Take Home Messages and Clinical Pearls

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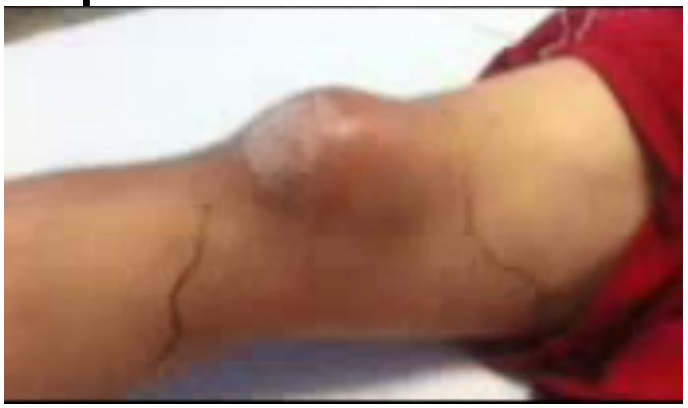
Disclosures

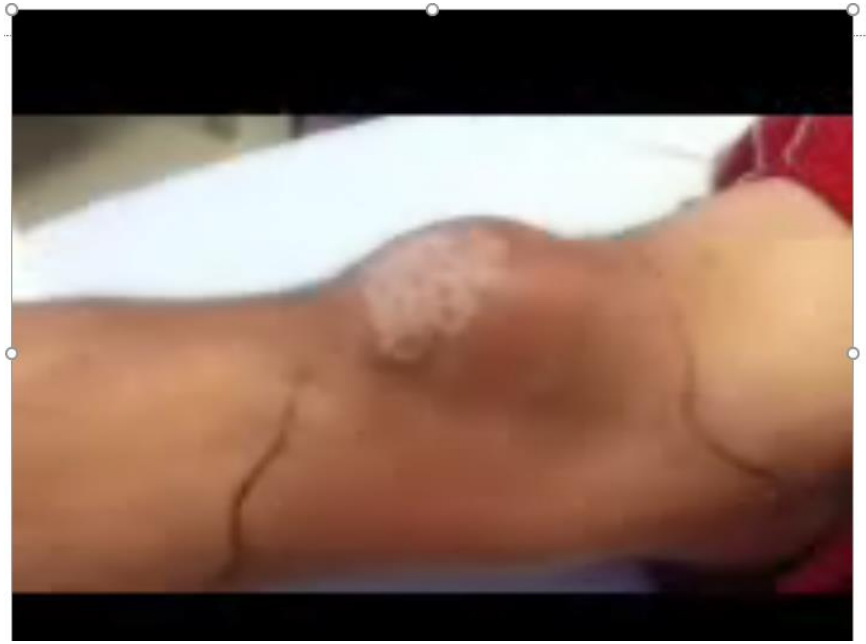
- Up To Date
- Genentech
- Bristol Myers Squibb
- Boehringer Ingelheim

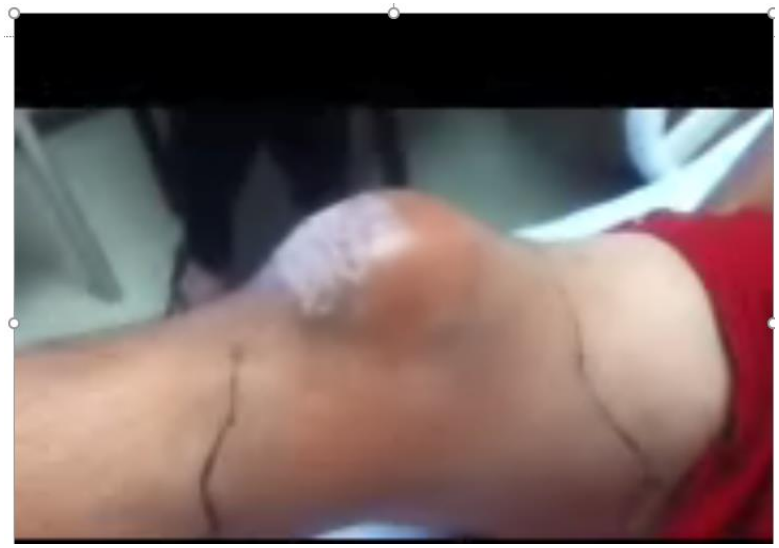
Teaching point:Distinguishing Bursitis vs arthritis on examination

- The ability to fully extend the knee with limited flexion indicates the process is outside the joint (ie bursa). In bursitis, intrabursal pressures increase with flexion and decrease with extension. FULL EXTENSION IS PRESERVED
- In a intra-articular process (ie arthritis/synovitis in a joint) the patient lacks the ability to fully extend the knee because intra-articular pressure increases in extension and is lowest in semiflexion.

