Mono-articular Joint Complaints

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  - Clinical focus: Transition Medicine
  - Research focus: MSK Ultrasound
Disclosures

- UpToDate: Author, Reviewer
“When an arthritis patient walks in the front door, I feel like leaving by the back…”
Objectives

1. Approach to the patient with monoarthralgia
2. Septic arthritis in detail
3. Microcrystalline arthritis in detail
4. Interspersed: Case-based questions
Making a Diagnosis

Clinical Assessment

Laboratory Testing

Diagnostic Imaging
Clinical Assessment

1. Pathophysiology
   • Inflammatory or non-inflammatory

2. Anatomy
   • Articular or not
   • Joint distribution

3. Chronology
   • Acute/explosive (hours or days)
   • Sub-acute (weeks)
   • Chronic/insidious (months or years)

4. Co-morbidities and risk factors
Acute Inflammatory Monoarthritis

Pain, warmth, swelling, and erythema, involving only one joint
Exam: Confirm “Mono” “Arthritis”

1. Perform a complete joint exam
2. How do you assess for effusion?
3. Examination should distinguish arthritis from peri-arthritis (bursitis or tendonitis)
4. Why is active versus passive ROM important?
Acute Monoarthritis: Likely Causes

1. Septic arthritis
   • Staph and Strep species (>90%)
   • Neisseria species
   • Other gram negatives

2. Microcrystalline disease
   • Acute gouty arthritis
   • Acute pseudo-gouty arthritis

3. Systemic rheumatic disease of one joint
   • Spondyloarthritis (PsA, ReA, AS, IBD)
   • Rheumatoid arthritis

4. Trauma or hemarthrosis
It’s swollen, now what?

1. Arthrocentesis (pre-antibiotics)

2. What do you need?
   - Syringes, needles, and tubes
   - Someone who knows how to do it.
   - Universal precautions
   - Prep: cleanser, lidocaine, gauze, and chuck
   - Give anesthesia time!

3. Any word of advice?

4. What do you send it for?
## Fluid WBC Analysis

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Not Inflamed</th>
<th>Sterile Inflamed</th>
<th>Septic Inflamed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WBC</strong></td>
<td>&lt;200</td>
<td>Up to 1K</td>
<td>1K – 100K</td>
<td>&gt;30K</td>
</tr>
<tr>
<td><strong>% PMN</strong></td>
<td>&lt;25%</td>
<td>25 – 50%</td>
<td>25 – 90%</td>
<td>&gt;90%</td>
</tr>
</tbody>
</table>
Fluid Crystal Analysis

A  B  C

© ACR
Fluid Crystal Analysis

Calcium Pyrophosphate Dihydrate (Pseudogout)

Monosodium Urate (Gout)
Interpretation of Inflamed Fluid

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<thead>
<tr>
<th>Gram Stain</th>
<th>Crystal Analysis</th>
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<tr>
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<td>Negative</td>
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<tr>
<td>Negative</td>
<td></td>
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<tr>
<td>Positive</td>
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## Interpretation of Inflamed Fluid

![Image of infected cells]

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<tr>
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Positive and negative results can indicate the presence of infection.
## Interpretation of Inflamed Fluid

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<td>Crystals AND Septic Joint</td>
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<th>Crystal Analysis</th>
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<tr>
<td>Negative</td>
<td>Negative: Many Options: RA, PsA, Lyme</td>
</tr>
<tr>
<td>Positive</td>
<td>Septic Joint</td>
</tr>
</tbody>
</table>
Risk Factors for Septic Arthritis

1. Immune-suppressed patient
   • Medications: steroids, chemotherapy, DMARDs
   • Co-morbidities: diabetes mellitus, cirrhosis, renal disease, asplenism, inherited immunodeficiency, HIV

2. Prosthetic joint: recent or established

3. Recent sepsis or invasive procedure

4. Intravenous drug user

5. Pre-existing damaged joints

6. Coagulopathy
Management: Septic Arthritis

1. Antibiotics
   - Empiric therapy: 3rd gen cephalosporin + vancomycin
   - Tailored therapy is ideal (beta-lactam)
   - Inferior alternatives: aminoglycosides, quinolone

