COMMON MISCONCEPTIONS IN RHEUMATIC DISEASE

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Common Misconceptions in Rheumatic Disease

- Gout
- Osteoarthritis
- Polymyalgia Rheumatica (PMR)
- Temporal Arteritis
- Rheumatoid Arthritis
Case 1: Recurrent podagra

- 68 year-old man with his 3\textsuperscript{rd} episode of acute pain and swelling in his first toe in the last 6 months
- Prior episodes resolved with OTC ibuprofen
- PMHx: HTN, CHF, CKD on HCTZ, ARB, ASA, prn ibuprofen
- Examination: pain/swelling/erythema over 1\textsuperscript{st} MTP; no tophi
Gout - “The Disease of Kings”

e.g., Henry VIII

Other famous gout sufferers: Alexander the Great, Christopher Columbus, Benjamin Franklin & Isaac Newton
Gout – Misconceptions

Who gets gout?

Gout is the “disease of kings”
- Gout is common across many socio-economic groups

Any adult is at risk for gout.
- Gout is quite rare among pre-menopausal women

Gout is a disease of obese drinkers.
- Alcohol (especially beer) & metabolic syndrome are risk factors but there are many others (and lean, non-drinkers also get gout)

Gout is a disease of middle-aged men
- Gout prevalence rises dramatically with age
Who gets gout? (continued)

Associations:
- Hyperuricemia
- CAD/HTN/diuretic use
- Renal disease
- Diabetes
- Diet: Alcohol/meat/seafood/fructose → risk
  Coffee/dairy → risk
- Trauma/Stress/Immobilization
- Age
- Heredity (especially among males in a family)
- Transplant recipients treated with cyclosporine
Gout: Prevalence

- Prevalence: 3.9% of adult population in U.S. & rising (Zhu et al., Arthritis Rheum. 2011;63:3136)

- Diuretic use, hypertension, obesity, transplantation medications → more gout

- Increasing sugar-sweetened soft drink consumption (with high fructose corn syrup) may be contributing to increasing hyperuricemia & gout (Choi HK, et al. BMJ 2008; 336;309)
Age is a powerful risk factor for gout

Prevalence (per 1000 patients)

Men | Women | Total

Age group (years)

Underwood M BMJ 2006;332:1315-1319
Gout – More misconceptions:
How to establish the diagnosis

The diagnosis requires aspiration and crystal-proof
- criteria do not require it
- standard of care allows clinical diagnosis

Elevated serum uric acid levels are diagnostically helpful
- most people at risk for gout for whom there’s suspicion of the disease have an elevated uric acid level

X-rays are diagnostically helpful in acute gout but not in chronic disease
- It’s the other way around!

Diet is key in the development of hyperuricemia & gout
- Genes probably matter more - diet accounts for ≤0.3% of variance in serum urate; genome wide single nucleotide variation accounted for nearly 25% \((BMJ 2018; 363: k3951)\)
“The Gout” by James Gillray, 1799
Diagnosis: Crystal proof is the gold standard

But, crystals need not be intracellular
ACR Criteria for the Diagnosis of Gout (1977)

A. Presence of MSU crystals in joint fluid, and/or
B. Presence of a tophus proven to contain MSU crystals, and/or
C. Presence of 6 of the following 12 clinical, laboratory, and radiographic phenomena:
   a. More than 1 attack of acute arthritis
   b. Development of maximal inflammation within 1 day
   c. Attack of monarticular arthritis
   d. Observation of joint erythema
   e. Pain or swelling in the first MTP joint
   f. Unilateral attack involving the first MTP joint (podagra)
   g. Unilateral attack involving tarsal joint
   h. Suspected tophus
   i. Hyperuricemia
   j. Asymmetrical swelling within a joint on x-ray films
   k. Subcortical cyst without erosions on x-ray films
   l. Negative culture of joint fluid for microorganisms during attack of joint inflammation

ACR, American College of Rheumatology; MSU, monosodium urate; MTP, metatarsophalangeal.

