

# Family Medicine Board Review 2011

Rheumatology Section  
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## 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
- 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, meta-carpal 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, a negative Rheumatoid Factor, and X-rays of her hands that demonstrate peri-articular osteopenia but no joint space narrowing or erosions.

## Case #1: Early Arthritis

Which of the following statements regarding this patient's symptoms are correct?

- A. Her age of onset is too young for RA
- B. Her morning and gelling symptoms are most consistent with an inflammatory arthritis
- C. The radiologic findings show no joint deformities, making an RA dx. unlikely
- D. She can't have RA if her rheumatoid factor is negative

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## Case #1: Early Arthritis

If positive, which of the following laboratory tests has the best predictive value in predicting whether she will develop rheumatoid arthritis?

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

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## Rheumatoid Arthritis

- RA is 2<sup>nd</sup> most common form of chronic arthritis (behind osteoarthritis)
- Has a prevalence of 1% in US adults
- Gender incidence 3:1 women:men
  - onset 4<sup>th</sup>-5<sup>th</sup> 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
  - Fatigue common
  - Significant weight loss (10%)
  - Low grade fevers (<38.3)

## 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

- Common labs
  - Anemia of chronic inflammation
  - Thrombocytosis
  - Elevated ESR, CRP
- 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

<u>At initial evaluation</u>	<u>OR (95% CI)</u>
Positive rheumatoid factor	1.7 (0.5-5.6)
Positive anti-CCP antibody	38.6 (9.9-151.0)

## Imaging



Rheumatoid Arthritis

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



Osteo-Arthritis

- Sclerosis
- Osteophytes
- Joint space narrowing

## Commonly used medications Monitoring and toxicity

- 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
- 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

## 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

## Commonly used medications Monitoring and toxicity

- 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?

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

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## Case #2

- A. Check a urinalysis, CBC, C3, C4  
Search for systemic involvement from SLE or other disease (low WBC, low complements, etc..)
- B. Check anti-ds DNA, Smith, and other ANA sub-serologies  
Again, looking for evidence of systemic lupus
- C. Substitute another agent for hydralazine  
Addresses most likely cause of symptoms
- D. Perform a kidney biopsy to rule out early lupus associated proteinuria  
Most likely has drug induced LE which is not often associated with organ involvement. Has other reason for 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 3<sup>rd</sup>-5<sup>th</sup> decade
  - ACR "Diagnostic" SLE criteria: Not intended for use in diagnosis, but can help guide general thinking of clinical context

## SLE: ACR 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 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)

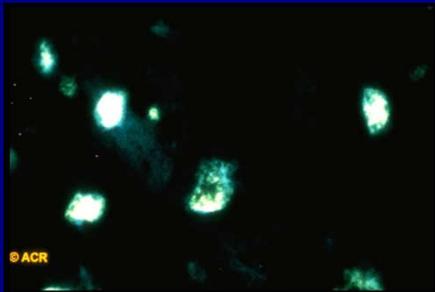
## Immunologic Disorder

One of the Following

- 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: Useful Facts of which the Family Practitioner should be Aware

- SLE patients are doubly susceptible to infectious complications 1. from SLE, itself, and 2. from the use of immunosuppressive therapies
- Infectious complications can mimic disease activity – so don't be fooled by questions like this:
  - A 40 year old woman with a six year history of lupus 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

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## 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

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## 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 Manifestations

- Headache (70-80% at one time or another)
  - Commonly dull, aching, often over the temporal area but can be anywhere
  - Scalp tenderness may be present
- Visual Changes
  - Present in up to a third of patients
  - Blurred vision, diplopia, amaurosis fugax often presage blindness
  - Monocular blindness can be abrupt without warning
  - If persists >24 hours can be permanent

## 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

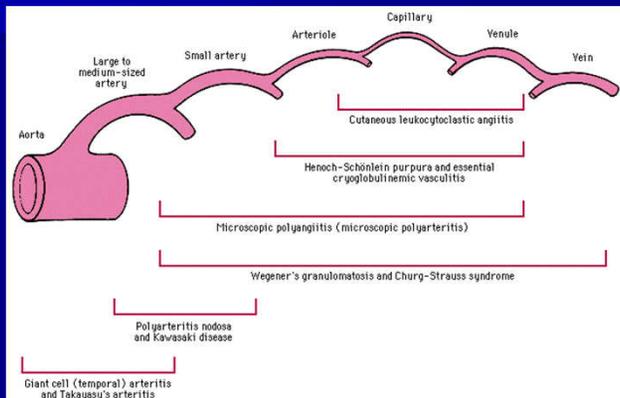
## Giant Cell Arteritis

- 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)

## Vasculitis Overview

Vessel Size	Some Clinical Features
Large <ul style="list-style-type: none"> <li>– Giant Cell Arteritis</li> <li>– Takayasu Arteritis</li> </ul>	Limb Ischemia, CVA
Medium <ul style="list-style-type: none"> <li>– polyarteritis nodosum</li> <li>– ANCA assoc, RA</li> </ul>	Renal/bowel infarction, mononeuritis, skin ulcers
Small <ul style="list-style-type: none"> <li>– Drug, SBE, cryos</li> <li>– ANCA assoc, etc...</li> </ul>	Glomerulonephritis, alveolar hemorrhage, palpable purpura

