

# Rheumatology Pearls

Primary Care Update  
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Paul Sufka, M.D.  
HealthPartners Rheumatology

No disclosures.

No off-label discussion.

## Topics

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- Common labs in Rheumatology
- Differentiating inflammatory from non-inflammatory arthritis
- Gout

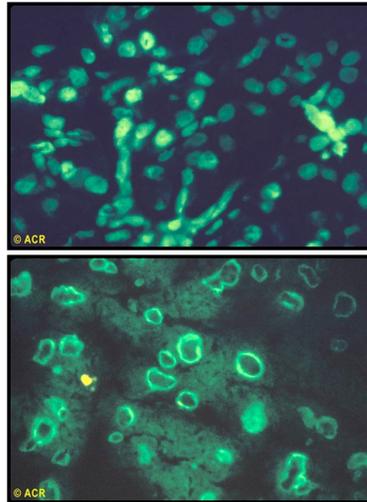
## Labs

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- ANA
- RF
- CCP

## ANA: Antinuclear Antibodies

- Autoantibodies that bind to contents of the cell nucleus
- Extremely common
  - Low titer (up to 1:160) - up to 20% normal individuals
  - Higher titers still found in up to 5% of normals
- Typically used to facilitate diagnosis of lupus and other connective tissue diseases.
- Negative ANA makes CTD highly unlikely, but positive doesn't rule in.



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## Some causes of positive ANA

- **Systemic autoimmune diseases**
  - SLE, Scleroderma, MCTD: nearly 100%
  - RA: 45%
  - Sjogren's, polymyositis, dermatomyositis, etc.
- **Organ specific autoimmune diseases**
  - Hashimotos, Graves', autoimmune hepatitis, PBC
- **Infections**
  - Viral: frequently seen w/ HCV, EBV, HIV, Parvovirus B19
- **Malignancy**
  - Other: IBD, pulmonary fibrosis

## When is an ANA indicated?

- Inflammatory polyarthritis
- Signs/symptoms that suggest SLE/ Sjogren's/Myositis/Scleroderma:
  - Raynaud's
  - Rashes
  - Oral ulcers
  - Eye inflammation
  - Sicca symptoms
  - Proximal muscle weakness
  - Cytopenias
  - Other organ involvement (nephritis)



Images: ACR Image Bank

## RF: Rheumatoid Factor

- Antibody to Fc portion of IgG
- Mostly used for diagnosis of rheumatoid arthritis
- Frequently seen in other rheumatic diseases and chronic inflammatory conditions
- Probably positive in ~4% of normal population, may increase to as much as 25% with aging

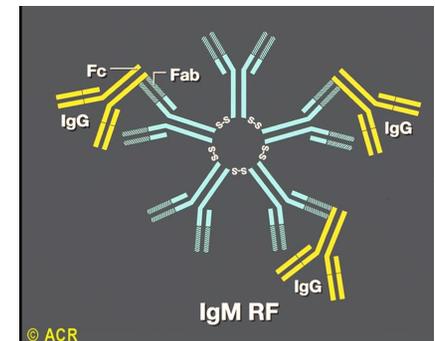


Image: ACR Image Bank

## Causes of Rheumatoid Factor

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- Rheumatic
  - RA: 26-90%
  - Sjogren's: 75-90%
  - Lupus: 15-35%
  - Others: MCTD, cryoglobulinemia, myositis, vasculitis
- Non-rheumatic
  - **\*\*\* Chronic Hepatitis C: 26-76% \*\*\***
  - Chronic Hep B, TB, endocarditis, syphilis
  - Pulmonary dz: sarcoid, pulmonary fibrosis, silicosis, asbestosis
  - Malignancy, PBC

## When is a Rheumatoid Factor Indicated?

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- When rheumatoid arthritis is suspected clinically
- In rheumatology, also helpful when looking for evidence of Sjogren's or cryoglobulinemia

## Cyclic Citrullinated Peptide (CCP) Antibodies

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- Strongly associated with rheumatoid arthritis and development of more aggressive/erosive disease
- Can be helpful in differentiating RA from other forms of arthritis, such as hepatitis C related arthritis (since RF often positive in both RA and Hep C)
- Often present for many years (with RF) before the onset of clinical arthritis

## Other notes on ANA and RF/CCP

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- No use in monitoring ANA titer or RF/CCP - not clinically useful
- Unless new symptoms occur, no reason to recheck ANA

## Arthritis history

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- Differentiate inflammatory vs non-inflammatory pain
- What is the pattern?
  - What joints are involved?
  - Acute, subacute, chronic? Additive, migratory, episodic?
  - Neck or back involved?
  - Tendons, enthesitis, or dactylitis?
- Other clues: Complete ROS

## Inflammatory pain

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- Improves with use
- Worsens with rest
- Prolonged AM stiffness (>30-60min)
- Synovial swelling with warmth
- Inflammatory effusions

