RAPID RHEUMATOLOGY REVIEW

The 13th Annual Richard C. Staab, DO Memorial Symposium

April 4th, 2025

Mary Hinojos Mamut, DO

DISCLOSURES

- NONE

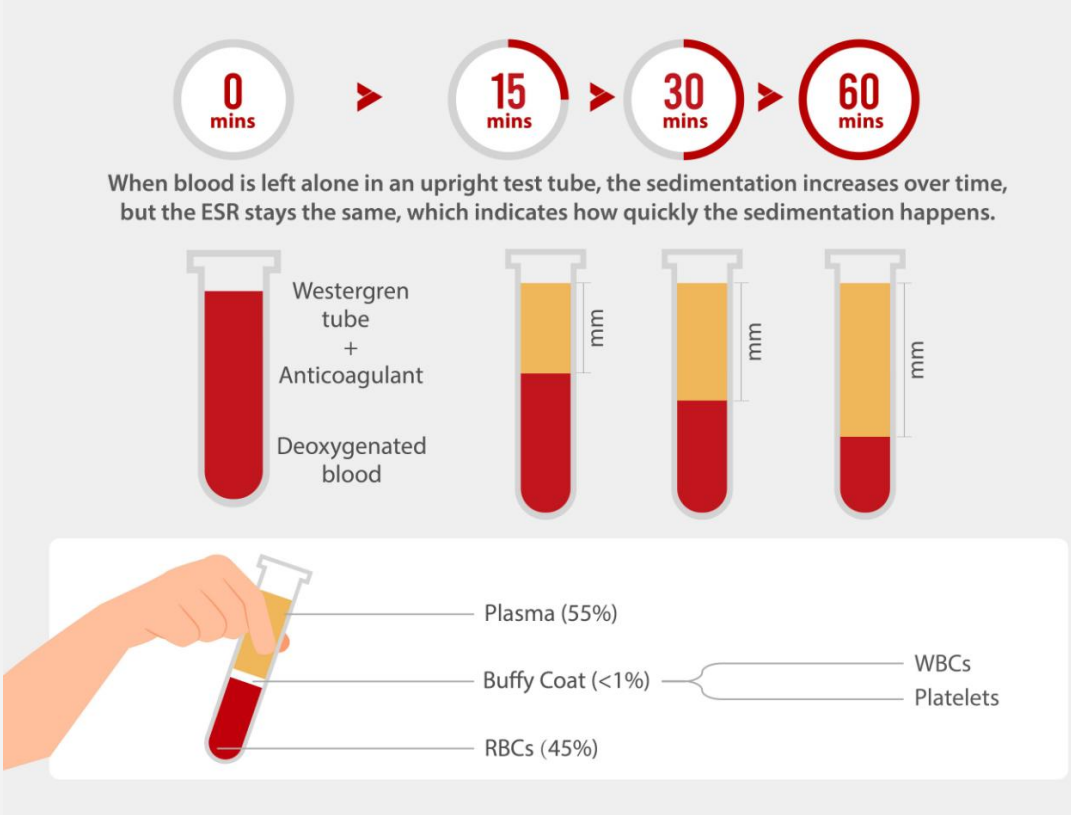
LEARNING OBJECTIVES

1. Understand autoimmune testing; it's implications and appropriateness of testing and interpretation
2. Be familiar with the initial work up in a patient that is believed to have an autoimmune disorder; what are the first steps in commonly seen rheumatologic disorders
3. Identify rheumatological emergencies

THE INFLAMMATORY MARKER

ERYTHROCYTE SEDIMENTATION RATE (ESR) AND C-REACTIVE PROTEIN (CRP)

- What is an ESR?
  - Distance in millimeters that RBCs fall within a specified tube over 1 hour
  - Increase is acute phase reactants leads to closer aggregation of RBCs (rouleaux formation), which causes them to fall faster => inc. ESR
- What is a CRP?
  - Acute phase reactant by the liver in response to IL-6 and other cytokines
  - Elevation occurs within 4 hours of tissue injury and peaks in 24 to 72 hours
  - In the absence of inflammatory stimuli, it falls rapidly, with a half life of about 18 hrs



https://www.mindray.com/content/xpace/en/media-center/blogs/quick-facts-about-esr-part-a.html

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ESR

A rough rule of thumb for the age-adjusted upper limit of normal for ESR (mm/hour) is: Male = age/2 and Female = (age + 10)/2.

- Markedly elevated ESR (>100 mm/hour)
  - Infection, bacterial (35%)
  - Connective tissue disease: giant cell arteritis, polymyalgia rheumatica, SLE, other vasculitides (25%)
  - Malignancy: lymphomas, myeloma, others (15%)
  - Other causes (25%)
- Markedly low ESR (0 mm/hour)
  - Afibrinogenemia/dysfibrinogenemia
  - Agammaglobulinemia
  - Extreme polycythemia (hematocrit > 65%)
  - Increased plasma viscosity

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THE ANA

ALL ABOUT ANTINUCLEAR ANTIBODIES

So what exactly is an ANA anyway?

ANA or **A**nti-**N**uclear **A**ntibody refers to antibodies against antigens in the nucleus ➠ like dsDNA, centromeres, ribonucleoprotein.

How are ANAs detected in the lab?

The immunofluorescence assay (IFA) is the main technique used to detect ANAs. Using fluorescence microscopy and serial dilution, a pattern and titer is reported.

What does a +ANA indicate, and what is the significance of the ANA titer/pattern?

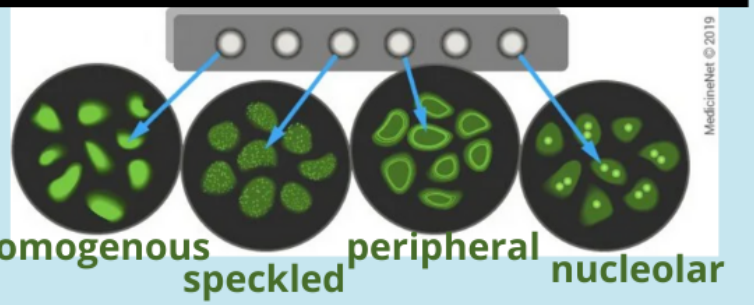
Positive ANA ≠ Autoimmune Disease!

+ANA can be seen in up to 33% of healthy adults, and should be interpreted in the context of other symptoms and physical exam findings

Titer: The higher the ANA titer, the more likely it will be clinically significant

Pattern: The ANA patterns are associated with different rheumatic diseases, but often not specific

What are the different ANA patterns?



Associations with Specific ANA Patterns

ANA Patterns & Associated Rheumatic Diseases

ANA Pattern	Associated Rheumatic Disease
Homogenous	• Systemic lupus erythematosus (SLE) • Mixed connective tissue disease (MCTD) • Drug-induced Lupus • Juvenile Idiopathic Arthritis (JIA)
Speckled	• Systemic lupus erythematosus (SLE) • Sjogren's Syndrome (SS) • Polymyositis/Dermatomyositis (PM/DM) • Systemic sclerosis or scleroderma (SSc)
Nucleolar	• Diffuse systemic sclerosis/scleroderma • Polymyositis
Centromere	• Limited systemic sclerosis/scleroderma
Peripheral	• Systemic lupus erythematosus (SLE) • Systemic sclerosis/scleroderma

Created by @MithuRheum @AnnKumfer

Interpreting +ANAs!

What **diseases** are associated with a **+ANA**?

Rheumatic Diseases

- Lupus (SLE)
- Systemic Sclerosis (scleroderma)
- Rheumatoid Arthritis
- Sjögren Syndrome
- Myositis
- Mixed Connective Tissue Disease (MCTD)
- Juvenile Idiopathic Arthritis
- Drug-Induced Lupus

Non-Rheumatic Diseases

- Malignancy
- Lymphoproliferative Disorders
- Infection
- Autoimmune Thyroid
- Autoimmune Hepatitis
- Primary Biliary Cirrhosis
- Drug-Induced
- Inflammatory Bowel Disease
- Interstitial Pulmonary Fibrosis
- Multiple Sclerosis

& More

AUTOANTIBODIES IN RHEUMATOLOGY

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	AUTOANTIBODIES	SIGNS & SYMPTOMS for DX	OTHER ASSOCIATIONS / RX
*	ANA (anti-nuclear antibody)	can be seen in SLE, RA, Myositis, Sjogren's, Scleroderma + other autoimmune diseases	
LUPUS (SLE)	ANA (anti-nuclear antibody) dsDNA (double-stranded DNA) Anti-Smith Anti-Ro (SSA) and Anti-La (SSB) Others (RNP, aPL antibodies)	**I** Immunoglobulins; **M** Malar Rash; **D** Discoid Rash; **A** Antinuclear Antibody (ANA); **M** Mucositis (Oral/Nasal Ulcers); **N** Neurologic **S** Serositis (pleuritis, pericarditis); **H** Hematologic (cytopenias); **A** Arthritis; **R** Renal (Lupus Nephritis); **P** Photosensitivity	• flare: classically ↑ dsDNA, ↓ C3/C4 • anti-histone = drug-induced lupus • +SSA x pregnancy: ↑ risk neonatal lupus • Libman-Sacks Endocarditis: nonbacterial thrombi on valves (usually mitral/aortic) • Causes of Death: renal, infection, CVD • Rx: hydroxychloroquine + immunosuppressant medications
ANTIPHOSPHOLIPID ANTIBODY SYNDROME	Anti-cardiolipin (aCl) B2 glycoprotein I (β2GP) Lupus Anticoagulant (LAC)	• Thrombosis (arterial or venous) or recurrent miscarriages • Laboratory Findings: positive aCL (>40), β2GP (>40) or LAC • Non-Criteria Manifestations: cutaneous (livedo reticularis), thrombocytopenia, neurologic, renal + others	• aCL antibodies ⇢ false +VDRL/RPR • Rx: anticoagulation with **warfarin**
SJOGREN SYNDROME	Anti-Ro (SSA) Anti-La (SSB)	• keratoconjunctivitis sicca [exocrine gland destruction] • joint pain, xerostomia, tongue fissuring may be seen • antibodies: +ANA, +RF, +SSA/+SSB can be seen	• dental caries, MALT lymphoma • focal lymphocytic sialadenitis on labial salivary gland biopsy
MCTD	Anti-U1 RNP (ribonucleoprotein)	Features of **SLE + scleroderma + polymyositis** • U1RNP antibodies (ANA speckled pattern)	
RA	Rheumatoid Factor (RF) Cyclic Citrullinated Peptide (CCP)	• inflammatory arthritis: joint pain/swelling which improves with use, AM stiffness >1hr, symmetric joint involvement • extra-articular manifestations: ILD, pleuritis, pericarditis, Felty syndrome, AA amyloidosis, scleritis, Sjogren's, Caplan	• swan neck, boutonniere deformity • Rx: steroids, disease-modifying agents (methotrexate), biologics (TNFα inhibitors), small molecule (JAKi)
Myositis (IIM)	Anti-Jo-1 Others: SRP, Mi-2, TIF1γ, MDA5	• symmetric proximal muscle weakness, rash in DM • dermatomyositis (DM): Gottron papules, heliotrope rash • Raynaud's phenomenon, interstitial lung disease (ILD)	• DM: perimysial, CD4+ T-cells • PM: endomysial, CD8+ T-cells
Scleroderma (Systemic Sclerosis, SSc)	Anti-centromere Scl-70 (DNA topoisomerase I) RNA Polymerase III	• **Limited** SSc ("CREST"): **C**alcinosis, anti-**C**entromere, **R**aynauds, **E**sophageal dysmotility, **S**clerodactyly, **T**elangiectasias • **Diffuse** SSc: widespread skin involvement, rapid progression, and early visceral involvement [↑ organ involvement]	• skin thickening, Raynaud's • other: renal (scleroderma renal crisis), pulmonary (ILD, pHTN), GI (GERD, esophageal dysmotility), and CV • scleroderma renal crisis ⇢ Rx ACEi
ANCA Vasculitis	P-ANCA (perinuclear) C-ANCA (cytoplasmic)	• **MPA**: no granulomas on biopsy, +**p-ANCA** (**MPO**) • **GPA**: sinusitis, nasal septum perforation, +**c-ANCA** (**PR3**) • **EGPA**: adult-onset asthma, cardiac, eosinophilia, ↑ IgE	• all can cause pulmonary/renal vasculitis, skin involvement, neuropathy • Rx: cyclophosphamide or rituximab

THANK YOU!