Table 2 The ACR/EULAR gout classification criteria*

<table>
<thead>
<tr>
<th>Step 1: Entry criterion (only apply criteria below to those meeting this entry criterion)</th>
<th>Categories</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least 1 episode of swelling, pain, or tenderness in a peripheral joint or bursa</td>
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<table>
<thead>
<tr>
<th>Step 2: Sufficient criterion (if met, can classify as gout without applying criteria below)</th>
<th>Categories</th>
<th>Score</th>
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</thead>
<tbody>
<tr>
<td>Presence of MSU crystals in a symptomatic joint or bursa (ie, in synovial fluid) or tophus</td>
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</table>

<table>
<thead>
<tr>
<th>Step 3: Criteria (to be used if sufficient criterion not met)</th>
<th>Categories</th>
<th>Score</th>
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<tbody>
<tr>
<td>Clinical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pattern of joint/bursa involvement during symptomatic episode(s) ever</td>
<td>Ankle or mid-foot (as part of monoarticular or oligoarticular episode without involvement of the first metatarsophalangeal joint)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Involvement of the first metatarsophalangeal joint (as part of monoarticular or oligoarticular episode)</td>
<td>2</td>
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<tr>
<td></td>
<td>One characteristic</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Two characteristics</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Three characteristics</td>
<td>3</td>
</tr>
<tr>
<td>Characteristics of symptomatic episode(s) ever</td>
<td>One typical episode</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Recurrent typical episodes</td>
<td>2</td>
</tr>
<tr>
<td>Erythema overlying affected joint (patient-reported or physician-observed)</td>
<td></td>
<td></td>
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<tr>
<td>Can’t bear touch or pressure to affected joint</td>
<td></td>
<td></td>
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<tr>
<td>Great difficulty with walking or inability to use affected joint</td>
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<td></td>
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<tr>
<td>Time course of episode(s) ever</td>
<td></td>
<td></td>
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<tr>
<td>Presence (ever) of ≥2, irrespective of anti-inflammatory treatment:</td>
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<td></td>
<td>Time to maximal pain &lt;24 h</td>
<td></td>
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<td></td>
<td>Resolution of symptoms in ≤14 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Complete resolution (to baseline level) between symptomatic episodes</td>
<td></td>
</tr>
<tr>
<td>Clinical evidence of tophus</td>
<td>Present</td>
<td>4</td>
</tr>
<tr>
<td>Draining or chalk-like subcutaneous nodule under transparent skin, often with overlying vascularity, located in typical locations: joints, ears, olecranon bursae, finger pads, tendons (eg, Achilles)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laboratory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum urate: Measured by the uricase method.</td>
<td>&lt;4 mg/dL (&lt;0.24 mmol/L)†</td>
<td>-4</td>
</tr>
<tr>
<td></td>
<td>6–&lt;8 mg/dL (0.36–&lt;0.48 mmol/L)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>8–&lt;10 mg/dL (0.48–&lt;0.60 mmol/L)</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>≥10 mg/dL (≥0.60 mmol/L)</td>
<td>4</td>
</tr>
<tr>
<td>Synovial fluid analysis of a symptomatic (ever) joint or bursa (should be assessed by a trained observer)†</td>
<td>MSU negative</td>
<td>-2</td>
</tr>
<tr>
<td>Imaging§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imaging evidence of urate deposition in symptomatic (ever) joint or bursa: ultrasound evidence of double-contour sign¶ or DECT demonstrating urate deposition**</td>
<td>Present (either modality)</td>
<td>4</td>
</tr>
<tr>
<td>Imaging evidence of gout-related joint damage: conventional radiography of the hands and/or feet demonstrates at least 1 erosion††</td>
<td>Present</td>
<td>4</td>
</tr>
</tbody>
</table>

http://goutclassificationcalculator.auckland.ac.nz/
Radiographs in acute gout: effusion/soft tissue swelling
Tophaceous gout: an indication for urate-lowering therapy
Case 2

A 79 y/o woman with hyperlipidemia on long-term statin treatment presents with sudden onset of diffuse aches and pains, especially in the shoulders and neck, and poor sleep. Physical examination is normal.

