolate mofetil, prednisone, etc...)

- Infectious complications can mimic disease activity
SLE: Useful Facts of which the Family Practitioner should be Aware

- Infectious complications were classically thought of as leading cause of mortality
- Growing evidence that ischemic heart disease now leading cause of mortality
  - Risk of CV disease in SLE patients is 7-50 fold greater (dwarfs diabetes and cholesterol and other "traditional" CV risk factors!!)
  - Care should be paid to minimizing other controllable cardiac risk factors (BP, cholesterol, smoking, etc.)
  - Cardiac symptoms should be treated seriously in all SLE patients, including young women, and on all board exams!!!

Case #3

A 72 year old woman presents complaining of profoundly increased pain and morning stiffness in her neck, shoulders low back and hips. She notes increased fatigue and a 10 pound unintended weight loss. No focal deficits are appreciated on her neurologic exam. Her PMH is notable for sciatica, hypertension, and COPD. Medications include HCTZ, Advair, and ibuprofen PRN. Xrays of her spine and hips are negative.

Case #3

All of the following are appropriate next steps in evaluating this patient except:

A. Start high dose prednisone 60 mg/day and arrange for urgent temporal artery biopsy
B. Question and examine the patient for more specific signs of Giant cell arteritis
C. Order an Erythrocyte Sedimentation Rate
D. Add 20 mg of prednisone empirically and assess her clinical response in 3-4 days

Polymyalgia Rheumatica

- Demographic
  - Women:men 2:1
  - Rare before age 50
  - Traditionally most common in whites of northern European lineage
- Clinical
  - Proximal musculoskeletal pain (shoulder girdle, neck> hips)
  - No true weakness like POLYMYOSITIS (this is not the same family of diseases!!!!!!)
  - Morning stiffness, gelling, and feeling OLD!!
  - Usually no palpable synovitis, although on ultrasound or MRI can see evidence of large joint bursitis
  - May have malaise, low grade fever
**PMR: More Clinical Features**

- Elevated ESR and/or CRP
- Association with Giant cell arteritis (But only 10-50% of time)
- **Rapid and dramatic response to MODEST doses of prednisone (<20 mg/day)**
  - No need to treat PMR with large doses of prednisone unless there is clinical suspicion of GCA
  - However, be wary of patients (and test questions) in whom one expects a diagnosis of PMR but there is no rapid response to modest doses of prednisone

**Giant Cell Arteritis Clinical Manifestations**

- **Demographics**
  - Same as PMR (May be part of spectrum of same disease)
  - 40-50% develop PMR (may precede, follow, or occur concomitantly)
  - Rare before age 50.
  - The most common vasculitis: increases in prevalence with each decade of life (less common in 50 year olds than in 80 year olds)

**Giant Cell Arteritis Clinical Manifestation**

- Jaw Claudication
  - Most specific symptom for GCA
  - Classic presentation is discomfort over masseter muscles with protracted chewing
  - This is not pain at temporal mandibular joint

- ** Constitutional signs are common in this SYSTEMIC disease**
  - Weight loss, Malaise
  - Low grade fever in up to half of patients
  - Cause of FUO in elderly
**Giant Cell Arteritis**

**Work-up**

- Establish pre-test probability of GCA using demographics, history, physical exam

**Laboratory Evaluation**

- ESR
  - >90% patients have an ESR >50; frequently >100
  - C-reactive protein may be more sensitive and be elevated in patients with normal ESR

- CBC
  - Normocytic anemia, thrombocytosis

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**Vasculitis Overview**

**Vessel Size**

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<thead>
<tr>
<th>Large</th>
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<tbody>
<tr>
<td>Giant Cell Arteritis</td>
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<tr>
<td>Temporal Arteritis</td>
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<tr>
<td>Limb Ischemia, CVA</td>
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<table>
<thead>
<tr>
<th>Medium</th>
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<tbody>
<tr>
<td>Polyarteritis nodosa</td>
</tr>
<tr>
<td>ANCA assoc, RA</td>
</tr>
<tr>
<td>Renal/bowel infarction, mononeuritis, skin ulcers</td>
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<table>
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<tr>
<th>Small</th>
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<tr>
<td>Drug, SBE, cryos</td>
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<tr>
<td>ANCA assoc, etc... palpable purpura</td>
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<tr>
<td>Glomerulonephritis, alveolar hemorrhage</td>
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**Giant Cell Arteritis**