The swollen knee: is it Arthritis or prepatellar bursitis?



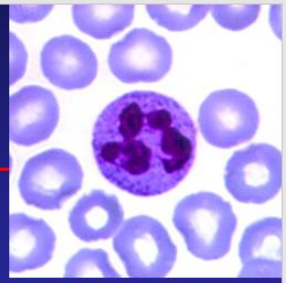




Acute Monoarthritis: Likely causes

- Septic arthritis (Staph, Strep mostly, Neisseria, Gram negatives less likely)
- Micro crystalline disease (gout, pseudogout)
- Systemic rheumatic disease of one joint or starting in one joint (RA, spondyloarthritis)
- Trauma or hemarthrosis
- *All aspirated fluid should be analyzed for cell count, culture and crystals.*

Fluid WBC Analysis



	Normal	Not Inflamed	Sterile Inflamed	Septic Inflamed
WBC	<200	Up to 1K	1K – 100K	>30K
% PMN	<25%	25 – 50%	25 – 90%	>90%

Acute Crystalline Arthritis

1. Uric acid level is not always helpful in acute gout.
2. Distribution of involvement may be helpful:Most common site: Peripheral extremities
   - Can include tendon sheaths and bursae
   - Rarely occurs centrally: SI joints, pubis, or discs
3. May co-exist with septic arthritis or other forms of crystalline arthritis (CPPD)
4. In bad polyarticular disease, patients can demonstrate features that resemble sepsis or RA.
5. Management of hyperuricemia is often unnecessary in the acute setting.

Clinical presentation: gouty arthritis

- Typical presentation:
  - acute
  - monoarticular or oligoarticular
  - lower extremity joints
- 1st MTP: involved in 50% of initial attacks; 95% involvement in recurring gout
- BUT: any joint and tendon in the body lined with synovium may be affected

Serum Uric acid

- The serum uric acid (SUA) ranges widely in gout, from “normal” to elevated
- A very low SUA (< 4-5 mg/dL) makes diagnosis less likely
- SUA may drop by 1-2 mg during an acute attack
- Goal for SUA in most patients with gout is 6 mg/dL <5 mg/dL for those with tophi

Acute gout options

- NSAIDS: especially in younger patients
- Corticosteroids (oral typically in a tapered dose, IM or IV and intra-articular)
- Colchicine: not more than bid, caution in renal failure, **avoid titrating to diarrhea**.
- Other agents like IL-1 blockade may be needed in rare cases.

Chronic gout therapy

- Allopurinol
- Febuxostat (black box warning regarding CV disease)
- Probenecid: not effective in renal failure

Recent recommendations for gout treatment (Fitzgerald et al Arthritis Care Research 2020)