2. Serial drainage with WBC analysis

3. Review all joints daily

4. Search for sources of infection

5. Get orthopedics on board if…
   - Any joint other than the knee
   - Any prosthetic joint is involved
   - The knee in a young person
   - Refractory to drainage and Abx
   - Osteomyelitis is present
Myth-Busting: Gout
Basic Principles of Gout

1. Clinical gout results from the convergence of two processes
   - Chronic hyperuricemia, with crystal deposition
   - Inflammatory response to the crystals
   - **NO SINGLE MEDICATION ADDRESSES BOTH**

2. There are different stages of gout
   - Clinically silent hyperuricemia
   - Intermittent acute gouty arthritis/tendinitis/bursitis
   - Chronic gouty arthropathy (with or without tophi)
Serum Uric Acid Measurement

1. Uric acid level stratifies a patient’s risk for developing clinical gout over a lifetime
   • *Hyperuricemia is not diagnostic of gout*
   • *Normal uric acid does not exclude gout*

2. Many factors affect a spot serum uric acid
   • Hydration and dietary status
   • Acute changes in renal function
   • Medications (esp. diuretics)
   • *Uric acid frequently DROPS in a gout attack*

3. Uric acid should also be used as a target of treatment in a patient with established gout.
   • *Goal: uric acid <6 mg/dL, or <5 mg/dL if tophi*
Hyperuricemia: Risk Factors

1. Un-modifiable risk factors
   • Family history of gout or hyperuricemia
   • Age and male gender
   • Co-morbidities: cardiac disease, renal insufficiency, heme malignancy, inherited metabolic defects

2. Modifiable risk factors
   • Diet: alcohol (beer), shellfish, organ meat, red meat, heavy dairy, high-fructose corn syrup
   • Medications: diuretics, cyclosporine, HAART
   • **Obesity**
   • Lead exposure
Acute Gouty Arthritis

1. Acute inflammatory arthritis/tendinitis/bursitis
   - Usually mono- or oligo-articular
   - Aspirate: inflammatory fluid with uric acid crystals
   - DON’T FORGET ABOUT PSEUDOGOUT!

2. Triggers are mostly innocuous or unpredictable
   - Recent trauma or repetitive overuse
   - Systemic inflamed state: surgery, infection
   - Fluctuations in uric acid: fluid shifts, diuretics, or someone messed with the allopurinol
   - Dietary indiscretion?

3. Treatment: Target the inflammation!
Pseudogout Arthritis: Risk Factors

1. History of pseudogout
2. Presence of chondrocalcinosis may be helpful
3. Concurrent trauma or inflamed state
4. Usually limited to the elderly
5. Altered metabolic states
   • Hemochromatosis
   • Hyper-PTH
   • Thyroid abnormalities
   • Low phosphate or magnesium
   • Acromegaly
Chondrocalcinosis
Acute Crystalline Arthritis: Themes

Management principles for gout or pseudogout

1. Early treatment is the most successful
2. It gets better on its own with time
3. Rest, ice, and analgesics help almost everyone
4. Try to avoid the orthopedics service
5. Don’t mess with the allopurinol in patients with gout
Acute Crystalline Arthritis: Medications

1. NSAIDS: assess co-morbidities and risks
   - Indomethacin 50 mg TID or 75 mg BID remains the most effective NSAID for acute gout

2. Corticosteroids: low doses are safe and effective
   - Intra-articular: directed therapy
   - Quick: IM/IV methylprednisolone 40 mg x1, then oral
   - Oral: Prednisone 20-30 mg daily, tapered by 5-10 mg every 4 days for a total of 12-16 days of treatment
   - Oral methylprednisolone is an alternative to prednisone in those with liver disease or a poor response to prednisone.
Acute Crystalline Arthritis: Medications

3. Oral colchicine: not as good for a bad attack
   • NEVER give intravenously
   • Now available in liquid formulation
   • 0.6 mg BID-TID for 1-2 days, then QD-BID
   • Expensive: Patient will often be unable to fill without a PA. Probenecid/colchicine 500/0.5 is cheaper.
   • CAUTION in renal compromise
   • CAUTION with medication interactions
   • Do NOT dose to the point of diarrhea!
   • Prophylaxis discussed later…
Acute Crystalline Arthritis: Pearls

