Rheumatology for Primary Care Webinar Series 2025

WHO, WHAT, WHEN, AND HOW TO REFER TO RHEUMATOLOGY

SESSION 2

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JANUARY 27, 2025

I have no conflicts of interest to declare related to the material being presented.

OBJECTIVES

After this webinar, participants will be able to:

- **Identify patients who would benefit most from a rheumatology referral**
- **Identify rheumatologic emergencies requiring urgent referral**
- **List the clinical information and initial laboratory and imaging work-up to include in your rheumatology referral for a variety of common presentations**
- **Develop a treatment plan for patients with a variety of rheumatic diseases while awaiting a rheumatologist's assessment**
- **Describe other outpatient services and the resources they provide for patients with a confirmed or suspected rheumatic disorder**

DELAYS IN THE PROVISION OF CARE

- Musculoskeletal problems account for a large and growing proportion of primary care provider (PCP) visits.
- A minority of patients who consult a healthcare provider for an MSK complaint will have a systemic rheumatic disease that warrants referral to a rheumatologist for diagnostic confirmation and initiation of appropriate treatment.
- Important delays in the recognition and treatment of rheumatic diseases exist and must be tackled through a variety of innovations and interventions.
- One aim of this webinar is to equip PCPs with the knowledge and tools to identify patient presentations that are in keeping with a systemic autoimmune rheumatic disease, request investigations, and initiate a management plan while waiting to see a rheumatologist.

WHAT DO RHEUMATOLOGISTS TREAT?

Systemic autoimmune connective tissue diseases	Juvenile idiopathic arthritis
Rheumatoid arthritis	Rheumatic disorders associated with metabolic, endocrine, and hematologic disease
Seronegative spondyloarthropathies	**Idiopathic inflammatory myopathies**
Crystalline arthritis	**Polymyalgia rheumatica**
Vasculitides	Miscellaneous disorders
*We frequently see but are often NOT the primary treating physicians for: osteoarthritis, non-articular regional MSK disorders, fibromyalgia	

A GOOD HISTORY AND PHYSICAL EXAM ARE THE MOST IMPORTANT PARTS OF THE EVALUATION OF A PATIENT WITH SYMPTOMS OF A RHEUMATIC DISEASE

LABORATORY TESTS MAY HELP CONFIRM YOUR CLINICAL DIAGNOSIS - THEY OFTEN WILL NOT MAKE IT

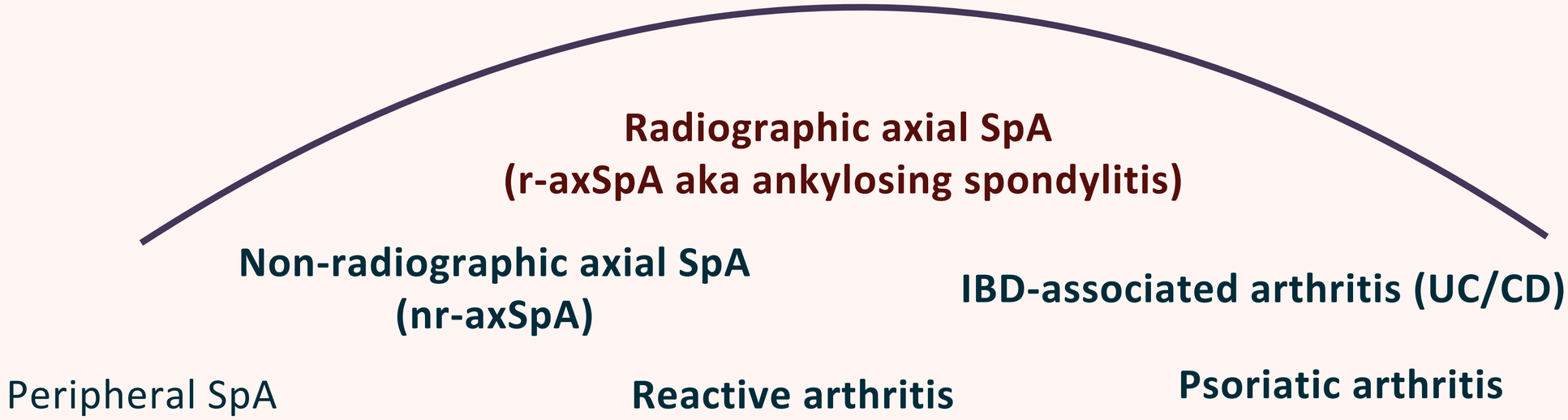
CASE 1

- Mr. A is a 25 year-old man who works in construction. He is new to your practice after moving from Quebec to the Ottawa region. He is seeing you for the first time today for chronic low back pain.

- He reports that he has had low back pain for at least the last 5 years. He was active as a teenager, playing hockey and soccer in school. He does not recall ever having a major injury but he attributes his pain to “wear and tear” injuries sustained while working. He has recently run out of a prescription for Tylenol 3s. He has been using Ibuprofen 600mg PO TID and Acetaminophen 4g per day over-the-counter with minimal relief.

Could Mr. A have a spondyloarthritis (SpA)?

SERONEGATIVE SPONDYLOARTHRITIS



A group of rheumatic diseases that share in common many clinical, radiographic, and serological features as well as genetic links (HLA-B27 association).

Shared rheumatologic features:			
Sacroiliac and spinal (axial) inflammation	Enthesitis (inflammation at the site of insertion of ligaments, tendons, joint capsule, or fascia to bone)	Peripheral, often asymmetric, inflammatory arthritis	Dactylitis (“sausage” digit)
Shared extra-articular and laboratory features:			
Ocular inflammation (acute anterior uveitis, conjunctivitis)	Inflammation of bowel mucosa	Psoriasis	NO association with RF = ‘seronegative’

INFLAMMATORY BACK PAIN

Characteristic features

- Onset - insidious, before the age of 45 years for patients with ankylosing spondylitis
- Duration > 3 months
- Associated with prolonged morning stiffness (>1 hour)
- Pain improves with movement, stretching, exercise but does not improve with rest
- Awakens patient in the second half of the night (classically, very early morning) with improvement upon getting up
- Good responds to NSAIDs (at 24-48h after a full dose of NSAID, the back pain is not present anymore or much better)
- Buttock pain (may alternate sides)

OTHER ARTICULAR AND EXTRA-ARTICULAR FEATURES OF SPONDYLOARTHRITIS

What to ask on history

- History of acute anterior uveitis or conjunctivitis
- GI review of systems for possible IBD (abdominal pain, weight loss, bloody stools)
- Personal or family history of psoriasis
- Diarrhea or non-gonococcal urethritis/cervicitis accompanying or occurring within 1 month before arthritis
- Enthesitis manifesting as plantar fasciitis, Achilles' tendonitis
- Dactylitis
- Tender and swollen peripheral joints