A number of conditions/questions are considered:

- Fibromyalgia (but no tender points)
- Statin-induced myalgia (but statin therapy unchanged for many years)
- Polymyalgia rheumatica (PMR)
- If PMR suspected, should she have a temporal artery biopsy?
PMR: Misconceptions

**PMR is a muscle disease**
- The name is confusing but NOT a muscle disease
- Pain is referred to muscles from inflamed joints, bursae, tendons
- Muscle is normal (motor exam, CK, EMG, biopsy)

**CRP is better than ESR (or vice versa) for dx or to monitor**
- The ideal inflammatory marker for PMR is not known
- Recommendation: pick one and go with it

**Treat to normalize ESR**
- Recommendation: treat the patient, not the ESR
- ESR rises with age (to correct: age/2) so driving the ESR to < 20 mm/hr is likely to provide risk > benefit

**Treat PMR as Temporal Arteritis until temporal artery biopsy returns negative**
- "pure" PMR does not require a biopsy or high dose steroids
• CRP more sensitive (98.9% vs. 91.5%) and predicted relapse better than ESR

• ESR reflected response to treatment better (ESR high in 13%, CRP in 42% after 4 weeks of treatment)

• IL-6 was even better: persistent elevation predicted relapse
Should Temporal Arteritis be entertained in all patients with PMR?

• Older literature: up to 15% of patients with PMR have temporal arteritis

• Larger studies suggest the “15%” rate may be an over-estimation:
  - 4.4% of 287 “pure” PMR patients had TA by bx
    (Myklebust Br J Rheumatol 1996;35:1161)

• The association is real:
  - vigilance is warranted in PMR
  - low incidence of “arteritic” complications in pure PMR
  - data do not support routine TA biopsy in all PMR
Other considerations in this case

**Fibromyalgia?**
- The latest criteria do not require tender points
- They require widespread pain and chronic, unexplained somatic complaints (e.g., fatigue, waking unrefreshed, cognitive dysfn)
- New onset fibromyalgia in a 79 y/o woman is unusual!

**Statin-induced myalgia after many years?**
- Statin-induced muscle toxicity may occur at any time (but usually early)
- May occur after months to years especially if dose is escalated or an interacting drug (e.g., clarithromycin) is added
An 82 y/o man presents with headache and jaw pain.

Temporal arteritis is suspected – how do these details help?

- A history of headaches for years
- His jaw pain occurs with the first bite rather than after a bit of chewing
- Another explanation for jaw pain
- A history of recent diplopia
- A normal ESR
Temporal arteritis: Misconceptions

The diagnosis of GCA is unlikely in absence of arteritic symptoms (eg, headache, jaw claudication)

- Prominent constitutional symptoms are common and may dominate the clinical presentation

- Includes: FUO, FTT, malaise, weight loss, anorexia

**Steroid-sparing treatment is warranted with initial treatment**

- No compelling evidence to support immediate, concomitant steroid-sparing agent (but this could change!)

The temporal arteries should be abnormal in TA

- A normal examination is the rule

Jaw pain = temporal arteritis

- It’s jaw claudication that’s suggestive
Temporal arteritis: defined

ACR Classification Criteria

- Age >50
- New headache
- Abnormal temporal artery (e.g., tender, diminished pulse)
- ESR > 50 mm/hr
- Positive biopsy (mononuclear cell infiltrate, granulomatous inflammation, giant cells)

With at least 3/5, Se=93%, Sp= 91%

For studies

To distinguish TA from other types of vasculitis

Criteria perform poorly in clinical practice
Temporal arteritis

Beyond the criteria: 2/3 female, ↑N. European descent, 15-25/100,000 among >50 y/o adults; target vessel restriction are prominent

Local features ("arteritic")
- visual loss/ION
- scalp, tongue necrosis
- jaw claudication
- cranial neuropathies
- aortitis, other arteritis

Systemic features
- PMR
- Fever
- Anorexia, wt. loss
- Abnormal LFTs (AP)
- Anemia (ACD)
Other presentations of temporal arteritis

- Fever of unknown origin
- CVA, TIA, diplopia, peripheral neuropathy
- Non-productive cough
- “SUO” – sed. rate of unknown origin (rare!)
- Incidental biopsy: e.g., gall bladder
- Weight loss, anorexia
Temporal artery findings in temporal arteritis

- prominent
- beaded
- tender
- pulseless
- erythematous
- irregular

But... exam often normal!
Temporal artery findings in temporal arteritis: scalp necrosis
Temporal Artery Biopsy

Transmural inflammation with giant cells at media-intima border, and narrowed lumen.  
What is the clinical utility of history, exam & ESR in the diagnosis of temporal arteritis?