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Can also access them via website:
www.rheumonepagers.com.

PHYSICAL EXAM!

Just a quick reminder of its importance

INFLAMMATORY ARTHRITIS

DIFFERENTIATING JOINT PAIN

INFLAMMATORY or NON-INFLAMMATORY?

ARTHRITIS IN SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES IS ASSOCIATED WITH **INFLAMMATORY** JOINT PAIN

	INFLAMMATORY Joint Pain	NON-INFLAMMATORY Pain
Timing of Pain	worse in the **AM**	worse in **evening**/lasts all day
Change w/ Activity	often **improves**	worse with **activity**
AM Stiffness	prominent, often >30-60min	if (+), usually lasts **< 30 min**
Swelling?	yes, often	usually no
Redness/Warmth?	sometimes	no

MANAGEMENT

INFLAMMATORY JOINT PAIN:

- consider referral to **Rheumatology**
- order **XR** of affected (painful) joints
- only check **labs** based on suspected condition:
  - **RF/CCP** (for RA) ⇢ if inflammatory joint pain
  - **HLA-B27** (for AS/SpA) ⇢ if inflammatory back pain
  - **ANA** ⇢ only if concern for SLE / scleroderma
  - **uric acid** ⇢ if concern for gout

NON-INFLAMMATORY JOINT PAIN: DO NOT SEND "AUTOIMMUNE"/RHEUM LABS

- consider **XR** of affected (painful) joints
- do **not** check **labs** ⇢ can get "false positives" esp. ANA)
- consider **acetaminophen** or oral/topical **NSAIDs** PRN
- consider **Physical Therapy,** exercises, orthotics
- osteoarthritis ⇢ f/u PCP, consider **Ortho referral**/injection
- chronic pain/fibromyalgia ⇢ consider **Pain Management**

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SIGNS OF INFLAMMATION SUGGESTIVE OF ACUTE SYNOVITIS

- Best indicator: distended joint capsule with warmth
- Synovial distention, warmth, limited range of motion
- Erythematous: Think acute septic or crystalline arthritis -> TAP IT!
- Good "rule of thumb" is to palpate the joint with enough pressure to blanche your distal thumbnail
- "Stressing" a joint – gentle passive range of motion
- What is crepitus?
  - Fine vs coarse

RA VS OA

Table 5-4.

FEATURE	RHEUMATOID ARTHRITIS	OSTEOARTHRITIS*
Symmetry	Yes	Occasional
Synovitis	Yes	Rarely†
Nodules	Yes	No
Digital infarcts	Seldom	No
Bony hypertrophy	No	Yes
Joint involvement		
DIP	No	Heberden's nodes
PIP	Yes	Bouchard's nodes
MCP	Yes	No‡
CMC	No	Thumb
Wrist	Yes	No§
Deformities	Swan neck Boutonniere Subluxation Ulnar drift	DIP or PIP angulation

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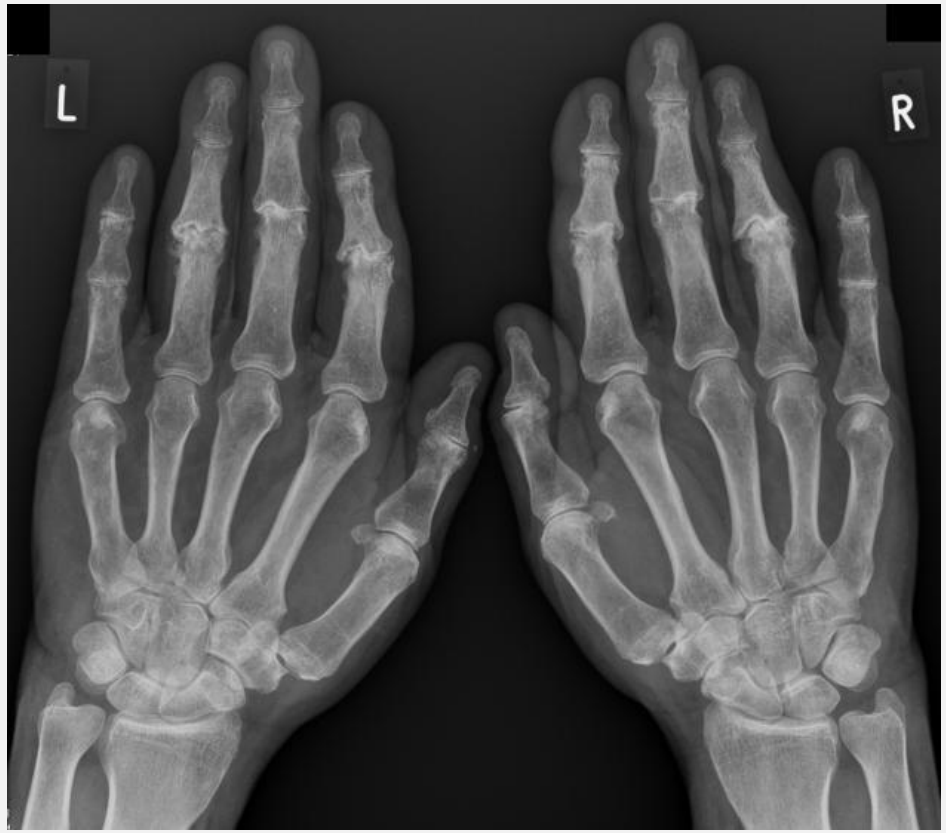
OA MANAGEMENT

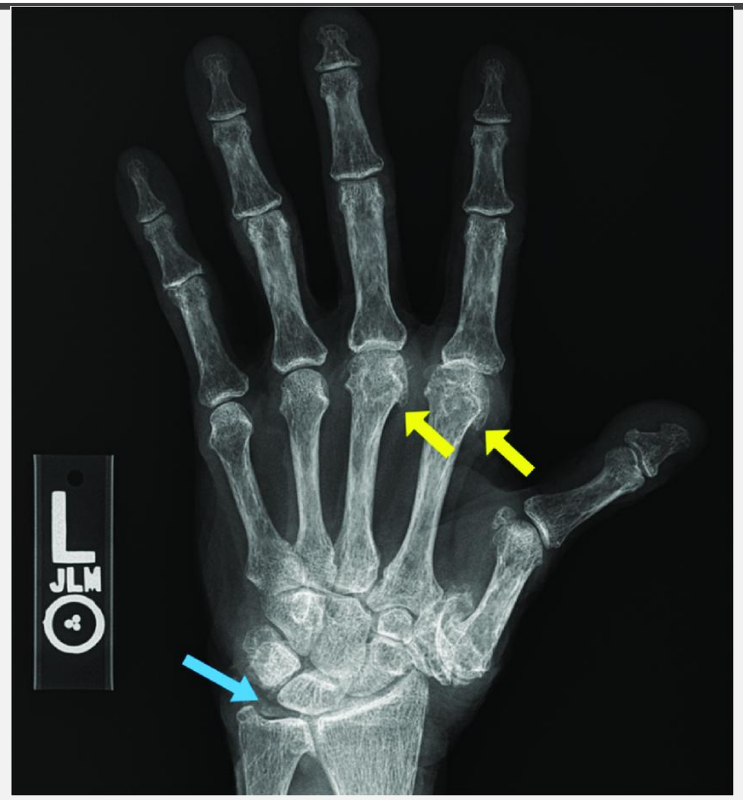
- XR, do NOT check labs (false positives), PT, orthopedics referral, pain management
- Weight loss (incorporate aerobic training, resistance training w/ muscle strengthening, and flexibility/ROM)
- Tai chi
  - Particularly effective in improving balance, pain, stiffness, and knee OA (1-3 x week for at least 3 months)
- Topicals
  - Diclofenac gel, capsaicin, arnica gel (apply to joint 2-3 x daily x3 weeks)
- Acupuncture (up to 12 weeks to improve short term symptoms hip and knee OA), yoga, moist heat for muscle relaxation, cold packs/ice after exercise to reduce swelling
- Oral NSAIDs, acetaminophen
- Intraarticular steroids
- Duloxetine
- Tramadol

EROSIVE (INFLAMMATORY) OA



https://radiopaedia.org/cases/erosive-osteoarthritis-1

CALCIUM PYROPHOSPHATE DEPOSITION DISEASE (CPPD)