INVESTIGATIONS AND TREATMENT

What to order if you suspect an axial spondyloarthritis and first-line treatment

- **Imaging:**
  - **First: X-ray of pelvis to assess for sacroiliitis, X-rays of C-T-L Spine**
  - **If still suspect spondyloarthritis but X-rays do not demonstrate sacroiliitis or are equivocal: Request MRI of the spine and sacroiliac joints (non-contrast, STIR sequence)** **must include that you are excluding axial spondyloarthritis on the requisition so protocolled appropriately by radiologist and SI joint views are included
- **Laboratory:** CBC, creatinine, ALT, C-reactive protein
- **Treatment: Trial full-dose NSAID for at least 4 weeks. If not effective, switch to another full-dose NSAID.**
  - Naproxen 500mg po BID
  - Diclofenac 50mg po BID-TID
  - Meloxicam 15mg po daily
  - Celecoxib 200mg po BID
  - **Referral to physiotherapy, smoking cessation**

Prednisone is not effective for axial spondyloarthritis. Do not prescribe for this indication. Instead use NSAIDs assuming no contraindication.

WHEN SHOULD YOU ORDER HLA-B27 TESTING?

- HLA-B27 is present in about 8% of the general population (**there is significant geographic variability)
- HLA-B27 may be present in as many as 85-95% of Caucasian patients with axSpA
- This test should not be used in all patients with chronic back pain
- Can increase probability of axial spondyloarthritis in patients with inflammatory back pain (IBP), but does not definitively rule in OR rule out a diagnosis of axial spondyloarthritis
- The probability of a patient with IBP who is HLA-B27 positive having an axial spondyloarthritis is much higher than a patient with IBP alone. A positive test in this scenario may help you prioritize requesting an MRI of the spine and SI joints
- Be aware of the limitations of this test and your next steps with a positive result before requesting it

CASE 1

- Mr. A describes lower back and buttock pain for the last 5 years. He reports morning stiffness of 1-2 hours. The intensity of the pain he experiences varies, but may occasionally awaken in from sleep at 3-4AM and he must get out of bed and stretch or move to alleviate it.

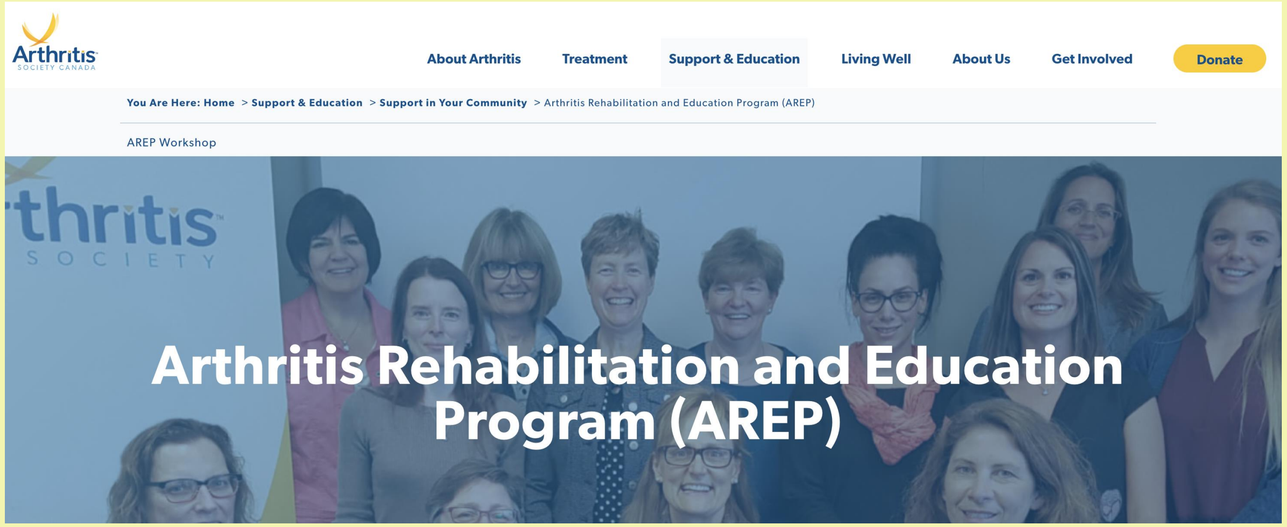
- He denies any swollen or tender peripheral joints. He does describe pain at the posterior ankles, where the Achilles inserts on the calcaneus. He has had swelling in this area as well in the past. He had an episode of plantar fasciitis 2 years ago that lasted at least 6 months. He has no personal history of IBD, psoriasis, uveitis, or recent GI or urogenital infection. There is a family history of psoriasis in a first-degree relative.

- An X-ray of the SI joints demonstrates bilateral sacroiliitis with erosive changes. His CRP was elevated at 25 (ULN <10). His other labs were unremarkable.

CASE 1

- You make a diagnosis of axial spondyloarthritis and have referred him to Rheumatology as well as to Physiotherapy. You provide him with information on how to self-refer to The Arthritis Society for patient education and counselling from a physiotherapist.

- You prescribe a trial of Naproxen 500mg PO BID x 4 weeks but his axial pain and stiffness still impair his quality of life and functioning. You stop Naproxen and try a second full-dose NSAID, Celecoxib 200mg PO BID, which he finds more effective and is tolerating well.



The Arthritis Society AREP services are only available for patients in Ontario.

Now Offering Virtual and In-person Care

To better safeguard your health, we now offer virtual care, from initial assessment to delivery of care and education, in a method that works best for you. Individual virtual care can be delivered by telephone, email and/or personal video*. Virtual group education programs are also available for registered clients.

To make a self-referral for a free appointment:

Call: 1800-321-1433 ext. 3307

Email: AREP@arthritis.ca

Health professional wanting to refer a patient:

referral form

Email: AREP@arthritis.ca

fax: 1.888.519.6869

** requires computer/laptop/tablet, internet/wi-fi access and email address*

CASE 2

- Mrs. B is a 65 year-old woman who recently retired from her job as a restaurant manager. She presents with a 6-week history of hip and shoulder girdle pain and stiffness that has been limiting her daily activities. She is stiff in the morning for at least 2 hours.

- Her past medical history is significant for hypothyroidism, osteopenia with no history of fragility fractures, and hypertension. She takes Synthroid, Vitamin D3 1000 units daily, and Hydrochlorothiazide.