**Temporal artery biopsy**

- If elect to pursue biopsy, initiate prednisone 40-60 mg/day
- Request 3-5 cm segment of artery.
- Unilateral biopsy is >90% sensitive
- 2 weeks of empiric prednisone does not significantly affect the sensitivity. Treat with large, long-term doses (40-60mg prednisone daily to start)

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**Vasculitis: Anatomic Schematic**
ANCA Associated Vasculitis: Quick Facts

- Wegener’s Granulomatosis: Renamed “Granulomatosis with Polyangiitis” (GPA) in 2010
  - Clinical
    + Sinus – chronic sx, necrotizing disease
    + Lungs – nodules, cavities, alveolar hemorrhage
    + Kidneys – glomerulonephritis, normal complements
  - c-ANCA – anti-proteinase-3 abs – 60-90% sensitive

- Microscopic polyangiitis
  - Clinical
    + Skin – palpable purpura, ulcers
    + Lungs – Diffuse alveolar hemorrhage
    + Kidneys – glomerulonephritis, normal complements
    + Neuro – mononeuritis multiplex
  - p-ANCA – anti-myeloperoxidase abs
    + MPA – 75% sensitive
    + Also abnormal with Churg-Strauss

- Treatment of both:
  - Cytotoxic therapies and corticosteroids
  - Recently, rituximab (B-cell depleting antibody) approved for GPA

Case #4

36 year old man complains of 3 weeks of a painful left knee and right ankle, dysuria, and new onset “severe athlete’s foot”. He had no previous illnesses. He endorses having had food poisoning for which he was treated successfully 6 weeks ago. On exam he has active synovitis at his left knee and right ankle, with heel spur pain and plantar fascitis on his right foot. Pustular scaling plaques with onycholysis were seen on his bilateral feet. Analysis of synovial fluid from his left knee revealed 14,000 WBC (91% PMNs) with negative cultures and gram’s stain. Urinalysis and urethral swab studies are negative for STDs.

Pustular scaling plaques

Case #4

Which of the following treatment approaches is least appropriate for this patient?

A. Prescribe diclofenac 75 mg TID until symptoms improve
B. Intra-articular injection of triamcinolone into the knee
C. Sulfasalazine therapy for persistent symptoms
D. Empiric ceftriaxone therapy
Seronegative Spondyloarthropathies

- General Characteristics
  - ANA, RF negative (seronegative)
  - Inflammatory arthritis of axial skeleton (SI joints and spine)
    - Sacro-iliitis
    - Syndesmophytes
  - Oligoarticular, asymmetric peripheral arthritis
  - Enthesitis
    - Inflammatory pain at point of tendon or joint capsule insertion on the bone
      - E.g. Achilles tendon or plantar fascia insertion at heel pain

A Word About HLA-B27

- Prevalence of B27 is high in Caucasians
- 95% of patients with B27 never develop spondyloarthropathy
- B27 is not useful diagnostic test in most situations
- Presence of HLA-B27 associated with more axial disease, uveitis

Reactive Arthritis

- Arthritis is a reaction to an infectious exposure that occurred 1-4 weeks before
  - Venereal Exposure
    - Chlamydia trachomatis
    - Male Patient may report an antecedent urethritis
  - Invasive enteropathic process
    - Salmonella, Shigella, Campylobacter, Yersinia
    - Patients report a prior episode of bloody or severe diarrhea
- Up to 50% may not identify an exposure

Classic Triad

- Described by the Prussian physician Hans Reiter in 1916
  - Arthritis
  - Conjunctivitis
  - Non-gonococcal Urethritis
- Triad is present MINORITY of Reactive arthritis cases
Reactive Arthritis

Clinical

- Disproportionately men, 3rd-5th decade
- Disproportionately affects lower extremities
  - Plantar fasciitis with heel spur pain on exam
  - Achilles tendonitis
  - Asymmetric knee or ankle arthritis
- Muco-cutaneous lesions
  - Painless oral ulcers
  - Keratoderma blenorrhagica (difficult to differentiate from pustular psoriasis)
  - Circinate balanitis – ulcerative urethritis
- Axial Arthritis
  - Asymmetric Sacro-iliitis
  - Asymmetric, bulky vertebral body osteophytes

Reactive Arthritis: Treatment

- NSAIDs of symptomatic benefit
- Sulfasalazine of some modest benefit for chronic peripheral arthritis
- Methotrexate likely of some benefit
- Anti-TNF medications for spinal and peripheral arthritis
- Controversial evidence suggesting possible benefit of combination antibiotics for Chlamydia associated reactive arthritis (not on boards!)