1. Uric acid level may not be useful in acute gout.

2. Distribution of involvement may be helpful:
   - Most common site: Peripheral extremities
   - Can include tendon sheaths and bursae
   - Rarely occurs centrally: SI joints, pubis, or disks

3. May co-exist with septic arthritis or other forms of crystalline arthritis (CPPD)

4. In bad polyarticular disease, patients can demonstrate features of sepsis.

5. Management of hyperuricemia is often unnecessary in the acute setting.
Chronic/Recurrent Gout
Chronic/Recurrent Gout

1. Principle: A disease of hyperuricemia
   - Treating only inflammatory episodes is effective for symptomatic gout but insufficient for chronic disease
   - Hyperuricemia associated with many disease states:
     ✓ Chronic arthropathy
     ✓ Chronic kidney disease
     ✓ Cardiovascular disease
2. Who should get treatment for hyperuricemia?

- All patients with clinical gout should be encouraged to modify risk factors: weight, diet, and possibly diuretics
- Indicators for anti-hyperuricemic medication:
  - Tophi
  - Erosive arthropathy
  - Multiple attacks
  - High recurrence risk
  - Uric acid nephropathy
  - Nephrolithiasis
Medications for Chronic Gout

1. Treat hyperuricemia!
   - Explain that treatment is usually “for life”
   - Goal uric acid: <6 mg/dL, or <5 mg/dL if tophi present
   - Almost all compliant patients can achieve this!

2. The agents
   - Xanthine oxidase inhibitors: allopurinol, febuxostat
   - Uricosurics: probenacid, losartan, Vit C, lesinurad
   - Recombinant uricase: pegloticase, rasburicase

3. Don’t lose your patient to a gout attack!!
   - Early in treatment: patients at high risk for gout attack
   - *Almost always co-preserve an anti-inflammatory such as low-dose colchicine, typically for months.*
1. Properly used, allopurinol is the most **effective** and **safest** agent for most patients with gout.

   • Allopurinol is generally safe, even at high doses.
   • OK to titrate allopurinol >300 mg daily, even in patients with CKD
   • OK to take allopurinol as a single combined dose, although absorbance is better with split dosing (at high doses).
   • **START LOW AND GO SLOW**
     - Start with 100 mg daily (50 mg in CKD)
     - Each month, test for uric acid and for toxicity (CMP, CBC/diff)
     - Based on labs, consider increasing daily allopurinol by another 100 mg (or 50 mg in CKD)
     - Titrate until the desired uric acid target is reached, then congratulate the patient, maintain the allopurinol, and reduce lab frequency to 4-6 months
     - Continue colchicine 6-12 months after achieving the uric acid target, then taper it off (e.g. every other day x1 month)
Allopurinol: Myth-busting

2. Try not to fumble the communication!
   • Usually no need to stop meds that raise uric acid
   • *Avoid losing your patient to an acute gout attack!*
     ✓ Co-treat with prophylactic agent (e.g. colchicine)
     ✓ This can be low-dose, and needs to be for months
     ✓ Rapid change in allopurinol can trigger an attack
   • Debate about WHEN to start treatment:
     ✓ I prefer to postpone ULT until after the acute attack resolves. It simplifies the message and allows the patient to demonstrate compliance.
   • Treatment failure?
     ✓ Under-dosing
     ✓ Non-adherence
3. Allopurinol toxicity

- Allopurinol undergoes mostly renal excretion, so titrate with caution in patients with CKD
- *Only very, very rarely is allopurinol nephrotoxic*
- Changes in LFTs or blood counts can be dose limiting
- Rash (3-5%) can portend a more serious reaction
- Slow dose escalation reduced risk of severe reaction
- Allopurinol hypersensitivity is severe and can be fatal: SJS, TEN, DRESS, DIL, ANCA vasculitis
- *Use allopurinol with caution, or not at all, in patients with high-risk HLA-B*5801: Korean, Han Chinese, Thai
Serum Urate Lowering with Allopurinol and Kidney Function in Type 1 Diabetes