- She tells you that in the last week, in addition to the shoulder and hip girdle pain, she has now developed swelling and pain at both wrists with decreased grip strength.

- On exam, you identify tender shoulders, wrists, and hips. You note that her wrists are swollen with reduced range of motion. You believe that 3 of her MCPs at both hands are swollen as well.

What is your differential diagnosis for Mrs. B?

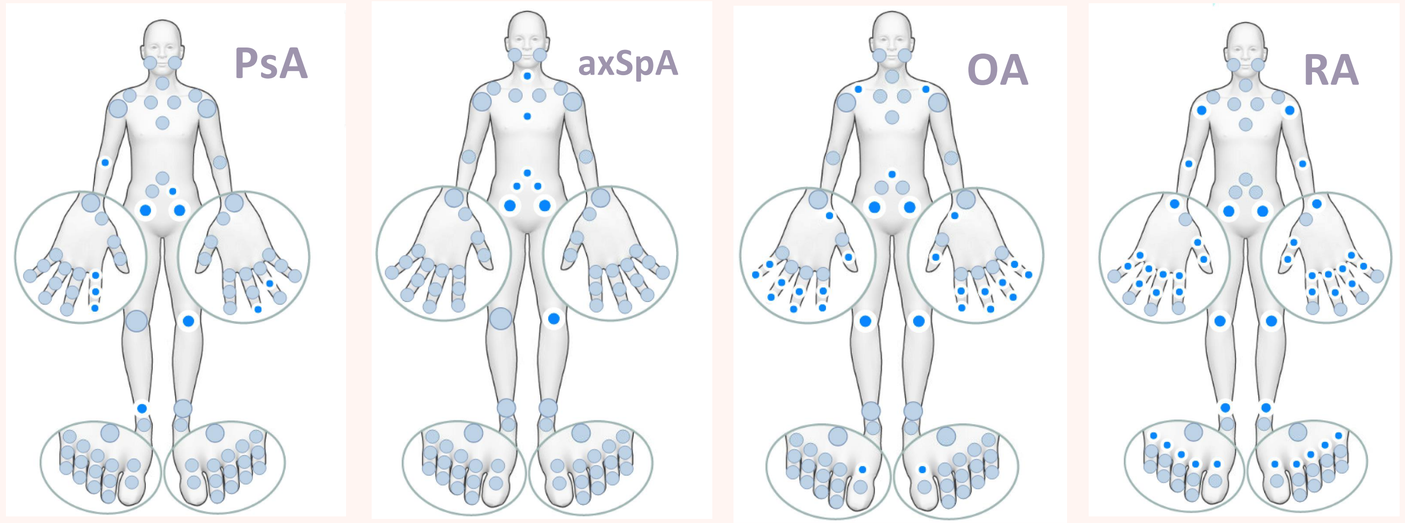
APPROACH TO PERIPHERAL JOINT PAIN

- Inflammatory vs. non-inflammatory features
- Duration of symptoms (<6 weeks vs. >6 weeks)
- Temporal pattern of joint involvement (migratory, episodic, additive)
- Distribution of joint involvement
- Patient demographics
- Extra-articular features

Migratory: Rheumatic fever, early gonococcal arthritis, Early Lyme disease, Whipple's disease

Additive: RA, Seronegative SpA, SLE

Episodic: Crystalline, palindromic rheumatism, auto inflammatory (i.e. FMF)



CASE 2

- **Differential diagnosis:**
  - **Viral arthritis**
    *Duration of symptoms long for this diagnosis
  - **Rheumatoid arthritis**
  - **Crystalline arthritis (polyarticular gout, CPPD arthritis)**
    *Unusual to have a first presentation of gout be polyarticular
  - **Peripheral seronegative spondyloarthritis**
    *Joint distribution not suggestive and no extra-articular manifestations
  - **Polymyalgia rheumatica**
    *Swollen wrists, small joints of hands excludes this diagnosis
  - **Paraneoplastic arthritis**
  - **Osteoarthritis**
    *Clear date of onset, inflammatory features by history, joint distribution and swollen joints on exam are not consistent with this diagnosis

- **Investigations:**
  - **Labs:** CBC, creatinine, liver enzymes, calcium, albumin, magnesium, phosphate, C-reactive protein, TSH, +/-uric acid, RF, +/-anti-CCP, viral serologies
  - **Imaging:** X-rays hands, wrists, feet, pelvis, chest, +/-U/S of shoulders

CASE 2

- You have requested X-rays of the hands, wrists, feet, pelvis as well as a chest-X-ray. The radiologist notes osteoarthritic changes at the PIPs of the hands and first MTPs but no erosions. No soft-tissue calcifications. The chest X-ray is unremarkable. You have requested an ultrasound of the shoulders but your patient has not yet been contacted for this appointment.

- Laboratory investigations are significant for a mild rise in C-reactive protein to 15 (ULN <10). Your patient also has a mild thrombocytosis and normoctyic anemia (Platelets 475, Hb 113). Renal function and liver enzymes are normal. RF is 50 (ULN <14).

- You suspect early rheumatoid arthritis.

- You prescribed Naproxen 500mg PO BID at your first visit 2 weeks ago. Your patient describes minimal improvement in her joint pain, swelling, and stiffness. You have referred her to be seen by Rheumatology but anticipate an 8-12 week wait. You have also referred her to The Arthritis Society.

- You elect to prescribe a course of prednisone to help manage her symptoms.

PREDNISONE

Low-dose (<10mg/day)	Moderate-dose	High-dose (1mg/kg/ay)
Polymyalgia rheumatica frequently tapering	Gout flare, bridging therapy for inflammatory arthritis with taper over 6-8 weeks while awaiting DMARD effect	Empiric treatment for giant cell arteritis
PMR taper: Prednisone 20mg PO daily with taper of 2.5mg/2 weeks until 10mg and then 1mg/month Return to smallest dose that was effective if flare with tapering x 2 weeks before re-starting taper	Gout/CPPD: Prednisone 30mg PO daily x 5 days, consider taper over another 5 days if polyarticular flare RA bridging: Prednisone 20-30mg PO daily with taper of 2.5mg per week (approx 8 weeks)	GCA empiric therapy assuming no visual loss or imminent visual loss: Prednisone 40-60mg PO daily x 1 month with taper of 10mg/2 weeks until 20mg then 2.5mg/2weeks until 10mg then 1mg/month

Mitigating glucocorticoid-related toxicity

- **Use smallest possible dose for shortest duration possible.**
- **Monitor blood pressure**
- **Monitor glycemias**
- **Add a PPI in patients with history of PUD, GERD, are on anti-platelet therapy or anticoagulation. Avoid concurrent use of other NSAIDs.**
- **Ensure adequate Vitamin D3 and Calcium supplementation.**
- **Counsel around smoking cessation and avoidance of excessive alcohol intake.**
- **Request a baseline BMD in patients starting >2.5mg/day of GC treatment for >3 months.**

CASE 2

- You prescribe Prednisone 20mg PO daily with a taper of 2.5mg/week.
- You ask her to stop the Naproxen.
- You ensure she has 1200mg of elemental calcium intake per day by diet or supplement. You refer her to the Calcium Calculator available online through Osteoporosis Canada. She is already taking recommended Vitamin D3 supplementation.
- You request a baseline BMD.
- In anticipation of her starting immunosuppressive therapy when sees the rheumatologist, you have requested Hepatitis B serologies (surface antigen, total core antibody, surface antibody) and Hepatitis C screen.