Case V

Question #1

55 year old male awakens with right knee pain and swelling one morning that worsens over next 48 hours until he has difficulty walking on that knee. He presents to your office complaining of knee pain, swelling, and low grade fever. His PMHx is notable for HTN and CKD with a baseline creatinine 2.1 (eGFR 45). On a recent Chem. 20 panel, uric acid level was elevated at 9.2. He denies any other joint pains, IVDU, or recent sexual contacts.

Your next best step in managing this patient should be to:

A. Order an Xray of the Knee
B. Recheck the patient’s serum uric acid level
C. Perform an arthrocentesis
D. Treat the patient empirically for presumed gout

Acute Gout

- Acute, usually self limited monoarticular inflammatory arthropathy
- Inflammatory response directed against monosodium urate crystals in synovium
- Usually but not always associated with hyperuricemia
- After attack, patient returns to normal during an asymptomatic inter-critical period that can last months or years
- Monosodium urate crystals precipitate around a UA concentration of 6.8, below the upper limit of “normal” in most US populations
Distribution of Serum Uric Acid Levels in Japan: 34,000 People

Acute Gout - Diagnosis
- **Definitive:** Crystal Identification – the only way!
  - Joint fluid examination under polarized microscopy with red compensator
  - Strongly negatively birefringent needle shaped crystals
- **Suspected:** Characteristic radiographic “gouty” corticated erosions away from joint space
- **Possible:** Classic clinical picture with elevated serum urate – not diagnostic however!!!!

Acute Gout - Key Points
- **Arthrocentesis is required to:**
  - Confirm the diagnosis of gout
  - Exclude infectious arthritis, which can coexist in cases of known gout (gram’s stain and Cx.)
- **X-rays of benefit for suspected diagnoses and to follow radiographic progression**
- **Serum urate level does not confirm or refute a diagnosis of gout but can be used to monitor therapy**
Case V, Question 2

Plain films demonstrate no acute changes, repeat uric acid level is now 10.7, and aspiration of the synovial fluid reveals numerous PMN’s, WBC count of 75,000, intracellular needle-shaped negatively birefringent crystals, and a negative gram’s stain. The patient is started on indomethacin and allopurinol 300 mg/day and sent home. Which of the following actions in this case was a mistake?

A. Allopurinol dose
B. Indomethacin therapy
C. The patient was not admitted and treated empirically with antibiotics pending results of synovial fluid cultures
D. Use of Allopurinol during acute phase of gout

Acute Gout Therapy

- Aimed at reducing the severity and duration of self-limited symptoms and reaching the “inter-critical period” sooner
- NSAIDs
  - Effective and rapid relief of symptoms
  - Contraindicated in patients with GI, Renal, or hypersensitivity concerns
- Corticosteroids
  - Intraarticular
  - Systemic
- Colchicine:
  - Low dose only (0.6 mg BID)
  - Not likely as effective as either NSAIDs or corticosteroids
- Uric Acid lowering therapy is now an option for some during acute flare

Chronic Gout - Therapy

- Goal: reduce serum uric acid level
  - Do not treat asymptomatic hyperuricemia
  - Prevention of future attacks: Lower serum uric acid associated with fewer attacks
  - Helps remove tophi/stores of uric acid
  - Goals of therapy, especially for tophi removal, are serum urate levels < 6.0. Max. dose of allopurinol is more than 200 mg/day in patients with normal renal function
Updates in 2012 Gout Guidelines

- Acceptable to start ULT in individuals during an acute flare provided there is adequate prophylaxis with anti-inflammatory agent (NSAID, prednisone, low dose colchicine)
- Starting allopurinol dose not to exceed 100 mg day.
  - Dose should be even less in those with renal insufficiency
  - HLA B5801 genotype testing recommended for populations with high allele frequency and risk of allopurinol hypersensitivity
- Hundreds-fold risk of developing severe DRES in Han Chinese, Thai, and some Korean patients

Urate Lowering Therapies

(More complete slides included at the end of syllabus)

- Probenecid: Uricosuric (under-excreters)
- Allopurinol: Blocks Xanthine Oxidase and uric acid production
- Febuxostat: Non purine xanthine oxidase inhibitor blocking uric acid production
- Pegloticase: Uricase – breaks down uric acid into water soluble metabolite

Case VI

- A 60 year old white female comes to your office for increasing right shoulder pain and limited range of motion. Her past medical history is notable for hypertension, nephrolithiasis, asthma, and a osteoarthritis of the knee that required a TKA two years prior. She takes only a beta blocker and inhaled corticosteroids. On examination, she has some tenderness of the supraspinatus tendon with minimal impingement with abduction, however – there is crepitus, diminished range of motion, and pain in the right shoulder with both abduction and external rotation. Shoulder and knee films are shown to the right.