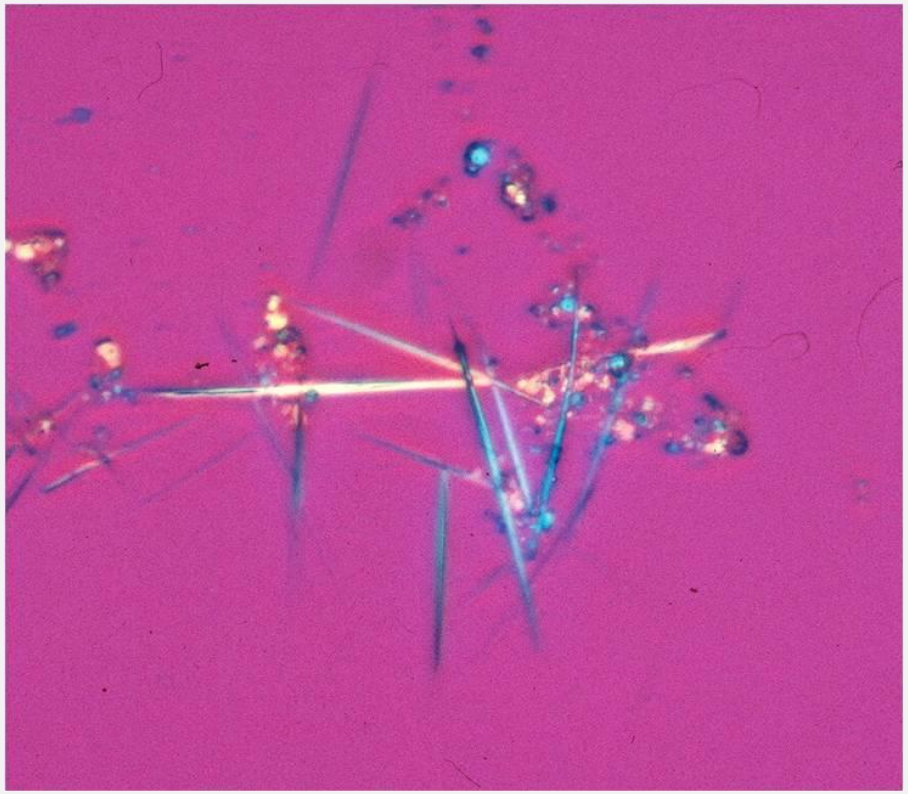


Radiographic Findings of Inflammatory Arthritis and Mimics in the Hands - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/year-old-male-with-CPPD-arthropathy-Severe-first-carpometacarpal-osteoarthritis_fig7_363308634 [accessed 13 Feb 2025]

GOUT

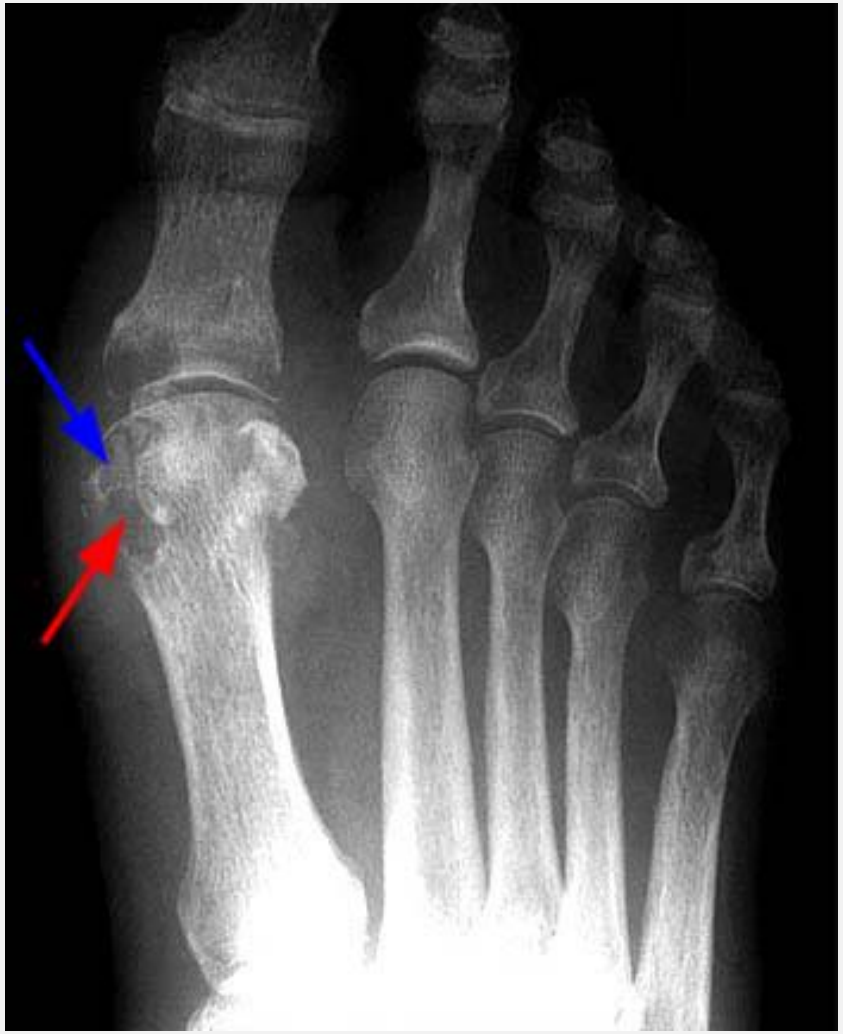
GOUT

- Most common inflammatory arthritis in US
- Hyperuricemia > 6.8 mg/dL
- Underexcretion of uric acid (UA) vs overproduction vs both
- Serum UA tends to **normalize during acute flare** in a third of patients
- Some develop tophi usually in 10 yrs of uncontrolled gout
- **Gold Standard**: aspiration of synovial fluid or tophi revealing monosodium urate (MSU) crystals

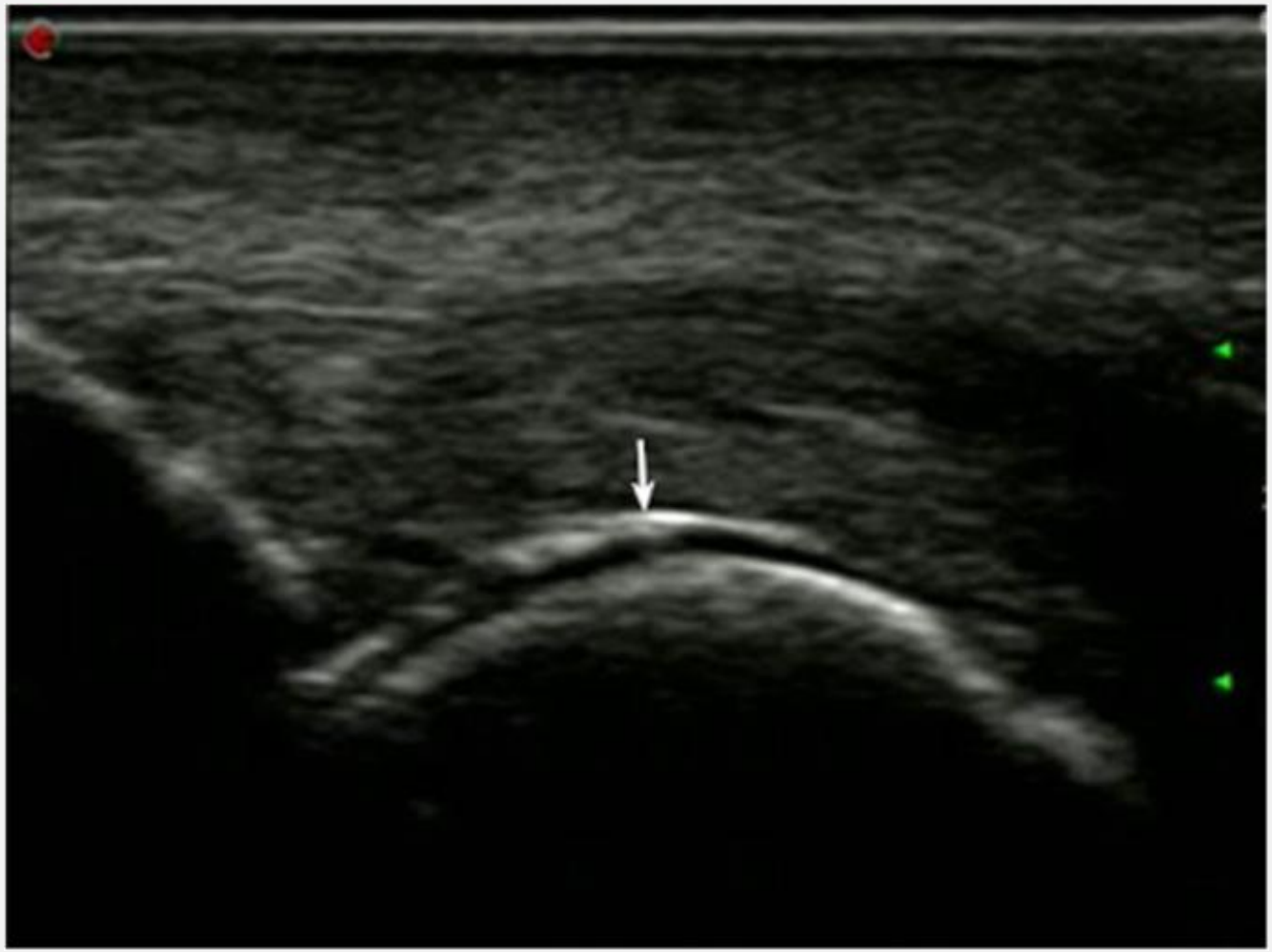


GOUT IMAGING

- X-ray with classic gout findings of punched out "rat-bite" erosion with overhanging edges. Do not typically see periarticular osteopenia unless late, progressed disease (as opposed to RA)
- Ultrasound with "double contour sign"
  - Operator dependent. But has 77% sensitivity and 84% specificity
- DECT scan to distinguish hard to diagnose gout vs other co-existing degenerative or inflammatory disease.



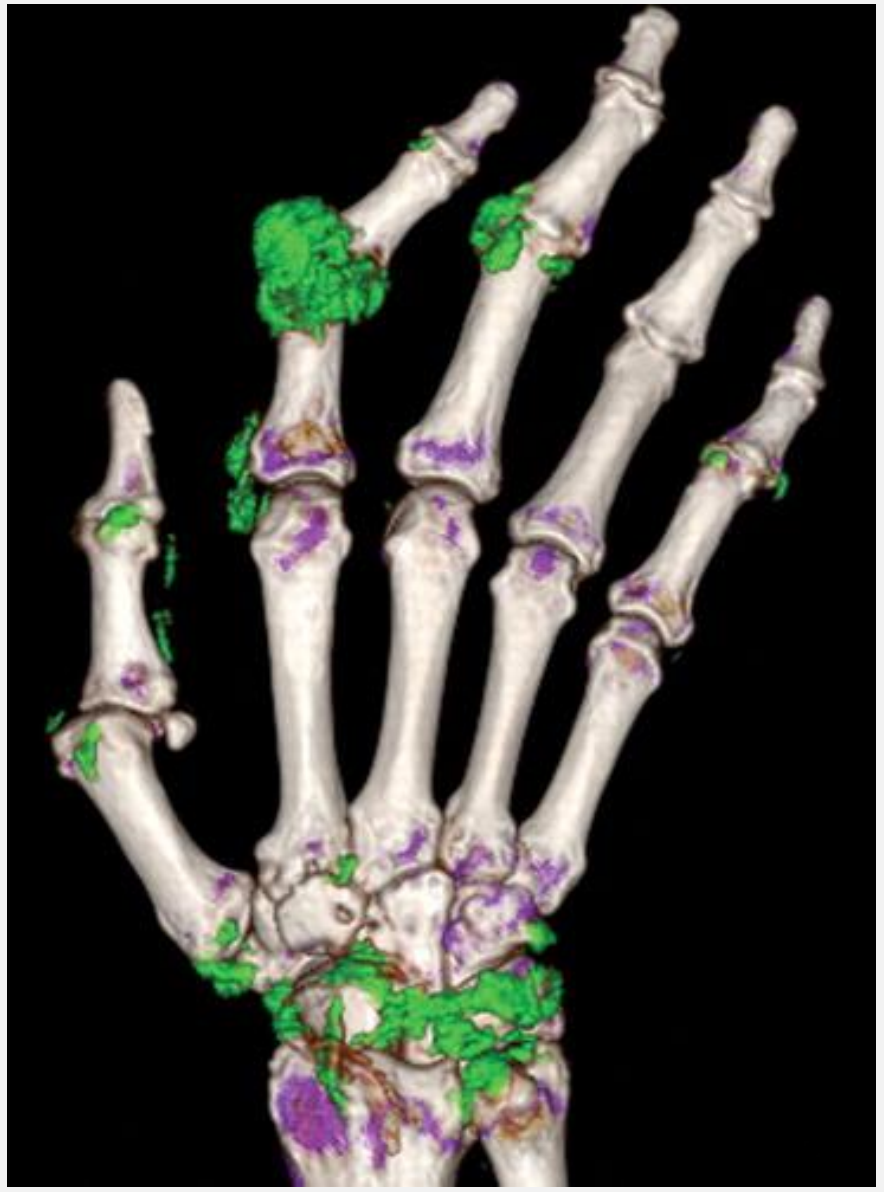
RadSource ©2022 https://radsource.us/gout/