CASE 3

- Ms. C is a 39 year-old woman who works as a chef. She has noticed that her finger tips blanch and turn blue with cold exposure in the last year. The attacks have become more frequent and are painful. She also describes new fatigue and puffy hands in the last few months.
- She had previously been in good health with no regular medications.
- In your office, she shows you pictures she has taken of her hands. You even note that a few of her finger tips appear purplish.

How can you differentiate between primary and secondary Raynaud's phenomenon?

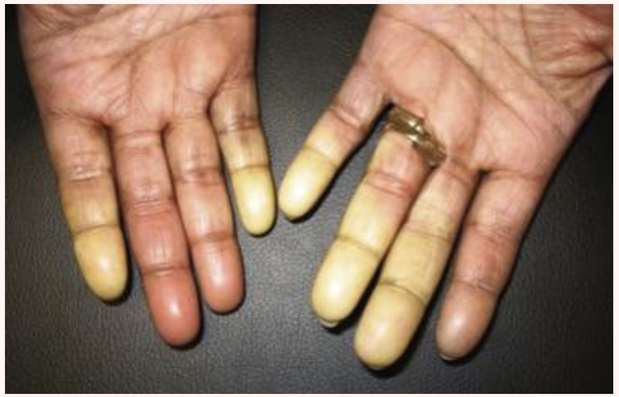


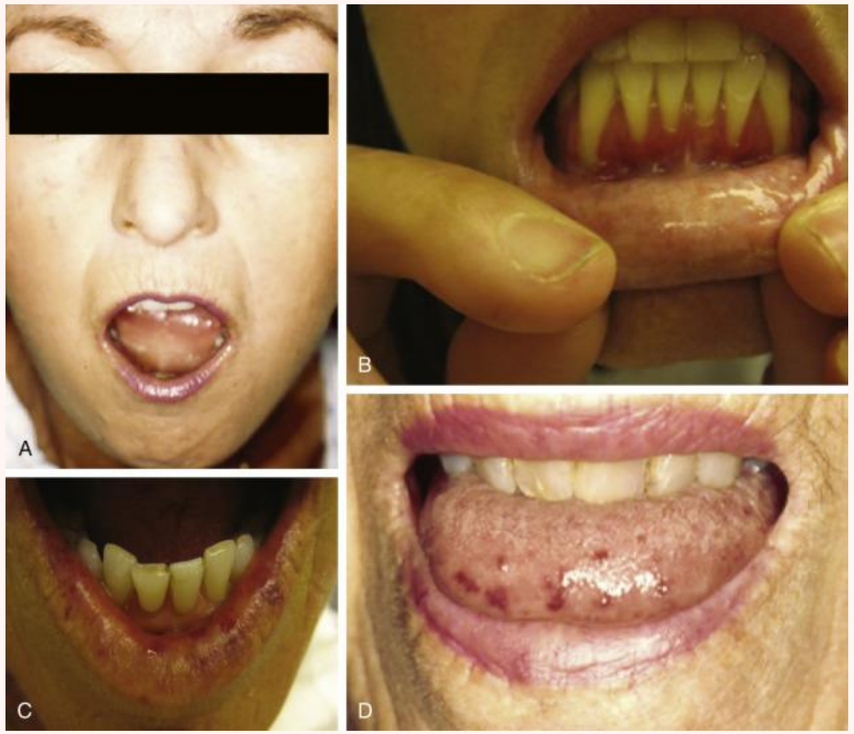
Image source: Firestein & Kelley's Rheumatology 11th ed.

RAYNAUD'S PHENOMENON

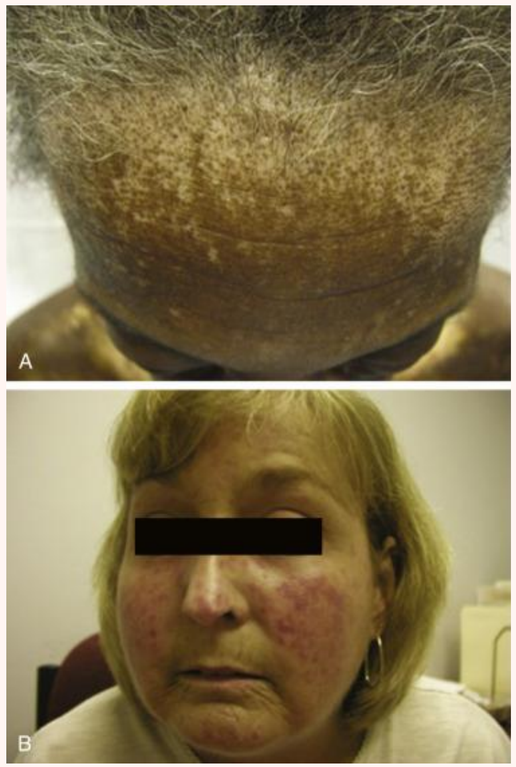
Primary versus Secondary Disease

- RP is an exaggerated vascular response of the digital arteries triggered by cold and stress.
- Diagnosis is based on a history of cold sensitivity and recurrent well-demarcated blanching of the tips of the fingers and/or cyanosis.
- **Primary RP:** No disease process is associated with the recurrent vasospasm. Young age of onset (teens to age 30 years), symmetric, no associated digital ulcerations, normal nail-fold capillaries, negative ANA.
- **Secondary RP:** In setting of **autoimmune connective tissue diseases**, obstructive vascular disease, hypothyroidism, cryoglobulinemia, hyperviscosity syndromes
  - CTD-related: Ask about arthralgias/arthritis, fever, muscle weakness, weight loss, rashes, photosensitivity, pruritus, sicca symptoms, skin tightening/thickening, puffy hands, symptoms of heart or lung disease, reflux or dysphagia, history of thrombosis
  - CTD-related: Examine for abnormal pulses, digital ulcers, digital pits, telangiectasias, skin thickening/tightening, calcinosis cutis, grossly abnormal nail-beds, malar rash, joint swelling/tenderness, puffy hands
  - CTD-related: Test for CBC, creatinine, liver enzymes, ANA, ENA, dsDNA, RF, C3 and C4 levels, urinalysis if concerns on Hx/Px