Case VI, Question #1

Which of the following features of this patient’s case, by itself, should prompt a more thorough diagnostic workup for her arthritis?

A. Osteoarthritis involving the shoulder
B. Total knee arthroplasty at age 58
C. Tenderness to palpation of the rotator cuff
D. Use of beta blockers
Osteoarthritis – **Key Point**

- Certain joints do not usually experience degenerative changes
  - Glenohumeral joint shoulder
  - Elbow
  - Ankle
  - Wrist
- Common joints affected by osteoarthritis
  - Acetabular joint of hip
  - Knee
  - DIP/PIP joints of hands/feet
  - AC joint of shoulder
  - Spine

**CPPD – Calcium Pyrophosphate Dihydrate Deposition Disease**

- Several distinct clinical forms:
  - Pseudogout (25%): Acute inflammatory monoarthritis mimics gout
  - Pseudo-RA (5%): Synovitis and degenerative changes of MCP’s (especially 2nd and 3rd)
  - Accelerated OA/DJD of unusual joints
  - Spinal Involvement (fever, neck pain)
  - Asymptomatic chondrocalcinosis

**CPPD Associations**

- Some Associated Metabolic Disorders
  - Hyperparathyroidism (This patient with renal calculi!)
  - Hemochromatosis
  - Hypothyroidism
  - Acromegaly
  - Ochronosis
  - Wilson’s disease
  - Others
Case V, Question 3

The patient is started on allopurinol at 100 mg/day which is eventually increased to 200 mg/day. However, the patient experiences a second, and subsequently third, painful attack of gout over the next eight months. A repeat serum urate level indicates that the patient’s uric acid level is now in the normal range at 6.9, however a foot film reveals the presence of a small tophaceous erosion in the 1st MTP joint. Your next best course of action is to do which of the following:

- A. Discontinue allopurinol for lack of efficacy and switch to daily colchicine
- B. Increase allopurinol to 300 mg./day and target a serum uric acid of less than 6.0
- C. Add colchicine to current allopurinol regimen
- D. Add prednisone to the current regimen
Extra slides: Chronic Gout – Serum Urate Lowering Therapies

- Probenecid: Uricosuric blocks tubular re-absorption or uric acid
  - Useful in patients who under-excrete uric acid (90%)
  - If need be, confirm under-excretion with 24 hr. uric acid <800 mg/24 hrs.
  - Do not use if:
    ✤ Tophi
    ✤ Renal Insufficiency
    ✤ Clear overproduction syndrome

Extra Slides: Urate Lowering therapy

- Febuxostat
  - Non-purine xanthine oxidase inhibitor (40 mg-80mg doses)
  - As it is not a purine:
    ✤ Can be tried for patients with allopurinol hypersensitivity
  - Has been used successfully in patients with mild renal insufficiency (unlike allopurinol)
  - Blocks xanthine oxidase: Like allopurinol, cannot be used with medicines that are metabolized by xanthine oxidase (leads to build up of azathioprine for example)

Extra slides: Chronic Gout – Serum Urate Lowering Therapies

- Allopurinol
  - Xanthine Oxidase Inhibitor
  - Blocks metabolism of purines to uric acid
  - Effective for both under-excreters and overproducers of uric acid
  - Careful use in patients with renal failure
  - Associated with hypersensitivity syndrome that is DIFFERENT from rash
    ✤ Fever, Steven’s-Johnson/TEN, hepatitis, marrow suppression, nephritis

Pegloticase

- Pegylated recombinant uricase (humans don’t have uricase like other animals)
- Metabolizes uric acid to allantoin which is 5-10 times more soluble than uric acid
- Can rapidly reduce uric acid levels and tophi
- Expensive and given as IV infusions
**Ankylosing Spondylitis: Quick Facts**

- **Demographic**
  - Men:Women 3:1
  - Most common onset during 3rd-5th decades
- **Clinical**
  - Skeletal
    - Axial skeleton arthritis – spine, sacro-iliac joints
    - Oligoarticular, affecting ankles, knees
  - Other
    - Anterior uveitis
    - Pulmonary fibrosis
    - Aortitis, aortic regurgitation
- **Radiologic studies**
  - Squared off vertebral bodies
  - Shiny corners of vertebral bodies
  - Syndesmophyes - fine, bony growths that bridge vertebral bodies