## Vasculitis: Anatomic Schematic



## 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 fasciitis 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 triamcinalone into the knee
- C. Sulfasalazine therapy for persistent symptoms
- D. Empiric ceftriaxone therapy

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## The Family of Seronegative Spondyloarthropathies

- Ankylosing Spondylitis
- Psoriatic Arthritis
- Reactive Arthritis
- Enteropathic Arthritis (associated with Inflammatory Bowel Disease)

## 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

- |                          |                     |                    |               |
|--------------------------|---------------------|--------------------|---------------|
| ■ Ankylosing Spondylitis | Psoriatic Arthritis | Reactive Arthritis | IBD Arthritis |
| 90%                      | 50%                 | 75%                | 40%           |
- 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, 3<sup>rd</sup>-5<sup>th</sup> 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. 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

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## 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

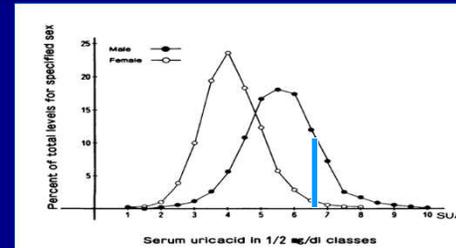


Fig. 1 Distribution of serum uric acid levels. Males:  $n = 15\ 712$ ,  $\bar{x} = 5.82$  mg/dl,  $SD = 1.14$  mg/dl. Females:  $n = 18\ 324$ ,  $\bar{x} = 4.33$  mg/dl,  $SD = 0.91$  mg/dl. (SI conversion:  $\text{mmol/l} = \text{mg/dl} \times 0.0595$ ).

## 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 and sent home. Which of the following actions in this case was a mistake?
  - A. Allopurinol therapy
  - B. Indomethacin therapy
  - C. The patient was not admitted and treated empirically with antibiotics pending results of synovial fluid cultures
  - D. None of the above

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## Acute Gout Therapy

- Aimed at reducing the severity and duration of 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)! No longer generic.
  - Not likely as effective as either NSAIDs or corticosteroids
- Uric Acid lowering therapy is not appropriate during acute gouty flare

## Chronic Gout - Progression

- Recurrent inflammatory arthritic attacks separated by diminishing inter-critical periods of normalcy
  - Monoarticular or polyarticular
    - Same joint
    - Spread to other joints
      - General rule of thumb: most commonly involved joints: distal (podagra) to proximal
- Chronic inflammation/synovitis with no inter-critical period
  - Recurrent attacks blend together and patient's symptoms never return entirely to normal between attacks
  - Eventually, chronic inflammation remains
- Tophaceous gout:
  - Can occur with all of the above
  - Uric acid containing tophi deposit in joints/tendons/soft tissues, can lead to erosions and deformities
  - Chronic synovitis and tophaceous deformities can be difficult to distinguish from other inflammatory arthritis such as RA

## 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 1<sup>st</sup> 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

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## Chronic Gout - Therapy

- Goal: reduce serum uric acid level
  - Lower serum urate 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

## 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

## Gout Therapy – Other Key Points

- Do not treat asymptomatic hyperuricemia
- Do not initiate uric acid lowering therapy during acute attack
  - When you do initiate uric acid lower therapy, DO use prophylaxis with either daily colchicine (0.6/day), NSAIDs, for at least 3 months
- Use colchicine properly
  - Low dose only for acute attacks (Very expensive and of mild efficacy)
  - Yes for prophylaxis during urate lowering therapy (now that no longer generic, this can be very expensive: \$5 a pill)
  - Does NOT lower uric acid levels, so not used to treat chronic tophaceous gout
  - But perhaps OK in that special patient intolerant of or refusing urate lowering therapy but who wants to decrease acute flares

## 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.

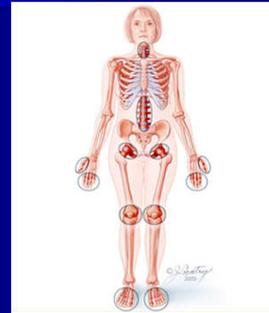
## Case VI, Question #1

- 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

## Case VI, Question #1

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## 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



## CPPD

- Several distinct clinical forms:
  - Pseudogout (25%): Acute inflammatory mono-arthritis mimics gout
  - Pseudo-RA (5%): Synovitis and degenerative changes of MCP'S (especially 2<sup>nd</sup> and 3<sup>rd</sup>)
  - 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

## Extra Study Slides

- Ankylosing spondylitis quick Facts
- Psoriatic arthritis quick Facts
- ANA quick facts
- Scleroderma
- ANCA associated vasculitis quick Facts
- Inflammatory myopathies quick facts
- Infectious arthritis questions and facts
- Extra slides on gout therapy

Good Luck!!!!