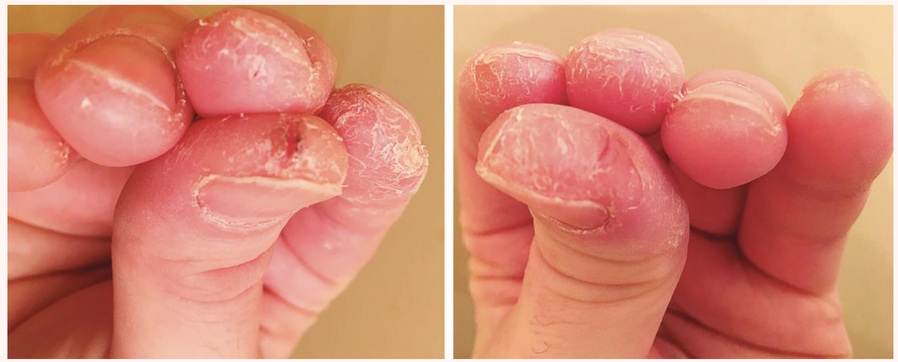
RP is common in the general population and usually follows a benign clinical course (3-15% population; 3-4:1 F:M)
Patients may be diagnosed with primary Raynaud's without having to go through specialized tests
Age of onset >40 years = suspicious for secondary RP



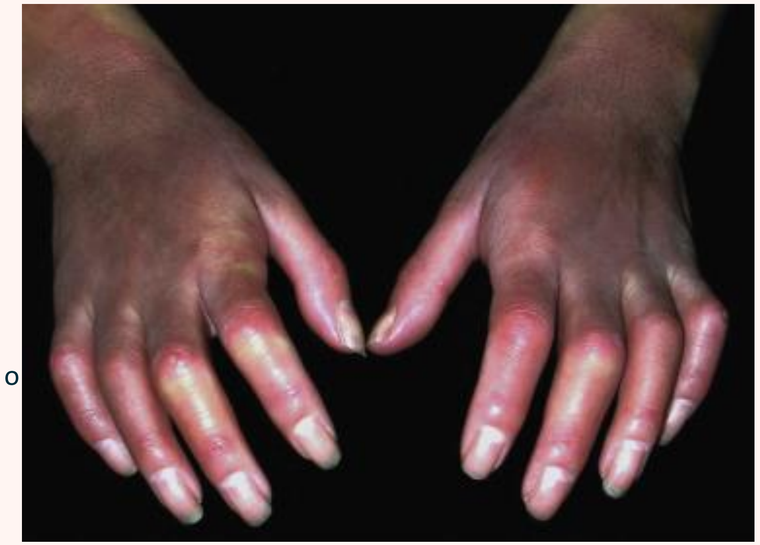
Decreased oral aperture, loosening of teeth with periodontal disease, telangiectasias on tongue and inner lip



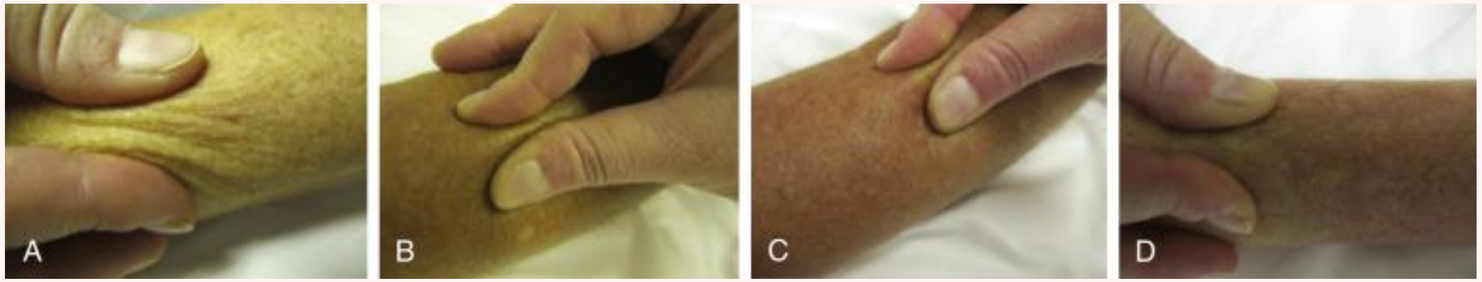
'Salt and pepper' skin changes, telangiectasis o cheeks



Mechanic's hands



Sclerodactyly



Skin tightening/thickening (from normal skin to completely tethered)

Images from: Firestein & Kelley's Rheumatology 11th ed, Chatterjee 2021

CASE 3

- After performing a review of systems and examining Ms. C, you suspect an underlying connective tissue disease is causing her Raynaud's Phenomenon.
- This is supported by the later age of onset, puffy hands, a few telangiectasias on the palms and face.
- You request an ANA, which returns as positive 1:640 titer, nucleolar pattern. Her ENA panel is negative. You refer her to Rheumatology for suspected systemic sclerosis.
- One month later, while still waiting to be seen by a rheumatologist, she calls you to report that she has been having headaches for the last 2 days. Her blood pressure at home in 160/90. At her last appointment, her blood pressure was 105/70.