- 21 studies between 1966 & 2000, n = 2680, with temporal artery biopsy information, 39% of referred patients had temporal arteritis (nearly all by biopsy) 
  
  \[ Smetana, JAMA 2002;287:92 \]

- History: jaw claudication and diplopia - \( \uparrow \) likelihood \( (LR = 4.2 \text{ & } 3.4) \), respectively)

- Examination: normal temporal arteries - \( \downarrow \) likelihood \( (LR = 0.53) \) 
  presence of beading, prominence, tenderness - \( \uparrow \) likelihood \( (LR = 4.6, 4.3, 2.6) \)

- ESR: normal value markedly reduced likelihood \( (LR = 0.2) \)
How is temporal arteritis treated?

• Gold standard: corticosteroids (but no controlled trials)
  - prednisone – 1 mg/kg/d (e.g., 40 to 80 mg/day) x 4-6 weeks, then taper by 5-10% every 2-4 weeks
  - duration of treatment: usually (but not always) years
  - parenteral corticosteroids if visual symptoms present
  - QOD prednisone not as effective
Are steroids enough?
- Once vision lost, usually permanent
- Treatment is to preserve vision in the other eye
- Effects on great vessels uncertain

Aspirin to preserve vision? – conflicting study results; most recent guidelines defer to other CV indications
(Rev Med Interne. 2016;37(3):154)

What about steroid sparing treatment?
- Methotrexate – conflicting results – 3 RCTs → 2 negative, 1 positive; meta-analysis suggests positive effect
(Arthritis Rheum 2007;56:2789)
- Tocilizumab (Actemra) – anti-IL-6 agent – FDA-approved in 2017 for TA - for all? For steroid-sparing effect?
Case 4: Polyarthritis

68 year-old woman complaining of fatigue and painful swelling in the hands, wrists and ankles for the last 2 months, now unable to help daughter with her grandkids

- Minimally improved with OTC ibuprofen
- PMHx: neg
- SHx: 50 pack years of smoking
- Examination: swelling, tenderness and loss of motion in MCPs, PIPs, wrists, & ankles

Questions:
- What are the most likely diagnostic possibilities?
- What work-up is appropriate?
A good story for Rheumatoid Arthritis (RA)

Consider:
- SLE, other rheumatic disease
- viral infection (parvovirus, hepatitis B, etc)
- fibromyalgia
- crystal-induced disease
- “inflammatory osteoarthritis”
Criteria for RA

The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for RA

Criteria to apply to those who:

- have at least 1 joint with definite clinical synovitis
- synovitis not better explained by another disease

A score of 6 out of 10 is needed for classification of a patient as having definite RA

A. Joint involvement -
   - 1 large joint: 0
   - 2-10 large joints: 1
   - 1-3 small joints: 2
   - 4-10 small joints: 3
   - >10 joints (at least 1 small joint): 5
Criteria for RA (cont’d)

B. Serology –
- RF and anti-CCP both negative: 0
- Low titer positive RF or anti-CCP: 2
- High titer RF or anti-CCP: 3

C. Acute-phase reactants
- CRP and ESR both normal: 0
- Either CRP or ESR elevated: 1

D. Duration of symptoms
  <6 weeks: 0
  ≥ 6 weeks: 1
RA Misconceptions

RA is erosive, nodular, “obvious”
- May be subtle!

RA occurs in young women
- Peak onset: ages 30-50; but 1/3 are > 60 for new dx
- Prevalence: 5% or more among those >65
- About 1 in 4 patients with RA is male

RF & anti-CCP are highly reliable
- RF only 65% sensitive, 85% specific
- anti-CCP has similar sensitivity; 95% specific

ESR & CRP are highly reliable
- Variable sensitivity; nonspecific

Treat with high dose steroids
- ≤ 20 mg/d of prednisone enough
Case 5: Polyarthralgia

72 year-old woman with hip, knee and hand pain for several years, perhaps 10 years with “swelling” of his fingers.