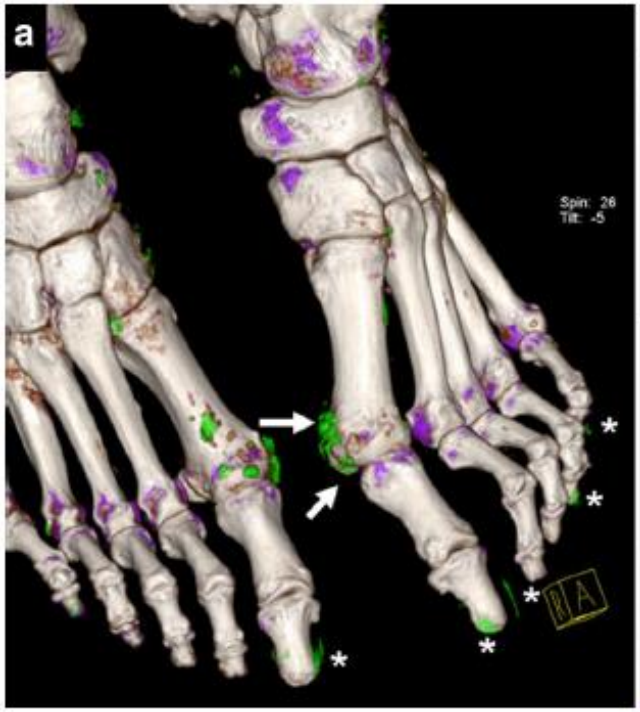
- Strong recommendations included initiation of urate lowering therapy (ULT) for all patients with tophaceous gout, radiographic damage due to gout, or frequent gout flares (2 or more per year)
- Allopurinol as the preferred first-line ULT, including for those with moderate-to-severe chronic kidney disease (CKD; stage >3);
- Using a low starting dose of allopurinol (≤100 mg/day, and lower in CKD, or febuxostat (< 40 mg /d)
- Treat-to-target management strategy with ULT dose titration guided by serial serum urate (SU) measurements, with an SU target of <6 mg/dL
- Continuing concomitant anti-inflammatory prophylaxis therapy for 3–6 months over < 3 months while beginning allopurinol or other ULT
- Allopurinol Testing for the HLA–B*5801 allele prior to starting allopurinol is conditionally recommended for patients of Southeast Asian descent (e.g., Han Chinese, Korean, Thai) and for African American patient

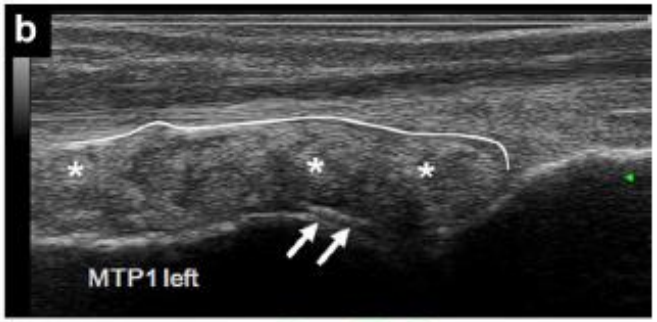
Clinical presentation: acute pseudogout

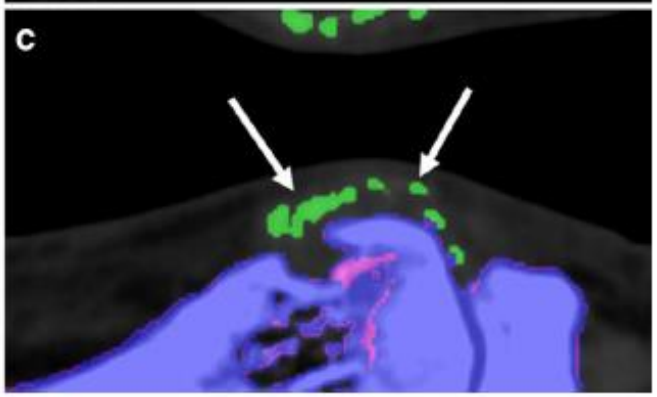
- Older adults
- Typically presents as an acute monoarticular arthritis, most commonly at the knee, shoulder.
  - big toe (gout) versus knee (pseudogout or gout)
- Can be febrile
- Chondrocalcinosis is common on x-ray

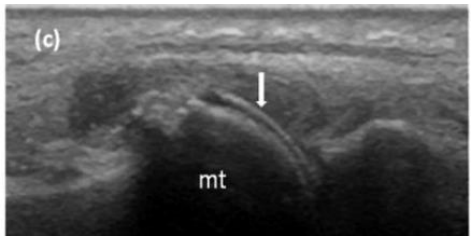
Chondrocalcinosis

Newer imaging for gout: Ultrasound and DECT (dual energy CT)









Rheumatoid Arthritis: Treatment

- **MTX - 1st line DMARD for most patients**
  - weekly dosing 15-25 mg PO or SQ
  - folic acid 1 mg daily to reduce side effect risks or leucovorin weekly 5-15mg
  - CBC, LFT, Creatinine monitoring
- "treat to target" (frequent monitoring + medication adjustment) improves long-term outcomes
- optimize treatment with current agent before making changes