SCLERODERMA RENAL CRISIS

- Characterized by **sudden and severe elevation of blood pressure** (usually >150/90 mmHg) with or without renal failure and microangiopathic hemolytic anemia. - Mimics malignant hypertension
- 5-year survival rate of SRC is approximately 65%
- SRC occurs in 5-10% of patients with scleroderma, mainly those with diffuse scleroderma (skin thickening/tightening proximal to the elbows and knees) and usually within the first 2-4 years from disease onset.
- Risk factors: Diffuse skin disease, exposure to corticosteroids, specific autoantibodies (anti-RNA polymerase III - not available on standard ENA panel)

Woodworth, T., Suliman, Y., Li, W. et al. 2016

MANAGEMENT OF RAYNAUD'S PHENOMENON

Non-pharmacologic and Pharmacologic Treatments

- **Non-pharmacologic:** Carry gloves, wear heated socks, use chemical heat packs (obtained at sporting goods, hardware stores), avoid cold. **Stop cigarette smoking**.
- **Pharmacologic:** First-line treatment is calcium-channel blockers
  - I.e. Nifedipine XL 30mg daily, can be up-titrated every 4 weeks to maximum tolerated dose that helps prevent vasospastic attacks
  - I.e. Amlodipine 2.5-5mg daily, can be increased by 2.5mg every 4 weeks to maximum tolerated dose that helps prevent vasospastic attacks
  - Counsel patients about risk of hypotension/dizziness, ideally monitoring blood pressure at home while titrating dose.
- **AVOID:** Triptans, ergots, Beta-blockers, stimulants (ADHD medications), OTC decongestants

CASE 3

- Ms. C's creatinine is 130 (from her usual baseline of 75µmol/L) and her Hemoglobin has decreased to 105 g/L from her baseline of 120 g/L. Her platelets have decreased to 90 000/µL from her baseline of 200 000/µL.

- Taking into consideration her new rise in blood pressure, the acute kidney injury, anemia, and your underlying suspicion that she has an underlying autoimmune connective tissue disorder, you are concerned this may all represent a severe manifestation of her disease.

- You page Rheumatology on call to discuss your concerns and together, decide it would be best if the patient is referred directly to the ER for urgent assessment of possible scleroderma renal crisis.

RHEUMATOLOGY EMERGENCIES

- Septic joint - primarily managed by Orthopedics/ID (but patients with underlying autoimmune inflammatory arthritis may be higher risk)
- Organ-threatening flare of a vasculitis (i.e. visual loss or imminent visual loss in giant cell arteritis)
- Organ-threatening flare of SLE (i.e. new renal failure)
- Scleroderma renal crisis
- Organ-threatening flare of myositis (i.e. rapidly-progressive interstitial lung disease)
- Macrophage activation syndrome (MAS)
- Infectious complications of immunosuppressive therapies

CASE 4

- Mrs. D is a 77 year-old woman who reports progressive pain in her hands. She finds she is having more difficulty knitting and carrying out tasks that require dexterity. She describes arthralgias involving the PIPs, DIPs, and first CMC of both hands of 10 years duration. More recently, in the last 6 months she endorses increased pain, swelling and warmth involving the DIPs and PIPs. She describes paresthesias in her finger tips and morning stiffness of about an hour.

- She is bothered by progressive deformities at her DIPs and PIPs.

- You request X-rays of her hands and wrists. The radiologist reports severe joint space narrowing involving the interphalangeal joints and first CMC. The MCPs are spared. There are central erosions at multiple PIPs. The radiologist concludes that the radiographic appearance is most in keeping erosive osteoarthritis.

What is erosive osteoarthritis and how is it treated?

EROSIVE HAND OSTEOARTHRITIS (EHOA)

- Sub-type of hand osteoarthritis, aggressive, predominantly affecting women
- Central subchondral erosions are noted on X-ray
- Patients may experience more symptoms of inflammatory joint pain (warmth, soft-tissue swelling, +/- erythema) than in nodal hand osteoarthritis. May describe a more “abrupt onset”, paresthesias in finger tips at night.
- Erosive OA targets primarily the DIPs and PIPs but spares the thumb bases and MCPs.
- May also see ankylosis (“fusion”) of the interphalangeal joint.
- Heberden’s and/or Bouchard’s nodes may co-exist.
- Management follows the same algorithm as other types of hand osteoarthritis. There is no available “disease-modifying” drug.

Favero M, Belluzzi E, Ortolan A, Lorenzin M, Oliviero F, Doria A, Scanzello CR, Ramonda R. Erosive hand osteoarthritis: latest findings and outlook. Nat Rev Rheumatol. 2022 Mar;18(3):171-183. doi: 10.1038/s41584-021-00747-3. Epub 2022 Feb 1. PMID: 35105980.

EROSIVE HAND OSTEOARTHRITIS

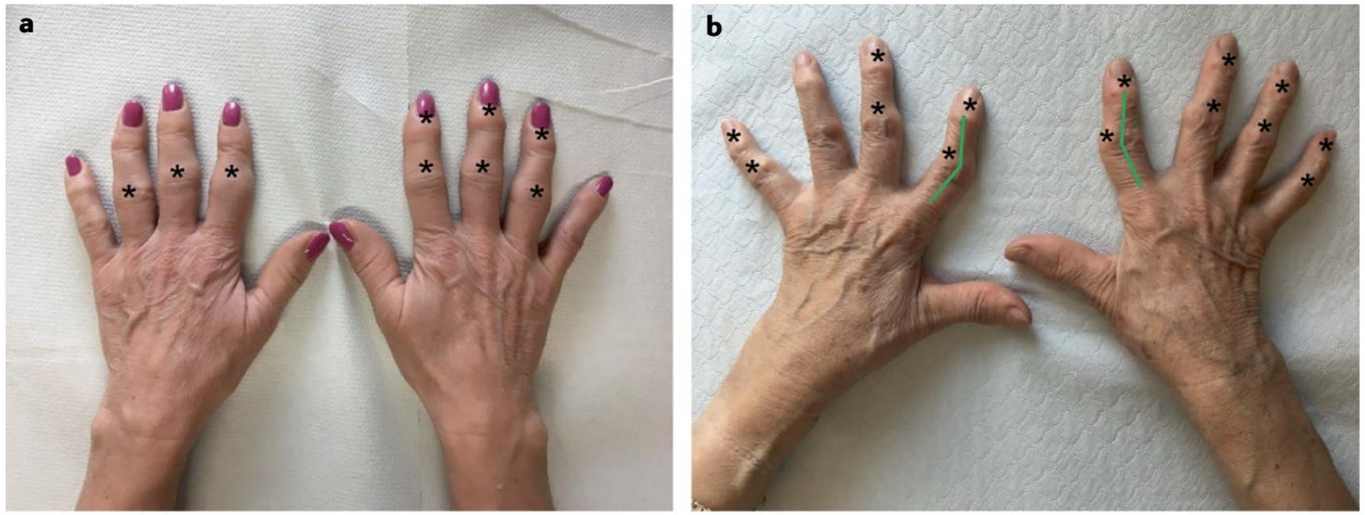


Fig. 2 | **Clinical features of erosive hand osteoarthritis. a** | Early-phase erosive hand osteoarthritis (EHOA), demonstrating soft swelling (marked by asterisks) of the proximal and distal interphalangeal joints. **b** | Late-phase EHOA, demonstrating deformity and bony enlargement (nodes) of proximal and distal interphalangeal joints (marked by asterisks) and subluxation at the proximal interphalangeal joint levels (highlighted by the green lines).