Sun, C., Qi, X., Tian, Y. *et al.* Risk factors for the formation of double-contour sign and tophi in gout. *J Orthop Surg Res* **14,** 239 (2019). https://doi.org/10.1186/s13018-019-1280-0

DECT – DUAL ENERGY CT SCAN

- Green for gout
- Purple for calcium
- Good modality if unable to aspirate joint, co-existing severe inflammatory or degenerative arthritis
- False negatives reported in early gout
- False positives seen especially with degenerative arthritis
- 63% sensitivity/92% specificity
- Can be hard to find a facility that performs this imaging as it is relatively newer technology.



Desai M, Peterson J, Warren H, Garner M. Clinical Utility of Dual-Energy CT for Evaluation of Tophaceous Gout. https://pubs.rsna.org/doi/10.1148/rg.315115510. Published September 6, 2011. Accessed January 12, 2022.

EXTRA-ARTICULAR MANIFESTATIONS OF GOUT

- Urate deposition has also been found in the following areas, leading to inflammation and chronic disease:
  - Myocardium[1]
  - Coronary Arteries
  - Prostate
- Uncontrolled gout has been found to be an independent risk factor for developing:[2]
  - Hypertension
  - Cardiovascular disease
  - Stroke
  - Chronic Kidney Disease
  - Metabolic syndrome

1. Frustaci A, Russo MA, Sansone L, et al. Heart Failure From Gouty Myocarditis: A Case Report. Annals of Internal Medicine. 2019;172(5):363. doi:https://doi.org/10.7326/l19-0486
2. Glasnović M. Giht kao sustavna bolest: sistemske manifestacije i komorbiditeti u hiperuricemiji [Gout as a systemic disease: systemic manifestations and comorbidities of hyperuricaemia]. Reumatizam. 2012;59(2):119-32. Croatian. PMID: 23745468.

WHEN TO START URATE LOWERING THERAPY?

- One or more tophi present on exam
- Any evidence of radiographic damage due to gout (ex: erosions on XR)
- More than one gout flare per year
- If only one gout flare but also have comorbidities such as CKD 3, Uric acid > 9 mg/dL, urolithiasis

- We do not treat asymptomatic hyperuricemia due lack of data thus far supporting this

TREATMENT APPROACH

- Treat to Target Serum Uric acid level < 6 or < 5 with tophi
  - Titrate the urate lowering agent to this goal. Serial labs with sUA level q 2-4 weeks while monitoring patient for side effects until at goal.
- Always start an anti-inflammatory agent at the same time as the ULT
  - Anti inflammatory agent should be taken daily and continued for at least 3-6 months.
- Review modifiable risk factors: diet, diuretics, weight loss efforts, volume depletion, etc.
- Do not stop ULT during flares. Not CI to start ULT during flare, but I do wait.
- ULT is a lifelong, chronic medication

ACUTE FLARE AND PROPHYLAXIS

- Colchicine 1.2mg x 1 at beginning of flare followed by 0.6mg 1 hour later.
- Colchicine 0.6mg QD or BID for 3-6 months
- It is safe in CKD with dosing changes if GFR < 30mL/min.
- Avoid in those w/ concurrent CKD AND severe hepatic disease.

- NSAIDs in those who can tolerate them (not for CKD, recent PUD, recent cardiac stent/CABG)

ACUTE FLARE AND PROPHYLAXIS

- Glucocorticoids – roughly 0.5-1 mg/kg at start of flare in those who cannot take NSAIDs, Colchicine, etc.
  - **Inpatient**: I like Solumedrol 80mg IV x 1, followed by PO Prednisone 40mg/d x 2-3 days, 30mg/d x 2-3 days, 20mg/d x 2-3 days, 10mg/d x 2-3 days, then stop.
  - **Outpatient**: Oral portion of steroid taper.
  - For prophylaxis, Prednisone 5-10 mg/day.
  - Intra-articular only when you are VERY confident there is no underlying infection.

ACUTE FLARE AND PROPHYLAXIS

- Canakinumab – IL-1β inhibitor by binding it to block interaction with its IL-1 receptor.
  - **FDA approved as of August 2023.** Dose:150mg subq x 1 ASAP at start of attack. It has a long half life of about 26 days.
  - If retreatment required, can give after at least 12 weeks from prior dose.
  - Was found to be superior to Triamcinolone in acute gout and superior to Colchicine in gout prophylaxis.
- Anakinra - IL-1 Receptor antagonist.
  - Used off-label for treatment of acute gout
  - Daily subq injection with high incidence of injection site reactions.
  - Increased risk of serious infections, neutropenia, although rare.

CHRONIC GOUT MANAGEMENT

- 1st Line Treatment: Allopurinol = purine-like Xanthine Oxidase Inhibitor (XOI).
- Start low and up-titrate slowly to goal sUA
  - Start at 100mg/day and up-titrate every few weeks based on sUA.
  - **If GFR < 30**, start at 50mg/d.
  - Some patients may need as high as 900mg/d of Allopurinol.
  - Two main causes of inadequate response to Allopurinol are
    - Poor Adherence
    - Under-dosed Allopurinol.
  - Can screen for HLA-B*5801 allele in susceptible populations (Asians, African Americans) as it has 150-500x increased risk for Allopurinol Hypersensitivity Syndrome. If positive, use febuxostat first instead.

CHRONIC GOUT MANAGEMENT

- 2nd Line Treatment: Febuxostat = non-purine selective XOI.
  - Start around 40mg/d and up titrate to 80mg/d if needed. Safe in CKD but limit to 40mg/d if GFR < 30
- 2nd line due to cost, and some cardiovascular concerns.
  - **CVD Black Box warnings**. Try other oral ULT in those with known CVD before Febuxostat. However, the trial studying this for Febuxostat had several flaws.

- Probenecid = Uricosuric that promotes uric acid excretion via inhibition of URAT-1 and GLUT-9 in renal tubules.
  - Used best when added onto a XOI.
  - AVOID if GFR < 50 due to lack of efficacy.
  - CONTRAINDICATIONS: nephro/urolithiasis, concomitant salicylates (Aspirin decreases effectiveness of Probenecid)
  - Numerous drug interactions and can increase serum concentrations of NSAIDs, many antibiotics, sulfonylureas, Heparin, Dapsone, Methotrexate, etc.

CHRONIC GOUT MANAGEMENT

- Any XOI and Azathioprine/Mercaptopurine drug interaction → higher levels of the immunosuppressant as AZA/MP are metabolized by XO. **Avoid this combination** as much as possible or use lower doses of the immunosuppressant if necessary.

CHRONIC GOUT MANAGEMENT

- Pegloticase = Recombinant pegylated Uricase which converts uric acid into Allantoin (5-10x more soluble)
  - IV q 2 wks. Cost-prohibitive also, therefore not 1st or 2nd line unless failed others and/or significant tophi burden.
  - CONTRAINDICATION: G6PD deficiency → increased risk of hemolytic anemia and methemoglobinemia. All must be screened for this prior to administration.
  - sUA levels down to undetectable.
  - Gout flare prophylaxis is mandatory as well as pretreatment with antihistamines, acetaminophen and steroids (if needed).
  - High rate of developing anti-pegloticase antibodies which are associated with anaphylactic infusion reactions. Check sUA prior to every infusion. If sUA rising > 6 prior two consecutive infusions, med is discontinued.
    - This risk is significantly diminished with concomitant use of DMARD therapy (ex: Methotrexate, Mycophenolate) to prevent antibody formation

ADJUNCTIVE RISK MODIFICATIONS

- Adjunct because > 80% gout due to urate underexcretion, not overproduction! Dietary changes will not have as much of an impact as pharmacotherapy itself.
- Weight loss efforts – obesity is a risk factor
- Treat any underlying Hyperparathyroidism, Hypothyroidism
- Diet
- Most common drug causes hyperuricemia:
  - Cyclosporine, Alcohol, Nicotinic Acid, Thiazides/Loop diuretics, Tacrolimus, Ethambutol, Aspirin (low dose), Pyrazinamide
- Uricosuric agents that can help lower sUA:
  - Losartan, Amlodipine, Atorvastatin, Rosuvastatin, Fenofibrate, high dose Salicylates, Leflunomide

SPONDYLOARTHROPATHY

SpA

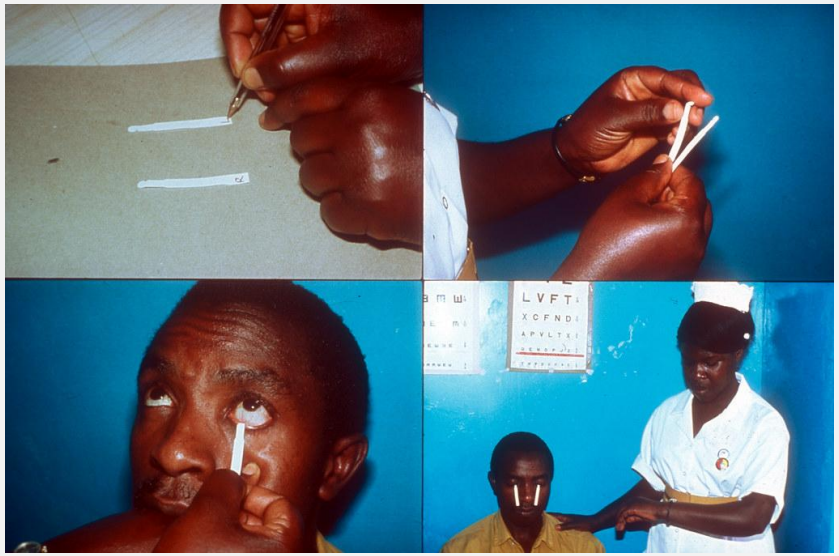
SPONDYLOARTHROPATHY

- Inflammatory back pain: Patient less than 40 yr (or onset before 40) with 3 out of 4 below has high likelihood
  - 1) morning stiffness of at least 30 min
  - 2) Improvement of back pain w/ exercise but not rest
  - 3) Awakening b/c of back pain and stiffness during the second half of the night only
  - 4) Alternating buttock pain
- HLA-B27
- Good response NSAIDs
- Uveitis/iritis, PsO, IBD or bowel complaints