Resistance to initial DMARD in RA:

- Triple therapy (Sulfasalazine, Hydroxychloroquine , MTX)
- Biologic or synthetic DMARD, often added to MTX -
  TNF inhibitors (multiple)
  - IL-6 receptor inhibitors (tocilizumab, sarilumab)
  - B cell depletion (Rituximab)
  - T cell co-stimulatory blockade
  - oral JAK inhibitors (tofacitinib, baricitinib,upadacitinib)
- role of corticosteroids:
  - useful adjunct at low doses (<10 mg)
  - many side effects, limit use

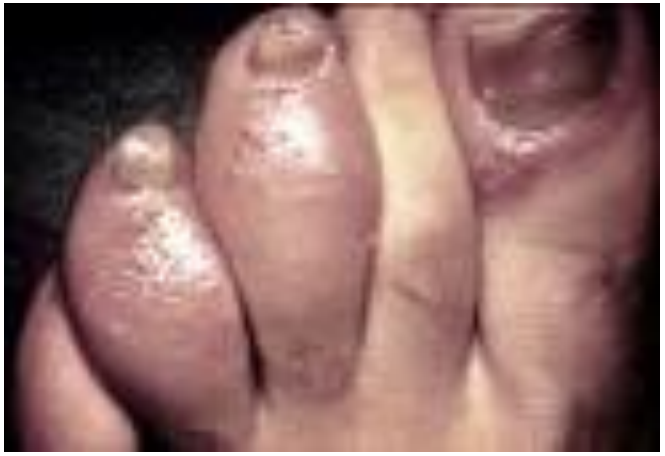
Singh Arthritis Rheumatol 2016

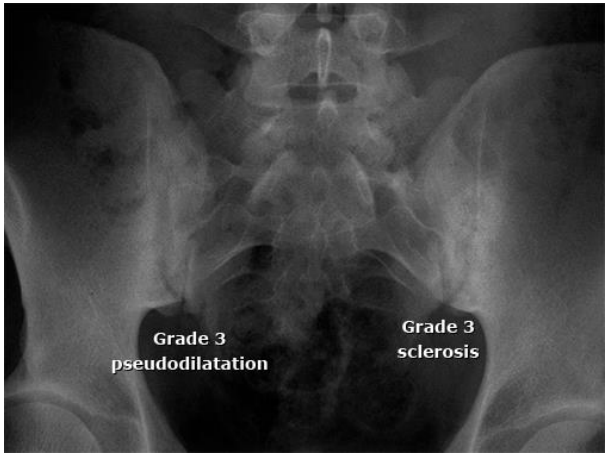
Take home message in RA

- Maximizing MTX is still a cornerstone of Rx in RA and likely lowers mortality in RA
- Patients starting on DMARDs like MTX or leflunomide or any biologic need to have an assessment of Hep B and C status.
- Assess for prior history of TB prior to DMARD or biologic therapy
- Shingrix /Pneumovax/flu vaccine advocated for such patients.
- The issue of Jak-inhibitor and risk of MACE (major adverse cardiovascular events) is an important consideration in treatment.
- The use of triple therapy with conventional DMARDs has been shown to be efficacious and cost effective compared to MTX/biologic combination based on recent data and may have lower risks of infection.

Spondyloarthritis

- Psoriatic arthritis (PsA)
- Inflammatory bowel disease
- Reactive arthritis
- Ankylosing spondylitis
- NSAIDS and DMARDs are effective but TNF inhibitors are often necessary for axial disease
- Secukinumab and Ixekizumab(IL-17) approved in AS and PsA and ustekinumab (IL-12/23 inhibition) in PsA





Few Notes About ANA Test

- ANA test was not designed as a screening test
- Up to 20% of healthy adults, particularly women, have a low titer ANA and do not go on to develop rheumatic diseases
- Causes of false positive tests:
  - Chronic infections (HIV, HBV, HCV, SBE)
  - Family history of rheumatic disease
  - Other autoimmune disease like GI or thyroid disease
  - Normal healthy people!
- Once a patient has a positive ANA, it does not need to be retested, unless symptoms change and there is an increased suspicion for a rheumatic disease

Autoantibodies in SLE

Antibody	Frequency in SLE	Clinical Significance
ANA	> 99%	High sens, low spec
anti-dsDNA	40%	High specificity, nephritis, often correlates with disease activity
anti-Smith	30%	High specificity
anti-RNP	30%	Raynaud's, arthritis, MCTD
anti-SSA/Ro	35%	SCLE, neonatal lupus, sicca symptoms
anti-SSB/La	15%	SCLE, neonatal lupus, sicca symptoms
APL abs	30%	Clotting diathesis

When to Think About Antiphospholipid Antibodies?