Images from:
Favero M et al Erosive hand osteoarthritis: latest findings and outlook. Nat Rev Rheumatol. 2022 Mar;18(3):171-183. doi: 10.1038/s41584-021-00747-3. Epub 2022 Feb 1. PMID: 35105980.

Kolasinski SL, et al 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. Arthritis Care Res (Hoboken). 2020 Feb;72(2):149-162. doi: 10.1002/acr.24131. Epub 2020 Jan 6. Erratum in: Arthritis Care Res (Hoboken). 2021 May;73(5):764. doi: 10.1002/acr.24615. PMID: 31908149; PMCID: PMC11488261.

Strongly recommended

Conditionally recommended

	HAND	KNEE	HIP
PHYSICAL, PSYCHOSOCIAL, and MIND-BODY APPROACHES	Exercise*		
	Self-Efficacy and Self-Management Programs		
		Weight Loss	
		Tai Chi	
		Cane	
	1st CMC Orthosis	TF Knee Brace**	
	Heat, Therapeutic Cooling		
	Cognitive Behavioral Therapy		
	Acupuncture		
	Kinesiotaping		
		Balance Training	
	Other Hand Orthoses***	PF Knee Brace**	
	Paraffin	Yoga	
		RFA	
PHARMACOLOGIC APPROACHES	Oral NSAIDs		
	Topical NSAIDs	Topical NSAIDs	
	I-A Steroids	I-A Steroids (Imaging-Guidance for Hip)	
	Acetaminophen		
	Tramadol		
	Duloxetine		
	Chondroitin	Topical Capsaicin	

REFERRING TO RHEUMATOLOGY

- ‘Arthritis’ vs. ‘arthralgia’
- If no evidence of swollen joints on physical exam, but still suspect an inflammatory arthritis, then will need imaging evidence of synovitis (ultrasound, MRI)
- **If suspect an inflammatory arthritis, but on physical exam cannot identify any swollen joints, try to avoid prescribing prednisone as may mask any subtle findings at the time of the rheumatologist’s assessment and delay definitive treatment.

INVESTIGATIONS TO INCLUDE IN YOUR RHEUMATOLOGY REFERRAL

- **Chronic inflammatory arthritis:** CBC, CRP, ESR, ALT, ALP, albumin, creatinine, urinalysis, HBV, HCV serologies, X-rays of affected joints (typically most high-yield hands/wrists/feet) and CXR
  - Rheumatoid factor, +/-anti-CCP
- **Axial spondyloarthritis:** CRP, ESR, CBC, ALT, ALP, albumin, creatinine, X-ray of spine and pelvis (SI joints). If no definite findings of spondyloarthritis on the X-rays, should include an MRI of the sacroiliac joints +/- spine
- **Autoimmune connective tissue disease:** CBC, CRP, ESR, ALT, ALP, albumin, creatinine, urinalysis, urine protein:creatinine (spot - ideally first AM), ANA, RF, ENA, dsDNA, C3/C4. CK - if muscle weakness.
- **Polymyalgia rheumatica:** CBC, CRP, ESR, creatinine. For differential: TSH, 25-OH Vit D levels, RF and anti-CCP (especially if peripheral arthritis), SPEP, Calcium, albumin, CK

COSTS OF RHEUMATOLOGY LABS

- **Covered by OHIP:** ANA, dsDNA, ENA, C3, C4, RF, cryoglobulins, SPEP
- **Not-covered by OHIP:**
  - Anti-phospholipid antibody testing (lupus anti-coagulation, anti-B2 glycoprotein, anti-cardiolipin) ($55-70 per test)
  - Anti-CCP ($55-83)
  - ANCAs (MPO, PR3), when ordered by PCP ($75)
  - AST ($18)

EXTRA CASE

- Mr. E is a 50 year-old man who presents with an acute monoarthritis of the right knee of 5 days duration. He is known for an accountant. He is sedentary. He is an ex-smoker with a 20PY history. He denies any alcohol or drug use.

- His past medical history is significant for longstanding psoriatic arthritis, diagnosed approximately 20 years ago, which has been well-controlled on Adalimumab 40mg SC every 2 weeks. He is also known for type 2 diabetes on insulin and coronary artery disease with an MI 10 years ago.

- Mr. E tells you that his now-retired rheumatologist diagnosed him with gout, 6 months ago after presenting with acute first MTP pain, swelling and erythema. This was treated with a 10 day course of Colchicine 0.6mg PO BID.

What is your differential diagnosis for Mr. E?

FORMULATING A DIFFERENTIAL DIAGNOSIS

Is this an acute or chronic monoarthritis?

Acute (<6 weeks)	Chronic (>6 weeks)
Infection (Bacterial including non-gonococcal and gonococcal)	Infection (**Lyme**, Mycobacterial, fungal)
Crystal-mediated	Monoarticular presentation of polyarticular inflammatory arthritis
Hemarthrosis	Osteoarthritis
	Avascular necrosis
	Charcot joint
	Rare: foreign-body synovitis, benign/malignant neoplasms, amyloidosis

SEPTIC ARTHRITIS

Risk Factors - Non-gonococcal

From the Rational Clinical Examination: Does This Adult Patient Have Septic Arthritis?

- **Older age (>80 years, LR 3.5)**
- **Diabetes mellitus (LR 2.7)**
- **Rheumatoid arthritis (LR 2.5)**
- **Recent joint surgery (LR 6.9)**
- **Hip or knee prosthesis and skin infection (LR 15)**
- **Fever (LR 1.7)**

Abnormal WBC, ESR and CRP have limited diagnostic power because of their low specificities.

Margaretten et al, 2007

EXTRA CASE

- Mr. E is referred to the ER because of a concern of a septic joint. There, he has a joint aspiration performed. Joint fluid is sent for gram stain and culture, cell count, and crystal analysis.
- The cell count is 30 000 WBC/mL with a neutrophil predominance. Gram stain is negative. Intra-cellular monosodium irate crystals are noted. A diagnosis of gout is made.
- He receives a prescription for Colchicine 0.6mg PO BID and is asked to follow-up with you.
- He calls your office 2 days later because of ongoing knee pain and now new diarrhea, limiting his ability to take Colchicine.