SJOGREN'S SYNDROME

SJOGREN'S

- Most common autoimmune disease in middle-aged women
- Seen in the setting of other autoimmune disease (primary vs secondary)
- SSA/B antibodies, 75-95% have RF, can be seronegative
- Dx gold standard minor salivary gland biopsy with lymphocytic infiltrate
  - Other testing: Schirmer's tear test, ocular surface staining (OSS) and tear break-up time (TBUT)
    - OSS and TBUT performed by ophthalmologist
- Antibodies not specific
- Mother with SSA and/or SSB have increased risk of infant with neonatal lupus or complete heart block (even if w/o clinic features), patient should be on HCQ in pregnancy to dec. risk of block
- Lymphoma (lifetime frequency 5-10% and usually NHL with a predominant subtype of MALT)
- Regular dental and eye exams



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GCA/PMR

And Ultrasound

POLYMYALGIA RHEUMATICA

- Patients age >/= 50 years
- Symmetric shoulder girdle and bilateral hip pain
- ESR >40 mm/hr and/or elevated CRP
- Negative RF and CCP
  - Late onset RA can mimic PMR
- Should respond completely to 20 mg daily of prednisone
- ESR should normalize within a month
- Fever or failure to respond to suggests giant cell arteritis or another diagnosis, such as lymphoma
- GCA occurs in approximately 15%

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GIANT CELL ARTERITIS

- Large vessel vasculitis
- Patients age >/= 50 years
- Constitutional symptoms, HA, jaw or tongue claudication, visual disturbance, scalp tenderness
- PMR noted in 40-60% patients w/ GCA
- Less than 5-10% with ESR <30 and normal CRP
- Gold standard for dx traditionally TA biopsy; Unilateral bx sensitivity 87% and additional/contralateral biopsies increase the sensitivity by 5%.
- Temporal artery duplex US which may show homogenous wall thickening "halo sign"
- **Intact vision**: prednisone 1 mg/kg (usually no more than 60 mg/day)
- **Threatened vision**: methylprednisolone 1G IV a day x3 days (**DO NOT WAIT!**)

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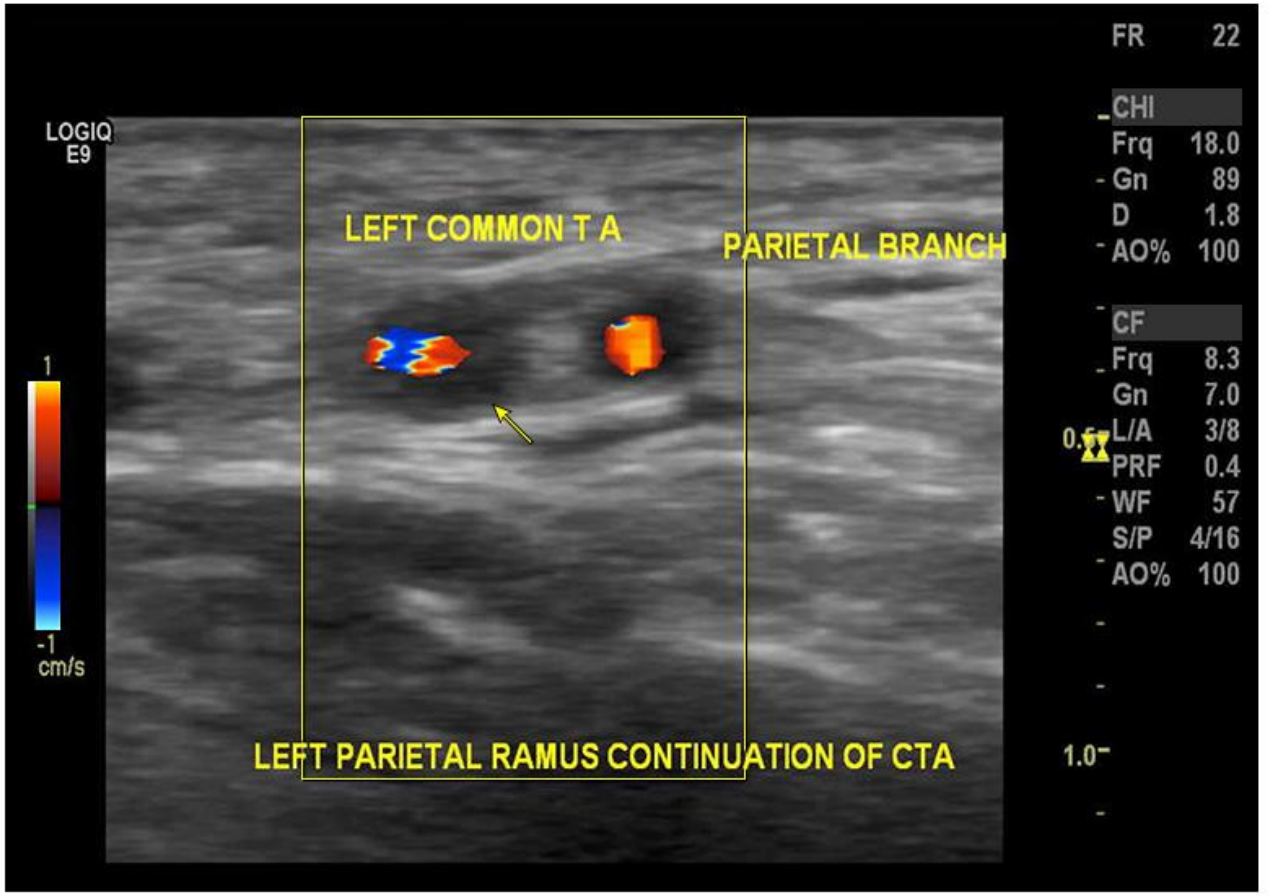
Arterial wall edema in giant cell arteritis



Ultrasound showing circumferential dark areas about the vascular lumens of the common superficial temporal artery and its parietal branch ("halo signs") in a patient with GCA. The halo sign results from hypoechogenicity of the vessel wall, attributed to mural edema.

GCA: giant cell arteritis, also known as Horton disease, cranial arteritis, and temporal arteritis.

Courtesy of William Docken, MD.

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EMERGENCIES

CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME (CAPS)

CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME (CAPS)

- Less than 1% of those with APS
- Initial presentation of APS in 50% of pts who develop CAPS
- Large vessel to microvascular. Venous and arterial.
- 3 or more organs simultaneously or within 1 week and histology showing predominately small vessel thrombosis in a patient with aPL abs
  - Lupus anticoagulant (LA), anticardiolipin antibodies (aCL abs), anti-β2GPI antibodies, and anti-phosphatidylserine-dependent prothrombin (anti-PS/PT) antibodies
  - Renal, CNS, pulmonary, cardiovascular, cutaneous, gastrointestinal, etc.
- Microangiopathic hemolytic anemia (MAHA) such as thrombocytopenia and schistocytes on peripheral blood smear
- Inciting event for CAPS is unknown in 45% of patients
- DDX: DIC, HIT and other anti-PF4 disorders, Primary thrombotic microangiopathies (such as TTP, HUS etc.), Vasculitis, Sepsis, Pre-eclampsia or HELLP

CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME (CAPS)

Definitive CAPS (if all 4 criteria met)

- Involvement of ≥3 organs, systems, or tissues
- Manifestations develop simultaneously or over <1 week
- Small vessel occlusion is confirmed histologically in at least one organ or tissue
- Presence of aPL (anticardiolipin antibodies, anti-beta2-glycoprotein I antibodies, and/or lupus anticoagulant) is documented twice, at least 12 weeks apart

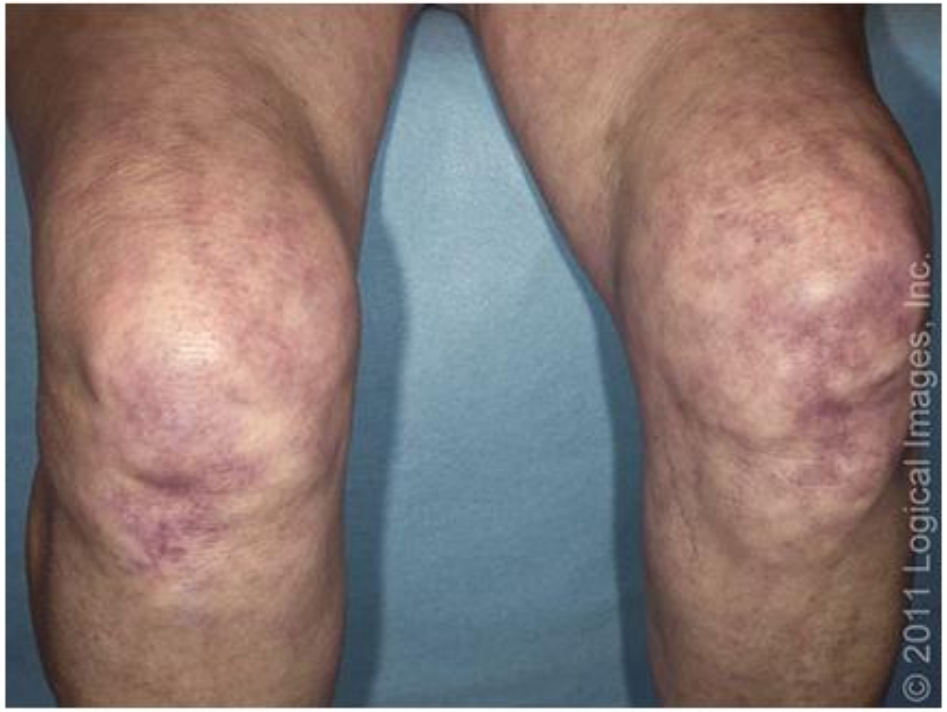
CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME (CAPS)

Treatment

- Methylprednisolone 1G IV a day x3 days followed by equivalent prednisone 1 mg/kg a day
- Intravenous unfractionated heparin and subcutaneous low molecular weight (LMW) heparin AND low dose ASA if without major bleed => warfarin with INR 2.0 to 3.0
- Therapeutic plasma exchange (TPE) or intravenous immune globulin (IVIG), but typically not both.
  - TPE is favored.
  - Check IgA before IVIG use.
- Refractory disease: rituximab or eculizumab (off-label)

CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME (CAPS)

Livedo reticularis



A red-blue, reticulated vascular network is present on the legs.