**Psoriatic Arthritis: Quick Facts**

- **Skin**
  - Arthritis seen in up to 15% of psoriatic patients
  - Psoriasis precedes arthritis for several years in 85% of patients
- **Peripheral Arthritis**
  - Oligoarticular, monoarticular (66% of patients)
  - Polyarticular (pseudo-rheumatoid presentation)
- **Axial Arthritis**
  - Sacro-iliitis early on usually unilateral
  - Bulky asymmetric vertebral body osteophytes
- **Dactylitis** – Sausage digits

**Quick Approach to an abnormal ANA**

- Establish clinical context (Use the criteria as guide)
- Follow-up with more specific sub-serologies
- Consider other causes of an abnormal ANA
  - Auto-immune thyroid disease
  - Alternative systemic connective tissue disease
  - Family history of autoimmunity
  - Seen in 10-15% of asymptomatic women
  - Associated with a medication

**Scleroderma**
Limited Scleroderma (CREST): Quick Facts

- **Background**
  - Women:men 4:1
  - Most common onset during 3rd-5th decades
- **CREST (Criteria – diagnosis 3 of 5)**
  - Calcinosis – subcutaneous deposits, fingers extensor surfaces
  - Raynaud’s
    - Most common first sign (>90%)
    - May involve fingers and toes,
  - Esophageal
    - GERD often severe, provider does not appreciate association
    - Dysphagia (food sticks in the mid-esophagus)
  - Sclerodactyly
    - Swelling of fingers
    - Skin thickened distal to the MCPs
  - Telangectasia
    - Squared off appearance on face, palms, mucosal surfaces

Diffuse Scleroderma: Quick Facts

- **Demographic**
  - Same as CREST
- **Clinical (Different than CREST)**
  - Cutaneous
    - Early disease may see scleredema of fingers hands
    - Sclerosis extends to dorsum of hands, forearms
    - May involve the face and trunk
  - Renal Crisis
    - Hypertensive emergency picture
    - Most common during scleredema phase
    - Associated with prednisone use
    - ACE-I’s are life saving therapy

Scleroderma – Other key points

- **Serology**
  - ANA >95% for both forms
  - Anti-centromere pattern 20-40% (specific for CREST)
  - Anti-SCL-70 pattern 20-40% (specific for Diffuse scleroderma)
- **Pulmonary Disease**
  - Isolated pulmonary hypertension seen in 10% of patients with CREST (common cause of death)
  - Interstitial lung disease, without pulmonary HTN more common in Diffuse scleroderma
- **Overlap Syndromes**
  - Scleroderma with elements of polymyositis, dermatomyositis

Inflammatory Myopathies: Quick Facts

- **Polymyositis, Dermatomyositis, Inclusion Body myositis**
- Proximal muscle weakness is hallmark of PM and DM, more distal weakness IBM
- Proximal muscle pain is NOT feature
- Severe disease can affect diaphragm and swallowing
  - Interstitial lung disease common
- Elevations of CK and Aldolase are common, higher levels in PM/DM than IBM
- DM>>PM>>IBM association with malignancy (PM/DM: ovarian>breast/lung/GI)
  - Workup for visceral malignancy appropriate for DM
- Treatment with corticosteroids and immunosuppressive therapies mainstay
**Infectious Arthritis Slides**

**Septic Arthritis – Key Points**

- Non gonococcal septic arthritis
  - Medical emergency: 50% morbidity and 5-15% mortality
  - Synovial WBC usually >50,000 but may be quite less early in course of infection or if partially treated
  - Staph and Strep most common pathogens
  - Treatment:
    - Total of 6 weeks of antibiotics, of which at least two weeks (if not longer) should be IV
    - Drainage of joint, which can be via serial arthrocentesis (as long as WBCs decreasing) until fluid stops accumulating...or surgical debridement

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**GC Arthritis - Key Points**

- Disseminated gonococcemia
  - Usually associated with fever, rash, and migratory tenosynovitis
  - Most common cause of a septic monoarticular arthritis in adults under the age of 40 (most commonly in the knee)
  - Synovial WBC usually 25,000-50,000 range
  - Responds rapidly to a course of an IV 3rd gen cephalosporin, such that total duration of therapy ONLY needs to be 10-14 DAYS.