MANAGEMENT OF GOUT

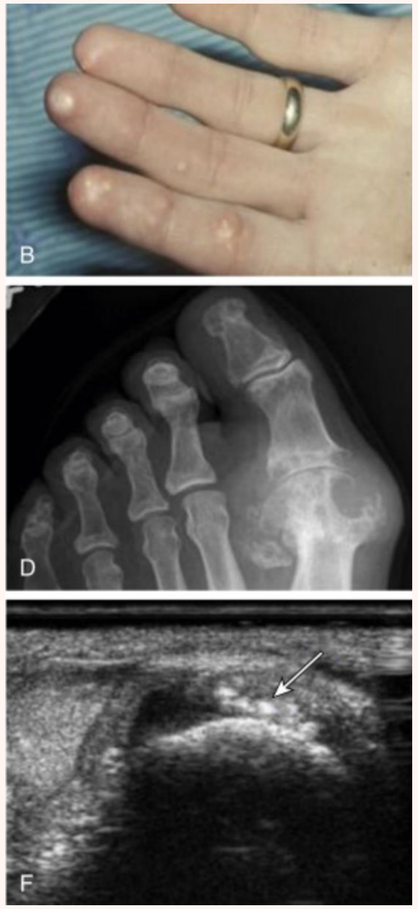
Acute Period - Control of Inflammation

Gout flares are typically self-limited over 1-2 weeks

"Intercritical period" between flares where there is no evidence of joint inflammation and the patient is asymptomatic

If persistently hyperuricemic, and treatment is not initiated, tophi and chronic gouty arthritis may develop

- **Acute management:**
  - **Oral steroid (i.e. Prednisone 30mg daily x 5-7 days) or intra-articular steroid (i.e. Depo-medrol 40mg to knee)**
  - **Colchicine (i.e. 1.2mg x 1 then 0.6mg 1 hour later, followed by 0.6mg BID - *must adjust for renal function)**
  - **NSAIDs (i.e. Naproxen 500mg BID, although no specific preference - often more difficulty to use because of patient comorbidities/contraindications)**



AGREE Trial Terkeltaub et al, 2010
Rainer et al, 2016

Image source: Firestein & Kelley's Rheumatology 11th ed.

MANAGEMENT OF GOUT

Chronic - Urate-lowering Therapy

Non-pharmacologic management: weight loss, avoidance of purine rich foods/beverages

Pharmacologic: "TREAT TO TARGET = uric acid <360µmol/L"

- **Allopurinol (purine analogue, xanthine oxidase inhibitor) - starting dose 50-100mg PO daily, titrate dose by 100mg every 4 weeks until reach target uric acid**
- Febuxostat (XOI) - starting dose 40mg PO daily, may be increased to 80mg PO daily
- **Flare prophylaxis: Colchicine 0.6mg daily (or lower if renally adjusted), NSAIDs, low-dose Prednisone x 3-6 months**

Indications for urate-lowering therapy
1 or more sc tophi
Radiographic damage (any modality)
Frequent flares (>=2/year)
> 1 flare but < 2/year (conditional)
First flare with CKD, eGFR<60 (conditional)
First flare with serum urate > 535 (conditional)
First flare with urolithiasis (conditional)

FitzGerald J et al, 2020

MANAGEMENT OF GOUT

Allopurinol Hypersensitivity Syndrome

- ***What is AHS?***

Rash + eosinophilia, leukocytosis, fever, hepatitis and progressive renal dysfunction

- ***What are the risk factors?***

Modifiable: Allopurinol starting dose, diuretic use

Non-modifiable: Time from start of treatment, HLA-B*5801, CKD, ethnicity, older age

- ***How can the risk be reduced?***

Avoid use of Allopurinol in HLA-B*5801 + patients, start at a low dose (50mg daily, and increase in 50mg increments in patients with GFR <60mL/min), educate patients about risk

Can still up-titrate Allopurinol to maximum dose of 800mg/day in patients with CKD

Stamp & Chapman, 2020

MANAGEMENT OF GOUT

Febuxostat and cardiovascular disease

- ***Can I prescribe Febuxostat in my patients with comorbid cardiovascular disease?***

Febuxostat should not be first-line. May consider in the event no other option (i.e. allergy to Allopurinol)

- **CARES Trial 2018** (Febuxostat vs. allopurinol): 6190 patients with history of gout and cardiovascular disease, median follow-up of 32 months. Primary endpoint = time to occurrence of any of a combination of CV events (CV death, MI, stroke, UA with urgent revascularization). Febuxostat showed increased risk of CV mortality and all-cause mortality (HR 1.34, 95% CI 1.03-1.73, 1.22 95% CI 1.10-1.47) however, was not associated with an increased risk of the combination of events composing the endpoint. No placebo arm. Majority of deaths occurred after discontinuation of drug.
- **FAST Trial 2020**: 6128 patients with gout in EU, >=60y + being treated with allopurinol. Continue versus switch to febuxostat. 1/3 had previous CV event, others had risk factors only. Median follow-up 4 years. No differences between the groups in overall mortality, CV mortality, or composite CV outcomes.

White et al, 2018; Mackenzie et al, 2020

MANAGEMENT OF GOUT

Other Common Questions

- ***Once it is determine that urate lowering therapy is indicated, when should it be started?***

ULT can be started during a flare (take advantage of the patient's motivation to begin treatment). Likely won't prolong or worsen a flare if you do.

- ***How long should I prescribe Colchicine prophylaxis for?***

ACR 2020 Gout Treatment Guidelines suggest Colchicine prophylaxis for 3-6 months. May require longer if frequent ongoing flares, but rarely need for > 1 year.

- ***How long should ULT be continued?***

Likely indefinitely. Minimize interruptions in ULT as much as possible to avoid unnecessary gout flares.

- ***Should I discontinue medications that my patient is already taking that are associated with hyperuricemia?***

Medications: diuretics, low-dose salicylates, calcineurin inhibitors (cyclosporine, tacrolimus)

No. If there is an indication for those treatments, then they can be continued.

Hill EM et al, 2015; Feng X et al, 2015; FitzGerald J et al, 2020

EXTRA CASE

- You check to make sure the final culture results from Mr. E's arthrocentesis are negative.
- You decrease the dose of his Colchicine to 0.6mg daily - may further decrease it to 0.6mg every other day if he still has ongoing diarrhea. Since you plan to initiate ULT, you prescribe this for 6 months.
- You prescribe Prednisone 20mg daily x 5 days with instructions to monitor his blood sugars closely and adjust his short-acting insulin as needed.
- You prescribe Allopurinol 100mg po daily to be increased in 4-6 weeks based on his serum uric acid. You provide him with a standing lab order for CBC, ALT, Creatinine, and Uric acid to be done every 4 weeks. You will instruct him to increase his Allopurinol by 100mg increments until you reach the target uric acid of <360µmol/L. You will then remain on that dose indefinitely.

QUESTIONS