## Noninflammatory pain

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- Worsens with use
- Improves with rest
- Minimal AM stiffness (<20min)
- Bony enlargement
- Crepitus, instability

## Recognizing joint inflammation

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Remember the 5 cardinal signs of inflammation:

1. Redness/erythema
2. Swelling
  - Look for loss of “dimples” around the joint & decreased skin lines over the joint
  - Feel for the edges of the joint to feel “squishy” or less distinct
  - Feel small joint swelling/effusions by pushing with one finger & sensing with the other
3. Tenderness
4. Heat
  - Normal joint should be cooler than surrounding tissues
5. Loss of function

## Loss of dimples around joint

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Image: ACR Image Bank

## Recognizing joint inflammation

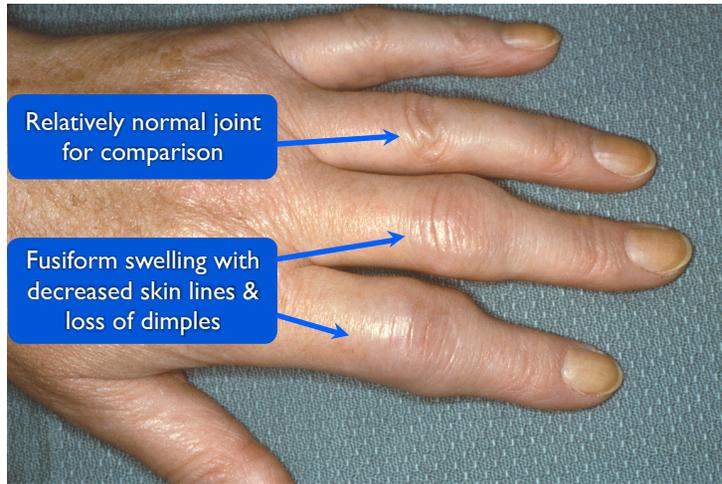


Image: ACR Image Bank

## Recognizing joint inflammation

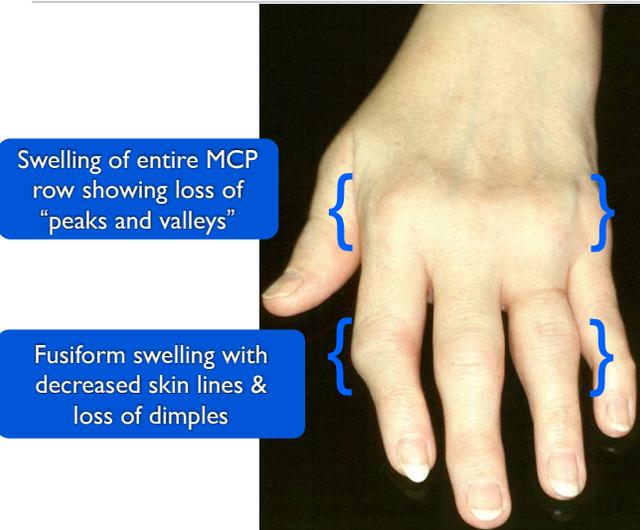


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## Rheumatoid arthritis



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## Osteoarthritis



Image: ACR Image Bank

## Osteoarthritis

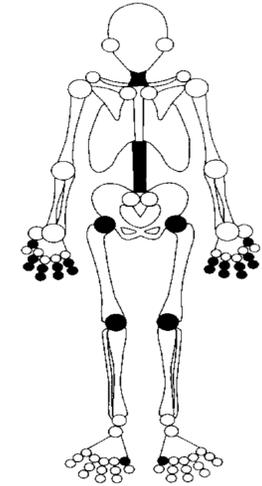
- Risk factors
  - Age (75% of pts >70yo)
  - Female
  - Hereditary
  - Mechanical stress (obesity, misalignments, injury)
  - Neuromuscular dysfunction
  - Metabolic (crystals, hemochromatosis)
  - Post-inflammatory



Image: ACR Image Bank

## Distribution of primary osteoarthritis

- Hands: DIPs, PIPs, CMC (base of thumb)
- Cervical and lumbar spine
- Hips
- Knees
- 1st MTP



## Most common patterns of inflammatory arthritis

- Monoarticular arthritis
- Asymmetric oligoarticular (2-4 joints)
- Symmetric polyarthritis
- Axial involvement

## Most Helpful Temporal Patterns

- Abrupt (<24 hrs): trauma, crystals, infection
- Migratory (few days in each joint): disseminated gonococcal infection, acute rheumatic fever, early Lyme
- Episodic/intermittent: crystals (gout, pseudogout), Lyme
- Additive: most common pattern & least specific