PULMONARY-RENAL SYNDROMES

PULM-RENAL SYNDROMES

- Pulmonary renal syndromes: diffuse alveolar hemorrhage, acute pneumonitis, rapidly progressing glomerulonephritis
  - Systemic lupus erythematous
  - Microscopic polyangiitis (MPA)
  - Granulomatosis polyangiitis (GPA)
  - Anti-glomerular basement membrane (GBM) syndrome
  - cAPS
  - Eosinophilic granulomatosis polyangiitis (EGPA)
    - Difficult to control asthma, chronic rhinosinusitis, and eosinophilia
  - Consider drug induced!

PULM-RENAL SYNDROMES

- Laboratory testing
  - ANA IFA, dsDNA crithidia, Smith, RNP, C 3/4, UA, PCR
  - ANCA: MPO, PR3 (PR3 specific!)
  - Anti-GBM
  - IgE level, peripheral blood eosinophilia ≥1000 cells/microL

  - Rule out infection!

ANCA ASSOC. VASCULITIS

PEXIVAS Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Plasma Exchange and Glucocorticoids in Severe ANCA-Associated Vasculitis

M. Walsh, P.A. Merkel, C.-A. Peh, W.M. Szpirt, X. Puéchal, S. Fujimoto, C.M. Hawley, N. Khalidi, O. Floßmann, R. Wald, L.P. Girard, A. Levin, G. Gregorini, L. Harper, W.F. Clark, C. Pagnoux, U. Specks, L. Smyth, V. Tesar, T. Ito-Ihara, J.R. de Zoysa, W. Szczeklik, L.F. Flores-Suárez, S. Carette, L. Guillevin, C.D. Pusey, A.L. Casian, B. Brezina, A. Mazzetti, C.A. McAlear, E. Broadhurst, D. Reidlinger, S. Mehta, N. Ives, and D.R.W. Jayne, for the PEXIVAS Investigators*

OTHER VASCULITIS

OTHER VASCULITIS

- Central nervous system vasculitis
- Polyarteritis nodosa (medium vessel) with GI bleed, perforation, or similar
- IgA vasculitis (small vessel) with renal or end organ damage

SCLERODERMA RENAL CRISIS

SCLERODERMA RENAL CRISIS

- Risk factors:
  - Diffuse skin involvement, steroid use, RNA poly III antibody (anti-centromere assoc. lower risk)
- Typically occurs within first 5 years disease onset
- Acute onset HTN, sometimes with feature of malignant HTN (10% occur in absence of HTN – sig. change from baseline such as 100/60 to 130/80
  - Increase in SBP of ≥30 mmHg above baseline, or an increase in DBP ≥20 mmHg above baseline
- AKI with normal urine sediment
- Start captopril regime with goal to return to BP baseline in 72 hours

- No radial arterial lines in scleroderma patient 2/2 risk hand necrosis

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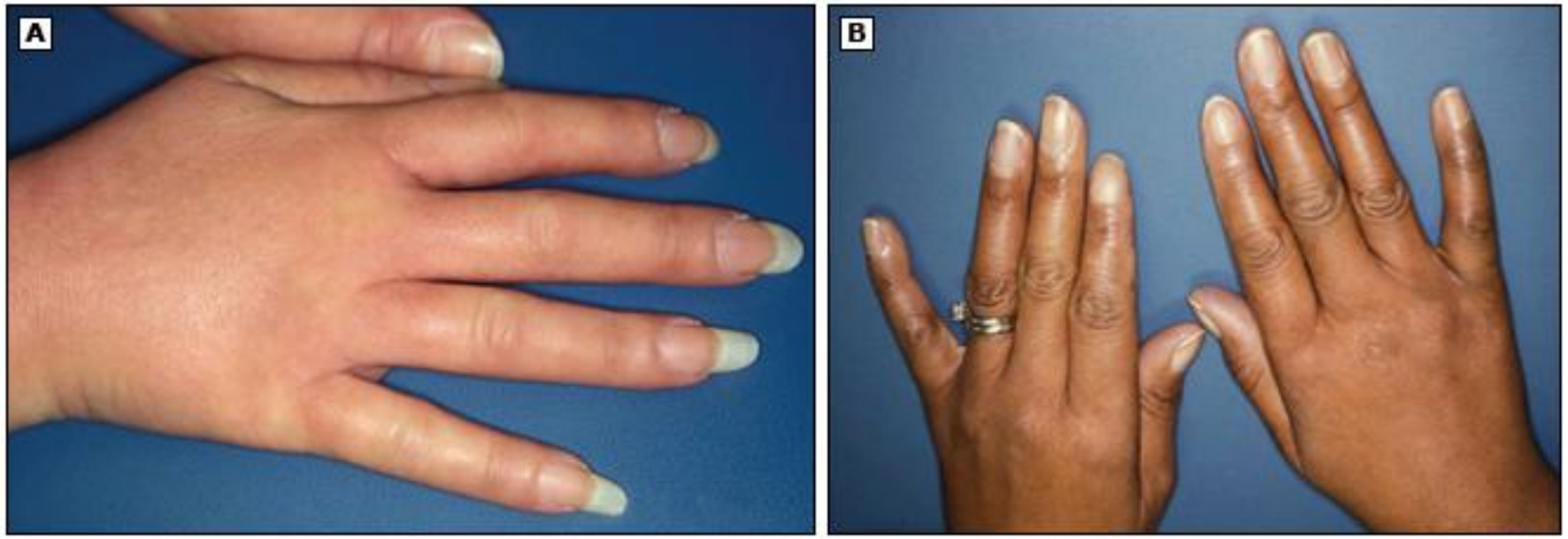
Puffy hands and shiny skin in early systemic sclerosis



(A) Diffusely puffy fingers are a common initial presentation.

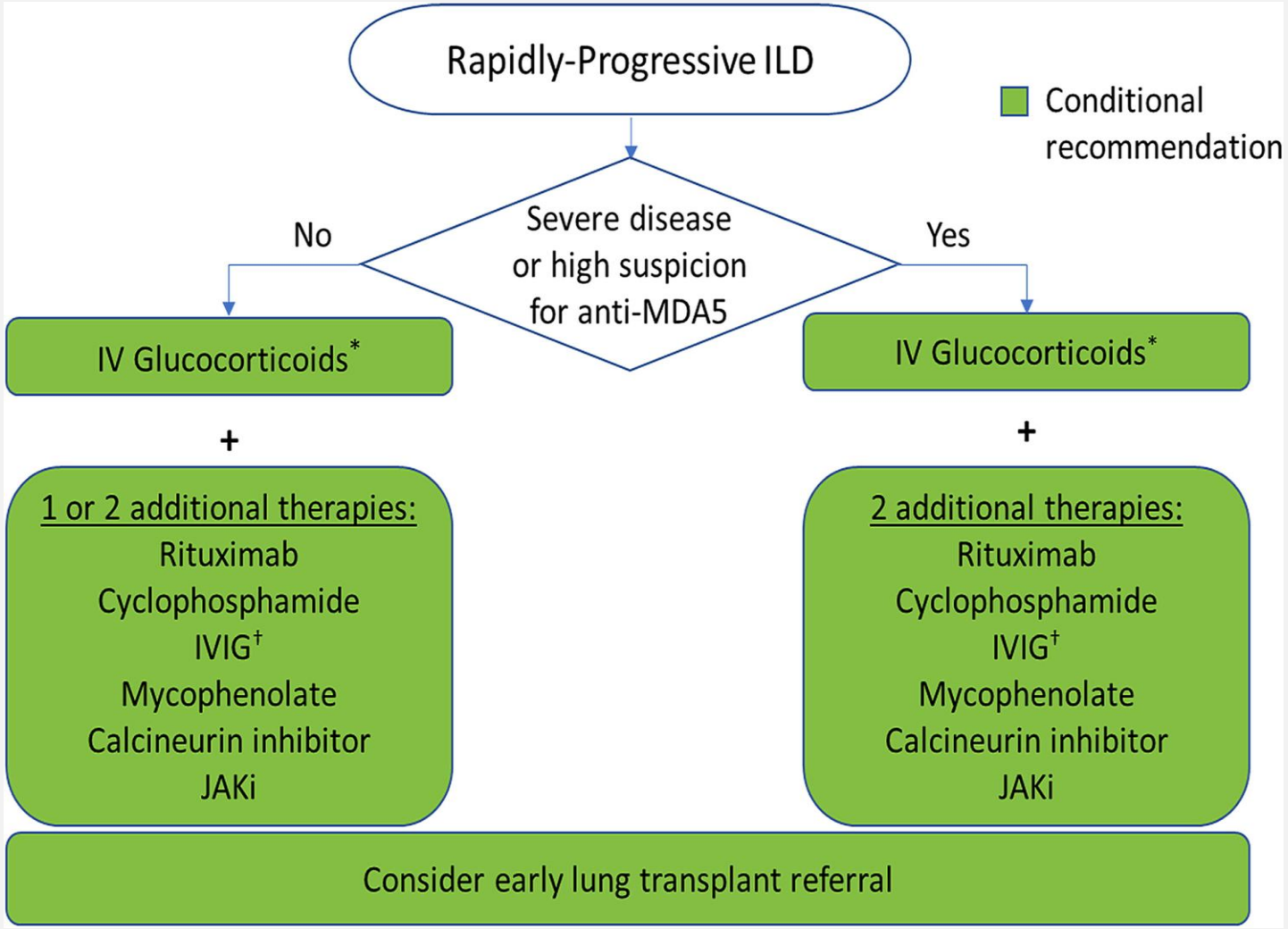
(B) Shiny skin suggests impending skin thickening.