## Extra Study Slides

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- Infectious arthritis questions and facts
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## Ankylosing Spondylitis: Quick Facts

- Demographic
  - Men:Women 3:1
  - Most common onset during 3<sup>rd</sup>-5<sup>th</sup> 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
  - Syndesmophytes - 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 3<sup>rd</sup>-5<sup>th</sup> 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
  - Telangiectasia
    - 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 sclerodema of fingers hands
    - Sclerosis extends to dorsum of hands, forearms
    - May involve the face and trunk
  - Renal Crisis
    - Hypertensive emergency picture
    - Most common during sclerodema 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

## ANCA Associated Vasculitis: Quick Facts

- Wegener's Granulomatosis: Renamed "Granulomatosis with Polyangiitis" (GPA) in 2010
  - Clinical
    - Sinus – chronic sxs, 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

## 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

## Case VII

- A 24 year old male presents to your office with the relatively sudden onset of acute pain and swelling in his left knee. Three months ago, he returned from a camping trip in the Pocono mountains during which he admits to having had one episode of unprotected sex as well as several episodes of diarrhea. A few weeks after, he developed a flu like syndrome and migratory polyarticular joint pains that eventually resolved. Currently, he reports some subjective fevers and difficulty bearing weight on his left leg. He denies any rashes, dysuria, redness of his eyes, or low back pain. Examination reveals a low grade fever with tenderness, warmth, and a moderate effusion in his left knee. CBC/WBC is mildly elevated, blood cultures are negative, and all other basic labs are normal. Plain films of the knee are unrevealing. Arthrocentesis of the knee yields:

■ Cell count	11,000
■ Crystals	None Seen
■ Gram's Stain	Negative
■ Culture	Negative

## Case VII, Question #1

- The least likely etiology for this patient's symptoms includes which of the following?
  - A. Reactive Arthritis: Because of a lack of other features consistent with Reiter's syndrome, such as urethritis or conjunctivitis
  - B. Gout: Because crystal examination is negative
  - C. GC Arthritis: Because synovial cultures are negative
  - D. Bacterial septic arthritis, because blood cultures are negative

## Case VII, Question #1

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## Case VII, Question #1

- Reactive arthritis is a sterile arthritis (for all current intents and purposes).
  - Only the MINORITY of patients have all three features of Reiter's syndrome.
- UA crystals are seen in the synovial fluid of 90+% cases of gout, so their absence is highly suggestive of an alternative diagnosis
- In GC arthritis, synovial cultures are positive in only 25-50% of cases
  - Negative synovial culture does not rule out GC
  - Recommended to culture blood and all inoculation sites (urethra, throat, and rectum if appropriate) to enhance yield
- Non Gonococcal Septic Arthritis: While synovial cultures are usually positive in 70-90% of patients, peripheral blood cultures are positive in only roughly 50-60% of patients.
  - Negative blood cultures, therefore, do not rule out bacterial arthritis.
  - Arthrocentesis is crucial, and if unable to perform, surgical sampling may be necessary

## Case VII, Question # 2

- You aspirate the knee a second time and then initiate therapy with ceftriaxone. The patient shows only mild improvement over the next 72 hours, both synovial cultures remain negative, and his synovial cell count remains just over 10,000 WBC.
- All of the following are reasonable statements EXCEPT
- A. The patient is unlikely to have GC arthritis without a rapid clinical response to appropriate antibiotics within 48 hours
- B. Non gonococcal bacterial arthritis does not occur in joints where the synovial cell count is less than 25,000
- C. Antibiotics are unlikely to be of much benefit in patients with reactive arthritis that is caused by enteric organisms
- D. Additional serologic testing would be appropriate for this patient

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## GC Arthritis - Key Points

- Disseminated gonococemia
  - 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 3<sup>rd</sup> gen cephalosporin, such that total duration of therapy ONLY needs to be 10-14 DAYS

## 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 WBC's decreasing) until fluid stops accumulating...or surgical debridement

## Case VII, Question #3

- Which of the following additional tests is likely to confirm this patient's diagnosis
  - A. Fungal serologies
  - B. Spirochetal Serologies
  - C. Brucella Serologies
  - D. HIV Serology

## Lyme Disease

- Which of the following additional tests is likely to confirm this patient's diagnosis
  - A. Fungal serologies
  - B. Spirochetal Serologies
  - C. Brucella Serologies
  - D. HIV Serology

## Lyme Disease

- Early: 7-10 days (within 1 month)
  - Erythema Migrans (20% patients may not have rash or notice they have it)
- Early Disseminated (Weeks-Months)
  - Arthralgias, fevers, fatigue, bell's palsy, AV block, multiple EM lesions, etc....
- Late persistent disease
  - Monoarticular arthritis, usually involving knee
  - Meningoencephalitis, cognitive impairment
  - Treatment with one month of oral amoxicillin or doxycycline. IV for recurrent arthritis after oral therapy

## Chronic Gout – Serum Urate Lowering Therapies

- Probenecid: Uricosuric blocks tubular re-absorption of 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

## Chronic Gout – Serum Urate Lowering Therapies

- Allopurinol
  - Xanthine Oxidase Inhibitor
  - Blocks metabolism of purines to uric acid
  - Effective for both under-excretors 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

## 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)

## 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