## Monoarthritis

- Most need to be aspirated
- Differential:
  - **INFECTION!!!**
  - **Gout**
  - **Pseudogout**
  - Fracture/hemarthrosis
  - Lyme
  - Osteoarthritis
  - Rarely: RA, psoriatic, reactive present as monoarthritis
- Workup:
  - Joint fluid: “the 3 C’s”
  - ESR/CRP
  - CBC, creatinine
  - Uric acid
  - +/- Lyme serologies/PCR
- Not indicated initially:
  - ANA, RF, CCP

## Synovial Fluid Analysis

“The 3 C’s”	Non-inflammatory	Inflammatory	Septic
Cell count/diff	<2000	2000 - ~50k	>50k
Crystals	None	+/-	+/-
Culture	-	-	Positive

## Oligoarticular arthritis

- Limited differential:
  - Crystals (gout, pseudogout)
  - Spondyloarthropathy (psoriatic, IBD, reactive)
  - Post-streptococcal & ARF
  - Lyme
  - Behcet’s
  - Gonococcal
  - Sarcoid
- Workup:
  - Varies greatly based on clinical suspicion

## Symmetric polyarthritis

- ROS may provide helpful clues
- A fair percentage is “seronegative” so a good exam is the most important part
- Limited differential:
  - Rheumatoid arthritis
  - SLE/other CTD
  - Hepatitis B/C
  - Viral (parvovirus)
  - Psoriatic
  - Vasculitis
  - Sarcoid
  - Still’s disease
- Initial workup:
  - CBC, creatinine, LFTs, UA
  - ESR/CRP
  - RF, CCP
  - Hepatitis B/C tests
  - ANA
  - +/- Parvovirus serologies
  - Joint xrays (esp hand/feet)
  - +/- CXR

## Quick review: rheumatoid arthritis

- RA affects ~1% of the population; female:male ratio is about 2:1
- Besides family history and genetics, smoking is the most important risk factor for development of disease
- RA is a symmetric inflammatory arthritis that mainly affects the small joints of the hands and feet, but larger joints and the cervical spine can also be affected
- Cartilage destruction and bone erosions are common, especially in patients with positive RF or CCP-antibodies
- Systemic manifestations include pulmonary disease, vasculitis, rheumatoid nodules, and eye disease
- Increased mortality is largely due to increased cardiovascular disease

Firestein, G. (2009). Kelly's Textbook of Rheumatology, 8th ed. Elsevier Saunders.

## ACR 2010 RA diagnostic criteria

New criteria are aimed at identifying newly presenting patients more quickly

### A. Joint involvement

- 1 large joint: 0 pts
- 2-10 large joints: 1 pt
- 1-3 small joints: 2 pts
- 4-10 small joints: 3 pts
- >10 small joints: 5 pts

### B. Serology

- Negative RF/CCP: 0 pts
- RF/CCP  $\leq$  3xNI: 2pts
- RF/CCP >3xNI: 3 pts

### C. Acute phase reactants

- Normal ESR/CRP: 0 pts
- Elevated ESR/CRP: 1pt

### D. Duration of symptoms

- <6 weeks: 0 pts
- $\geq$ 6 weeks: 1 pt

6 points needed for diagnosis

Exception: rheumatoid nodules or erosions present  
(also need to rule out other causes)

Arthritis Rheum 2010; 62(9):2569

## Multiple patterns of psoriatic arthritis

- DIP disease
- Oligoarthritis
- Polyarthritis
- Arthritis mutilans
- Dactylitis/tenosynovitis
- Enthesitis
- Axial disease



Images: ACR Image Bank

## Dactylitis



Image: ACR Image Bank

## DIP joint involvement

- If involved, think OA, psoriatic arthritis, gout
- If psoriatic arthritis, usually nail pitting is present
- DIPs spared in RA



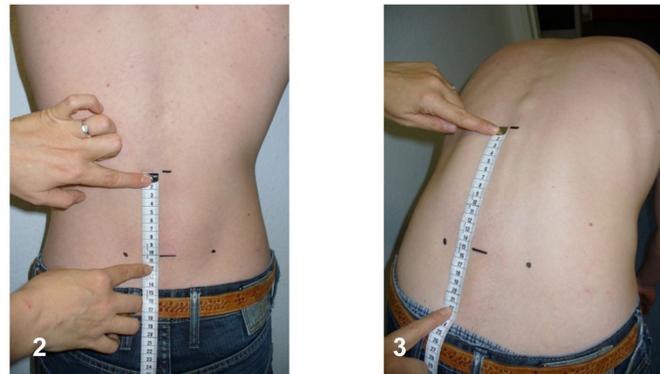
## Enthesitis



## Axial joint involvement

- Axial joint involvement, usually starting from the bottom up
- **Typical symptoms are inflammatory spine/buttock pain**
- Exam findings: decreased spine mobility, SI joint tenderness
- Associated with HLA-B27
  - Keep in mind HLA-B27 is positive in 8-10% of caucasians
- Confirmed radiographically