INFLAMMATORY MYOPATHY/ILD

IMFLAMMATORY MYOPATHY/ILD

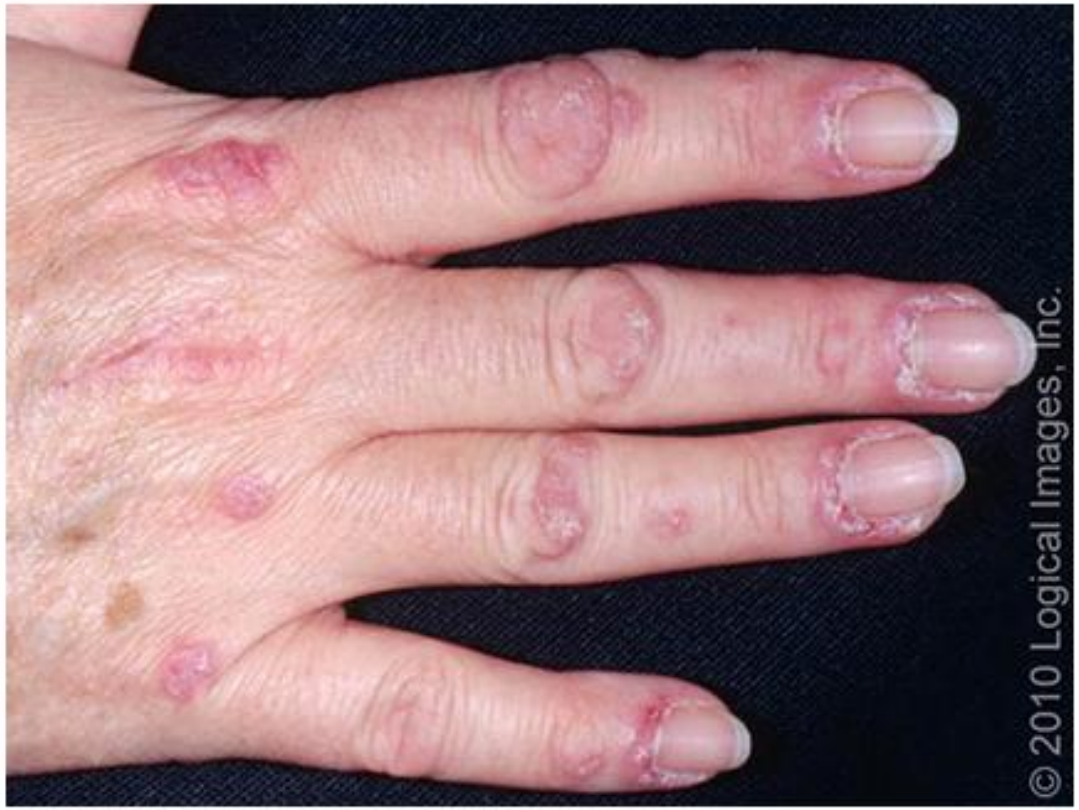
- The EMERGENCY: Myositis/antisynthetase syndrome with rapidly progressing dysphagia or dyspnea/ILD
- Characteristic cutaneous findings, muscle weakness, and laboratory evidence of myositis -> no need for biopsy
- May be hypomyopathic or amyopathic
- Anti-HMGCR autoantibodies with or without a history of statin use
  - NO statins! NO ezetimibe! PCSK9 inhibitors ONLY!
- Anti-MDA5 DM w/ rapidly progressive ILD => steroid pulse plus two additional therapies
- Anti-TIF1-γ and anti-NXP2 high association malignancy (if juvenile, risk low)
  - Malignancy w/u at diagnosis

2023 American College of Rheumatology (ACR)/American College of Chest Physicians (CHEST) Guideline for the Treatment of Interstitial Lung Disease in People with Systemic Autoimmune Rheumatic Diseases



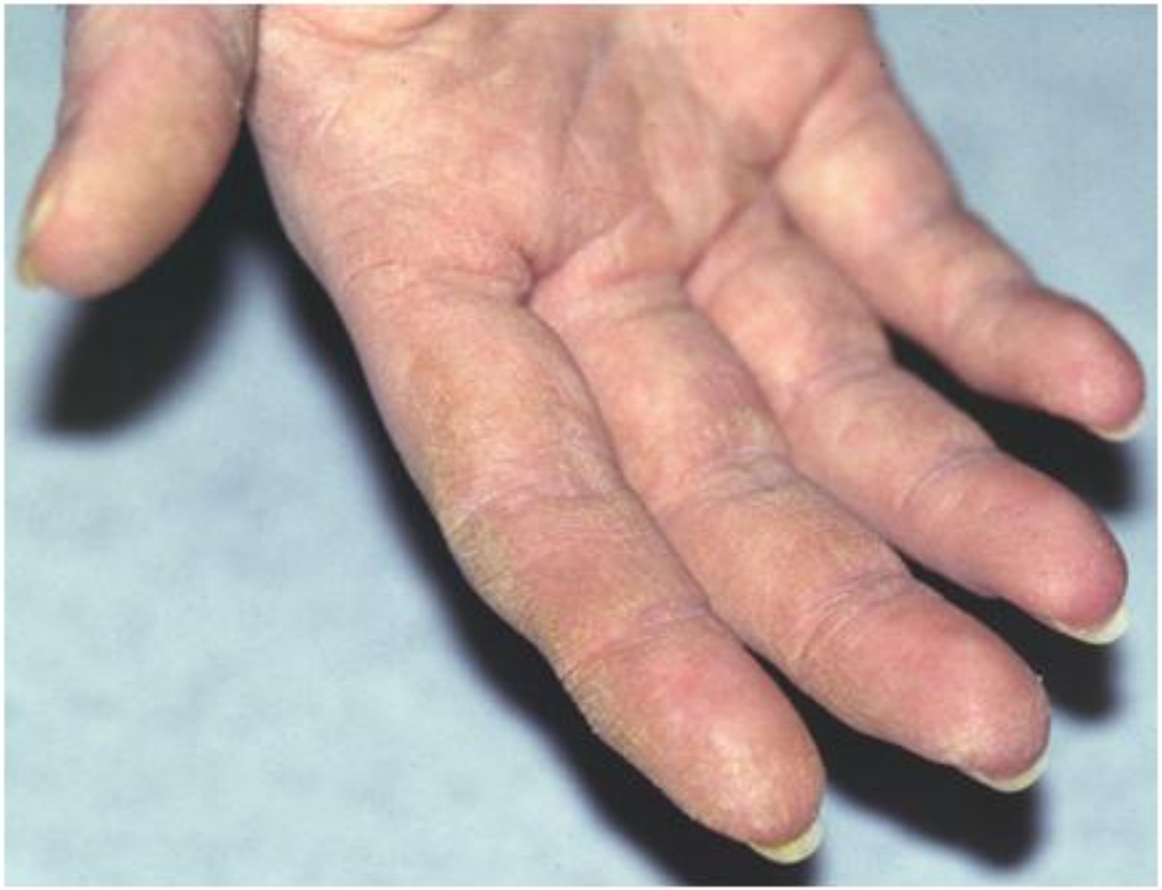
Arthritis & Rheumatology, Volume: 76, Issue: 8, Pages: 1182-1200, First published: 08 July 2024, DOI: (10.1002/art.42861)

Gottron's papules in dermatomyositis



Multiple violaceous, scaly papules are present overlying the joints on the dorsal hand.

Mechanic's hands in a patient with antisynthetase syndrome



Courtesy of John H. Stone, MD, MPH.

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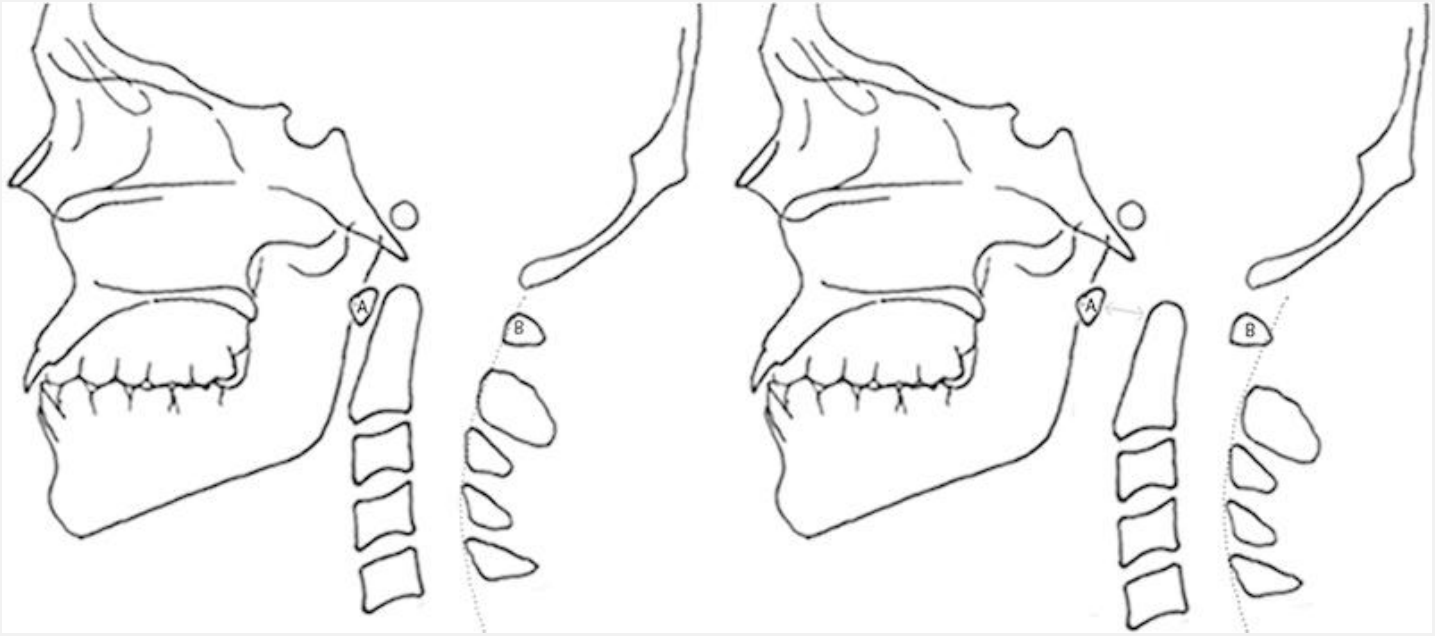
ATLANTO-AXIAL SUBLUXATION

ATLANTO-AXIAL SUBLUXATION

- Atlanto-axial subluxation with symptoms (Seropositive or erosive RA) – neurosurgery and inline intubation/direct laryngoscopy



Yang SY, Boniello AJ, Poorman CE, Chang AL, Wang S, Passias PG. A review of the diagnosis and treatment of atlantoaxial dislocations. Global Spine J. 2014 Aug;4(3):197-210. doi: 10.1055/s-0034-1376371. Epub 2014 May 22. PMID: 25083363; PMCID: PMC4111952.