• Symptoms are worse at night, with use, after sitting still, mildly better with acetaminophen

• Examination: bony enlargement of proximal and distal interphalangeal joints (PIPs & DIPs), loss of motion in hips and knees

• X-rays show typical findings of osteoarthritis

• What diagnostic tests are warranted? What treatment is appropriate? Should she be referred to an Orthopedist, a Rheumatologist, or both? Or, neither?
A good story for osteoarthritis (OA)
OA Misconceptions

- **OA is an inevitable part of aging**
  - Common but not inevitable
- **OA does not occur in young/middle-aged adults**
  - It does, but then it deserves an explanation
- **There is no treatment for OA**
  - There is no cure, but there are treatments
- **Indications for surgery are determined by the surgeon**
  - Determined **together**: by patient & surgeon
OA questions

- Diagnostic testing?
  - X-rays to confirm but largely unnecessary when story is so good in older individual
  - may be important if “too young for OA” or atypical locations

- Refer to Orthopedist? If surgery/procedure under consideration (see Indications, next slide)

- Refer to Rheumatologist? To help with decision for surgery, r/o other conditions if diagnosis is uncertain, procedure (joint injection)
Treatments for OA

• Non-medications
  • loss of excess weight
  • Exercise/Physical Therapy
  • Orthotics/Braces/Splints/Occupational Therapy
  • Yoga, Tai Chi, Aquatic Therapy

• Medication
  • Analgesics, Anti-inflammatory, Duloxetine, Gabapentin

• Surgery
  • Joint replacement
  • Indications: Failed other Rx; poor quality of life (pain, declining function)
    - imaging compatible with end-stage disease
    - good surgical candidate…..and willing
Secondary OA

- Consider when OA present in atypical location or atypical patient (e.g., elbow, young adult)

THE CHARMIN

- Trauma
- Hypermobility
- Endocrinopathy
- Crystal-induced
- Hemarthrosis
- Avascular necrosis
- Rheumatic disease
- Metabolic (esp. iron overload)
- Infection
- Newborn (congenital) or No good reason
Case 6: Recurrent podagra (revisited)

- 68 year-old man with his 3rd episode of acute pain and swelling in his first toe in the last 6 months
- Prior episodes resolved with OTC ibuprofen
- PMHx: HTN, CHF, CKD on HCTZ, ARB, ASA, prn ibuprofen
- Examination: pain/swelling/erythema over 1st MTP; no tophi
- What is the best treatment for his acute symptoms?
- What is the best treatment to prevent recurrence?
Acute gout treatment: misconceptions

*Indomethacin is the best treatment for acute gout.*
- It works well but it’s by far the most toxic NSAID

*High-dose colchicine is an effective and well-tolerated treatment option for acute gout.*
- major improvement within 24 hrs. in < 40%
- diarrhea is a limiting side effect
- low-dose colchicine less toxic
  (1.2 mg, then 0.6 mg 1 hr later)

*High-dose steroids are first-line therapy for gout.*
- NSAID therapy is typically first-line
- prednisone, 20-40 mg/d, is usually enough (with taper over 5-10 d)
Chronic gout treatment misconceptions

*Urate-lowering therapy (such as allopurinol or febuxostat) should not be started during an acute attack.*

- Urate-lowering therapy can be started along with treatment for acute attack followed by prophylaxis (e.g., low dose colchicine) per 2012 guidelines

*Allopurinol should not be dosed higher than 300 mg/day.*

- FDA-approved maximal dose: 800 mg/d
- gradual up-titration starting at 100 mg/d or less; may need > 300 mg/d

*Allopurinol should be prescribed only in low doses (or not at all) for patients with renal dysfunction.*

- starting in low dose with up-titration well-tolerated even with renal dysfunction
• Only the 2nd placebo controlled trial of colchicine treatment for acute gout
• Compared colchicine treatment at high dose (HD), 4.8 mg over 6 hours, with low dose (LD), 1.8 mg over 1 hour, and placebo (P) among 184 patients with acute gout
• Response (>50% pain reduction w/in 24 hrs w/out rescue Rx): HD: 38%, LD: 33%, P: 15%
• Adverse events: HD: 77% diarrhea (20% severe), 17% vomiting; LD: 23% had diarrhea
• Conclusion: efficacy similar (but low!), toxicity higher with HD
Thank you for your attention!