## Modified Schober's test



Sacroillitis



Normal



Images: ACR Image Bank

Squaring

Syndesmophyte

Romanus lesion  
"shiny corner"

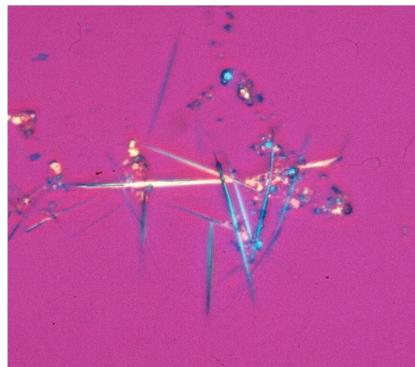


Image: ACR Image Bank

## Gout



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Images: ACR Image Bank

## Gout Review

- Gout is caused by crystal deposition of monosodium urate secondary to **hyperuricemia (uric acid >6.0mg/dL)**
- Acute gout typically presents as rapid onset of severe inflammation in the affected joint.
- In most cases the 1st metatarsophalangeal (MTP) joint is the first joint involved (podagra)
- The natural history of gout is to worsen over time, with more frequent and diffuse joint flares, and development of tophi
- Strongly correlated with the metabolic syndrome and increased risk of cardiovascular disease

## Gout Diagnosis

- Crystal proof of gout is preferred (although not always possible)



Arthritis Rheum 1998;41(4):736  
Image:ACR Image Bank

## Diagnostic “Rules” for Acute Gout

- Male sex: 2 pts
- Previous patient-reported arthritis attack: 2 pts
- Onset within 1 day: 0.5 pts
- Joint redness: 1.0 pts
- Involvement of 1st MTP: 2.5 pts
- HTN or  $\geq 1$  vascular syndromes present, including CHF: 1.5 pts
- Serum uric acid  $>5.88$  mg/dL: 3.5 pts
- Gout present in 80.4% with score  $\geq 8$
- Gout present in 2.8% with score  $\leq 4$
- Suggest joint aspiration for score 5-7

Arch Intern Med. 2010;170(13):1120-1126.

## Acute Gout Management

- **Steroid injection:** preferred if 1-2 joints involved
- **NSAIDs:** use with caution in elderly, kidney/liver disease, h/o bleeding
- **Colchicine:**
  - Label: 1.2mg (two tabs) at start flare, another 0.6mg one hour later
  - What we often do: 0.6mg once-twice daily until flare resolves
  - Will be most effective if started within 24 hours of onset of flare
  - Dosing may be limited by renal impairment; diarrhea common
  - Price can now limit use (Colcrys)
- **Prednisone:** usually need at least 20-40mg; caution in diabetes, infection, anxiety
- **Anakinra:** IL-1 receptor blocker (key cytokine in crystal arthritis), expensive but highly effective, given SQ daily, injection site reactions; caution in infection

NEJM 2011; 364:443  
Arthritis Res Ther 2007; 9:R28

## Chronic Gout Management

The most important part of chronic gout therapy is lowering the uric acid  $\leq 6.0$

## Chronic Gout Management

- **Reasons to start urate lowering therapy:**

- At least 2 attacks per year
- Tophi or erosive disease
- Nephrolithiasis
- Uric acid crystalizes at  $>6.0$ : lowering eventually reduces flares and causes tophi resorption
- Initiate therapy 2-4 weeks after acute flare resolved
- **Most patients require prophylaxis against gout flares for 1-6 months**
- Colchicine qday-BID preferred, can also use low dose prednisone or NSAIDs with appropriate caution



NEJM 2011; 364:443  
Images: J Musculoskel Med 2011;28:23

## Urate Lowering Agents

- **Allopurinol**

- Starting dose 50-100mg, increased q3-4 wks until serum urate  $\leq 6.0$
- Most patients need 300mg/day, but can dose up to 800mg with normal renal function
- Use with caution in impaired renal function, but recent study suggests may be safe to use with similar incidence of side effects
- Rash in ~2%; allopurinol hypersensitivity (can be life threatening) in 0.1%

- **Febuxostat (Uloric)**

- Second-line agent for when have contraindications (rash/hypersensitivity) or inadequate response to allopurinol
- Labeled as safe for  $GFR \geq 30$  or with mild-moderate hepatic impairment

NEJM 2011; 364:443  
Arthritis Rheum 2011; 63(2):412

## Final Pearls

- Since ANA is positive in about 20% of normal patients, it should only be checked when inflammatory arthritis or other autoimmune disease is suspected clinically.
- Be sure to check patients with a positive RF for hepatitis C.
- In chronic gout, the most important thing is to lower uric acid level below 6.0, but don't forget to have a plan to prevent/treat flares that occur in this process.