- Multiple early miscarriages
- Thrombocytopenia
- Stroke/TIA in younger patients
- DVT/PE
- Patients with lupus

Antiphospholipid Syndrome (APS): Major Criteria

- Clinical criteria:
  - Arterial thrombotic event
  - Venous thrombotic event
  - Recurrent pregnancy losses
    - 3 or more consecutive losses at < 10 weeks
    - 1 or more unexplained deaths of a morphologically normal fetus $\geq$ 10 weeks
    - 1 or more premature births before 34 weeks because of placental insufficiency/pre-eclampsia

PLUS

- Laboratory criteria:
  - Anticardiolipin IgG or IgM moderate-high titer (>40 GPL units)
  - Beta2-glycoprotein 1 IgG or IgM moderate-high titer (>40 GPL units)
  - Lupus anticoagulant positive
  - ***On 2 separate occasions 12 weeks apart***

Patients who should be evaluated for antiphospholipid antibodies

- SLE patients
- Patients under age 40 with CVA, MI no obvious risk factors
- Recurrent venous or arterial clots
- Women with recurrent first trimester pregnancy losses, or second trimester loss
- Some advocate the use of prophylactic aspirin therapy in those with positive antibodies. This therapy has not been shown to decrease the risk of clotting events except in patients with co-existing SLE.

Raynauds phenomenon

- **Primary Raynaud's:** common in young women (teens and twenties), may have a family history of this as well, ANA mostly negative.
- **Onset of Raynaud's in adults after the age of 35 concerning for the development of a rheumatic syndrome and is termed secondary Raynaud's**
- Digital ulcers, pitting scars in fingers, abnormal capillary microscopy and presence of autoantibodies suggest the development of an underlying rheumatic syndrome.

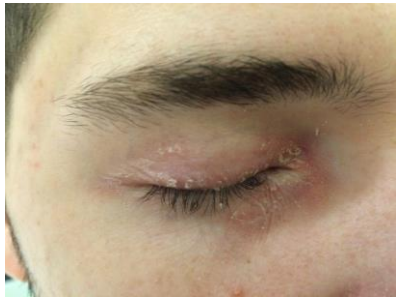
Key points in Scleroderma

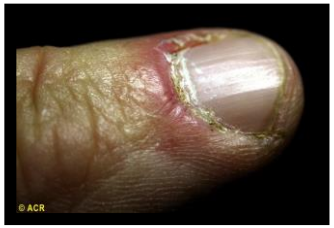
- Recognize the presence of concomitant Raynaud's and GERD as a possible clinical manifestation of underlying limited scleroderma and therefore the long-term risk of pulmonary hypertension
- ILD occurs in diffuse SSc>limited SSc but can occur in both
- Avoid high dose steroids in SSc in SSc pts. (increased risk of renal crisis)
- Pulmonary hypertension is a complication of long standing scleroderma of mostly the limited variant and treatment that improve morbidity and possible mortality are available now.
- Newer treatments and clinical trials ongoing and offer hope for better therapies