Effects of Allopurinol on the Progression of Chronic Kidney Disease

Cardiovascular Safety of Febuxostat or Allopurinol in Patients with Gout

William B. White, M.D., Kenneth G. Saag, M.D., Michael A. Becker, M.D., Jeffrey S. Borer, M.D., Philip B. Gorelick, M.D., Andrew Whelton, M.D., Barbara Hunt, M.S., Majin Castillo, M.D., and Lhanoo Gunawardhana, M.D., Ph.D., for the CARES Investigators*

N Engl J Med 378;13  NEJM.org  March 29, 2018

Assessment of Cardiovascular Risk in Older Patients With Gout Initiating Febuxostat Versus Allopurinol
Population-Based Cohort Study

Circulation. 2018;138:1116–1126. DOI: 10.1161/CIRCULATIONAHA.118.033992
My Conclusions re: ULT

1. Allopurinol remains the preferred xanthine oxidase inhibitor when choosing uric acid lowering therapy.

2. Allopurinol is generally safe in doses greater than that traditionally thought.

3. Allopurinol does not appear to preserve kidney function, although this conclusion was based on patients with uric acid levels mostly in the normal or slightly high range.

4. Febuxostat should not be cast aside entirely
   - Important role as the only feasible option in most patients with allopurinol hypersensitivity
   - Studies have shown conflicting evidence about mortality risk in patients on febuxostat compared to allopurinol
   - Reserve extra time for conversation about risks/benefits, especially in patients with cardiovascular risk factors
Conclusions: Gout

1. Try to secure a crystal-proven diagnosis
2. Non-invasive imaging modalities help diagnose gout and determine extent of disease burden
3. Treat inflammatory phase of acute gouty arthritis with anti-inflammatory agents
   • NSAIDs, corticosteroids, colchicine, ice, rest
4. Use anti-hyperuricemic agents when indicated
   • Tophi, erosions, nephrolithiasis, multiple attacks
   • Allopurinol, febuxostat, probenecid, pegloticase
5. Overlap #3 and #4, often for months
6. PLEASE don’t mess with my allopurinol
Case Examples
58 y.o. alcoholic man presents to clinic with rapid severe knee pain, swelling, and altered gait. He has psoriatic arthritis, on adalimumab. No other complaints. Imaging as shown. Joint aspiration: 30 cc non-bloody cloudy fluid, crystals (shown), 50,000 WBC/mm³, 95% PMN.

**What is the most appropriate next step?**

A. Contact orthopedics for “washout”
B. Send home with Rx for cefalexin
C. Intra-articular steroid injection
D. Wait for gram stain results before A-C
Crystal Analysis
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Question 2:

A 42 year old otherwise healthy woman presents with mild left knee discomfort but lots of swelling. The swelling has been progressing for weeks, without much pain or any associated systemic symptoms. Joint aspiration: 90 cc non-bloody slightly cloudy fluid with 12,000 WBC/mm³, 65% PMN, no crystals, and negative Gram stain. Which of the following would be most likely to provide a diagnosis?

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B. Serum lyme serology
C. Serum ANA test
D. MRI of the affected knee
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Comments on Lyme Testing

1. Too big a topic for this talk
2. Proper sequence: Start with a screening ELISA, and then do a Western blot only as a confirmatory test.
3. Lyme result can be negative in early disease (*immunologic window*), but are invariably positive in established disease.
4. Avoid fishing expeditions and “specialty lyme laboratories”, especially in patients without clinical features of Lyme disease.
5. Be prepared to interpret a positive result!
One dot is placed randomly within the county of residence for each confirmed case. Though Lyme disease cases have been reported in nearly every state, cases are reported based on the county of residence, not necessarily the county of infection.
Reported Cases of Lyme Disease — United States, 2018
When to Call Us

1. Any rheumatology patient
2. Any complex patient
3. The exam is equivocal
4. You would like to have procedural oversight or to review synovial fluid yourself.
5. Tap is dry, but exam suggests fluid is present
6. At 2 A.M., remember that ortho is in-house 😊
Summary

1. History and exam should prove that acute monoarthritis is “acute” “mono” and “arthritis.”
2. A hot joint is septic until proven otherwise.
3. Arthrocentesis with synovial fluid analysis is the procedure of choice and guides empiric therapy.
4. Don’t mess with the allopurinol.
Disclosures

• UpToDate: Author, Reviewer
Additional Reading for William Osler