OTHER EMERGENCIES

OTHERS TO CONSIDER

- Macrophage activation syndrome (HLH in the setting of rheumatologic disorders)
  - Please consult heme/onc as well
- Transverse myelitis, Neuromyelitis Optica
- Seizures in SLE/neuropsychiatric SLE
- Symptomatic extra-pulmonary sarcoidosis

IMMUNE RELATED ADVERSE EVENTS

(aka irAEs)

Immune checkpoint inhibitors by mechanism

Drug mechanism	Drug name
Anti-PD-1	▪ Nivolumab ▪ Pembrolizumab ▪ Cemiplimab ▪ Dostarlimab ▪ Retifanlimab ▪ Toripalimab ▪ Tislelizumab
Anti-PD-L1	▪ Atezolizumab ▪ Avelumab ▪ Cosibelimab ▪ Durvalumab
Anti-CTLA-4	▪ Ipilimumab ▪ Tremelimumab
Anti-LAG-3/anti-PD-1	▪ Relatlimab and nivolumab

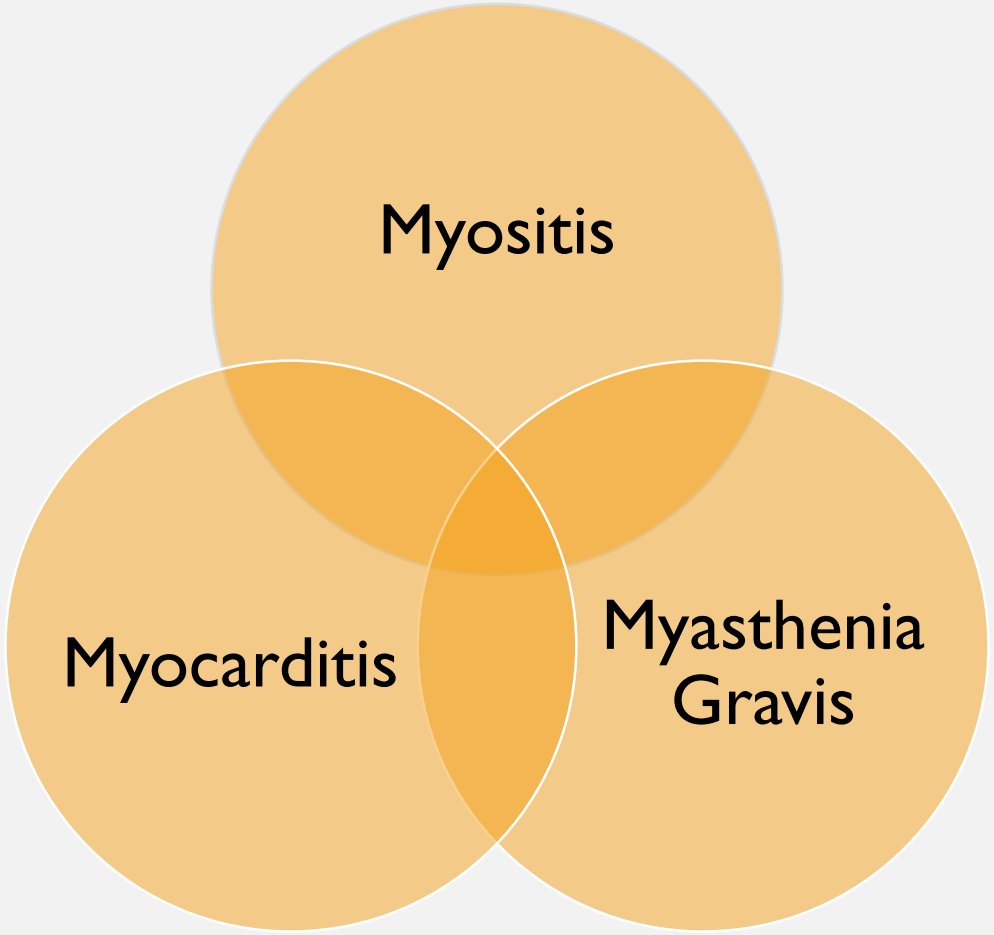
ADVERSE EVENTS

Common irAEs:

- •Dermatologic
- •Diarrhea/colitis
- •Hepatotoxicity
- •Pneumonitis
- •Endocrinopathies

Less common: renal, exocrine pancreas, central nervous system, cardiovascular, hematologic, eye, and rheumatologic and musculoskeletal systems.

MMM



REMINDERS

INPATIENT TIPS

- Rule out infection.
- Rule out malignancy.
- ANA and other antibodies may be present in infections and malignancies without associated connective tissue disease. Treat infection before autoimmune w/u!
- Monoarticular inflammatory arthritis is infection until proven otherwise.
- Is it drug-induced?
- Immune related adverse events (irAEs) should be a consideration with the use of check point inhibitors and similar in the treatment of malignancy.
- Initiate work-up for the rheumatologic concern and obtain biopsies when appropriate.
- Infection is the most likely reason a patient with a diagnosed rheumatologic disease is in the ICU.

DMARDS: CONVENTIONAL AND BIOLOGICS

CONVENTIONAL

- Hydroxychloroquine
- Sulfasalazine
- Methotrexate
- Leflunomide
- Azathioprine
- Mycophenolate

BIOLOGICS

- Common biologic targets include tumor necrosis factor (TNF), interleukin-6 (IL-6), interleukin-1 (IL-1), CD20 (on B cells), etc.
- New malignancy diagnosis – should be held
- How can you help?
  - Quant TB test
  - Hepatitis panel
  - Fasting lipid panel
  - Vaccinations (Live vaccinations CI while on immunosuppressive therapy)
  - Staying up to date on age appropriate and risk appropriate cancer screening test (including skin checks!)

PERI-OPERATIVE MED MGT

MEDICATIONS TO CONTINUE

MEDICATIONS TO CONTINUE THROUGH SURGERY		
DMARDs: CONTINUE these medications through surgery. (All patients)	**Dosing Interval**	**Recommended timing of surgery since last medication dose**
Methotrexate	Weekly	Anytime
Sulfasalazine	Once or twice daily	Anytime
Hydroxychloroquine	Once or twice daily	Anytime
Leflunomide (Arava)	Daily	Anytime
Doxycycline	Daily	Anytime
Apremilast (Otezla)	***Twice daily***	***Anytime***
SEVERE SLE-SPECIFIC MEDICATIONS††: CONTINUE these medications in the perioperative period in consultation with the treating rheumatologist.	**Dosing Interval**	**Recommended timing of surgery since last medication dose**
Mycophenolate mofetil	Twice daily	Anytime
Azathioprine	Daily or twice daily	Anytime
Cyclosporine	Twice daily	Anytime
Tacrolimus	Twice daily (IV and PO)	Anytime
Rituximab (Rituxan)	***IV Every 4-6 months***	***Month 4-6***
Belimumab (Benlysta)	***Weekly SQ***	***Anytime***
Belimumab (Benlysta)	***Monthly IV***	***Week 4***
Anifrolumab (Saphnelo)†	***IV Every 4 weeks***	***Week 4***
Voclosporin (Lupkynis)†	***Twice daily***	***Continue***

Goodman, S.M., Springer, B.D., Chen, A.F., Davis, M., Fernandez, D.R., Figgie, M., et al. American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline for the Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty. Arthritis Care Res 2022. https://doi.org/10.1002/acr.24893

MEDICATIONS TO HOLD

MEDICATIONS TO WITHHOLD PRIOR TO SURGERY***		
BIOLOGICS: WITHHOLD these medications through surgery		**Recommended timing of surgery since last medication dose**
Infliximab (Remicade)	Every 4, 6, or 8 weeks	Week 5, 7, or 9
Adalimumab (Humira)	Every 2 weeks	Week 3
Etanercept (Enbrel)	Every week	Week 2
Golimumab (Simponi)	Every 4 weeks (SQ) or every 8 weeks (IV)	Week 5 Week 9
Abatacept (Orencia)	Monthly (IV) or weekly (SQ)	Week 5 Week 2
Certolizumab (Cimzia)	Every 2 or 4 weeks	Week 3 or 5
Rituximab (Rituxan)	2 doses 2 weeks apart every 4-6 months	Month 7
Tocilizumab (Actemra)	Every week (SQ) or every 4 weeks (IV)	Week 2 Week 5
Anakinra (Kineret)	Daily	Day 2
IL-17-Secukinumab (Cosentyx)	Every 4 weeks	Week 5
Ustekinumab (Stelara)	Every 12 weeks	Week 13
Ixekizumab (Taltz)†	***Every 4 weeks***	***Week 5***
IL-23 Guselkumab (Tremfya)†	***Every 8 weeks***	***Week 9***
JAK inhibitors WITHHOLD this medication 3 days prior to surgery*		
Tofacitinib (Xeljanz):	***Daily or twice daily***	***Day 4***
Baricitinib (Olumiant)†	***Daily***	***Day 4***
Upadacitinib (Rinvoq)†	***Daily***	***Day 4***
NOT-SEVERE SLE: WITHHOLD these medications 1 week prior to surgery	**Dosing Interval**	**1 week after last dose**
Mycophenolate mofetil	Twice daily	**1 week after last dose**
Azathioprine	Daily or twice daily	1 week after last dose
Cyclosporine	Twice daily	**1 week after last dose**
Tacrolimus	Twice daily (IV and PO)	**1 week after last dose**
Rituximab (Rituxan)	Every 4-6 months	Month 7
Belimumab IV (Benlysta)	***Monthly***	***Week 5***
Belimumab SQ (Benlysta)	***Weekly***	***Week 2***

Goodman, S.M., Springer, B.D., Chen, A.F., Davis, M., Fernandez, D.R., Figgie, M., et al. American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline for the Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty. Arthritis Care Res 2022. https://doi.org/10.1002/acr.24893

INTEGRATIVE MEDICINE

Complements medical therapy

MEDITERRANEAN DIET

McKellar, G., et al., A pilot study of a Mediterranean-type diet intervention in female patients with rheumatoid arthritis living in areas of social deprivation in Glasgow. Ann Rheum Dis, 2007. 66(9): p. 1239-43
Skoldstam L., Hagfors L., Johansson G.: An experimental study of a Mediterranean diet intervention for patients with rheumatoid arthritis. Ann Rheum Dis 2003; 62: pp. 208-214

DIETARY

- Increase omega-3 fatty acids (salmon, walnuts, flaxseed, hempseed)
- Introduce anti-oxidants such as Vitamin E (800 units daily), Vitamin C (250mg 2x/day), selenium (in nuts or 100mcg daily)
- Avoid exacerbating factors (coffee, tobacco, alcohol)
- High fiber diet

Smedslund G., et. al.: Effectiveness and safety of dietary interventions for rheumatoid arthritis: a systematic review of randomized controlled trials. J Am Diet Assoc 2010; 110: pp. 727-735.

SUPPLEMENTS

- Turmeric 0.5-1g 2-3x/day
- Fish oil 3g/day
- Ginger 500 mg capsules at a dose of 1 g two or three times a day. Can increase up to 4 g daily.
- Vitamin D

Ernst E., and Chrubasik S.: Phyto-anti-inflammatories: a systemic review of randomized, placebo-controlled, double-blind trials. Rheum Dis Clin North Am 2000; 26: pp. 13-27
Proudman S.M., James M.J., Spargo L.D., et al: Fish oil in recent onset rheumatoid arthritis: a randomised, double-blind controlled trial within algorithm-based drug use. Ann Rheum Dis 2015; 74: pp. 89-95

EXERCISE AND WEIGHT MANAGEMENT

- Aquatic exercise (30 min 1-2x/week for 4-6 weeks)
- Light weight training → increase muscle strength around joints to improve stability
- Aerobic exercise → improve mood, decrease weight and fatigue
- Physical and Occupational therapy → improve range of motion and strengthen muscles

THANK YOU. QUESTIONS?