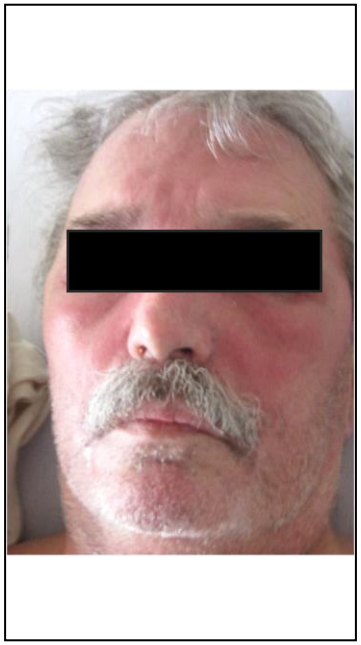
Inflammatory myopathies

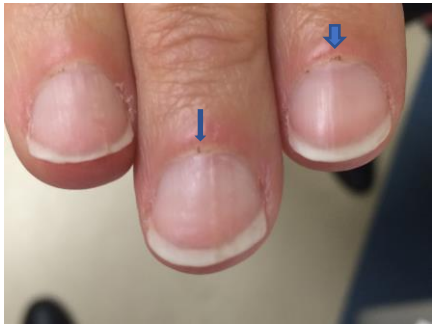
- Immune mediated muscle injury
- Usually CK and aldolase (and often transaminase) elevated
- MRI show characteristic inflammation
- Muscle biopsy can offer distinctions regarding diagnosis
- Disorders include:
- Polymyositis/Dermatomyositis (PM, DM)
- Overlap myositis
- Inclusion body myositis (IBM)
- Immune mediated necrotizing myositis (including statin related)

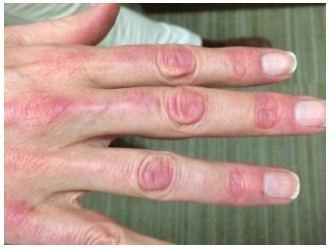
Teaching Phenotypes: Dermatomyositis









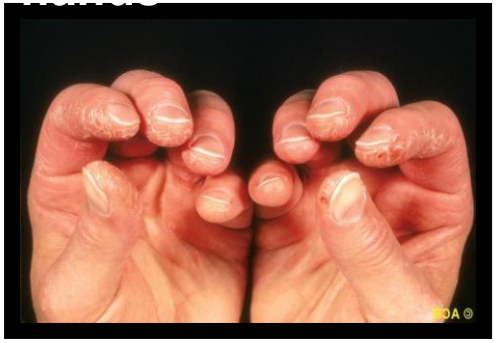


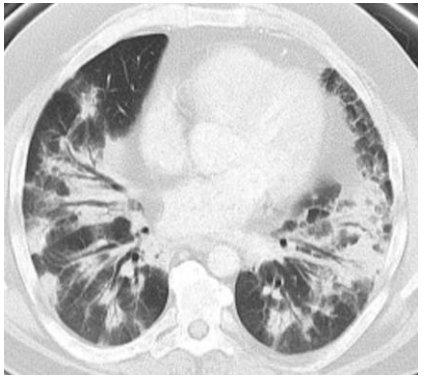
Inflammatory myositis:other points

- Amyopathic DM can occur (skin and lung but no muscle disease)
- If you have a patient being treated for “inflammatory myositis” especially with distal extremity weakness and they are not improving consider the possibility of inclusion body myositis
- Remember morbidity linked to respiratory complications (interstitial lung disease)

Antisynthetase syndrome:morbidity is associated with lung disease!

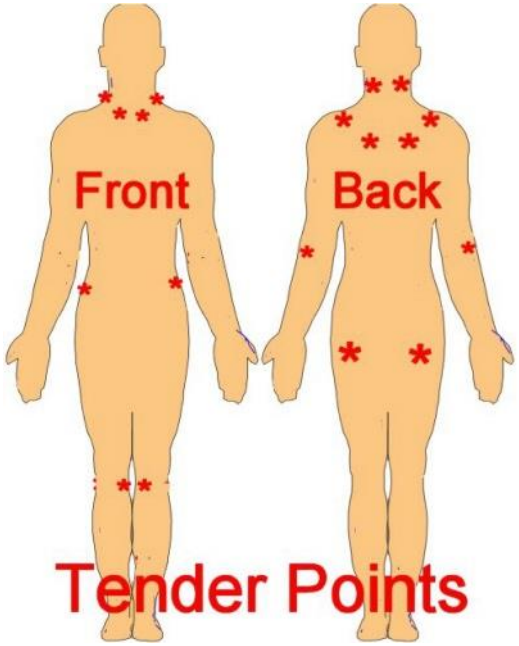
- Fever
- Mechanics hands
- Raynauds
- Inflammatory Arthritis
- *ILD (can be severe)*
- Myositis
- Typically associated with Jo-1, PL-12, PL-7 ab amongst others recently discovered





Fibromyalgia

Non-inflammatory
Pain without objective findings
Sleep disturbance
Mood disorders
Normal labs



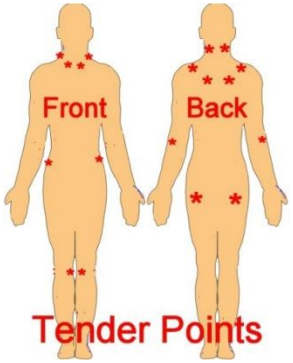
Polymyositis

Painless weakness
Proximal>Distal
CK elevated
Inflammatory markers
EMG - insertional irritability

Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein

- Can help distinguish inflammatory vs non-inflammatory conditions
- However—nonspecific
- CRP can be elevated in obesity
- ESR increases with age
- ESR/CRP can be normal early in systemic rheumatic illness
- It will never be diagnostic, but can help support your differential diagnosis

Fibromyalgia :What to do?



- Examination
- Typically tender to touch around joints
  - Bursas, paraspinal muscles, sometimes just the skin is painful
- Make sure no joint swelling
- Check labs:
  - CBC, TSH, ESR, CRP, chemistries, CPK, vitamins (B12 or D)
- Avoid checking RF or ANA unless indicated
- Be very careful about considering this diagnosis in the elderly!

Fibromyalgia Treatment

- Multidisciplinary treatment of symptoms
  —pain, brain fog, fatigue, insomnia
- Education
- Sleep interventions
- Exercise
- Cognitive behavioral therapy
- Medications, if not improving with non-pharmacologic treatment
  - Published studies of medications FDA approved for fibromyalgia show 30% improvement in pain
  - Benefits may not outweigh risks/side effects in some patients

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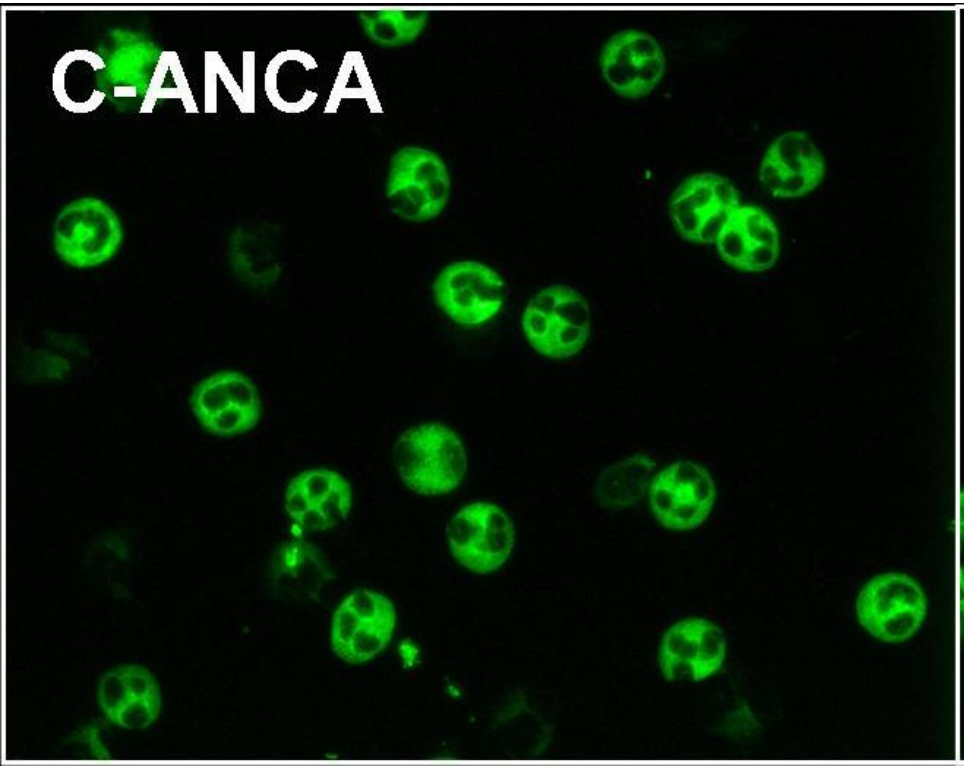
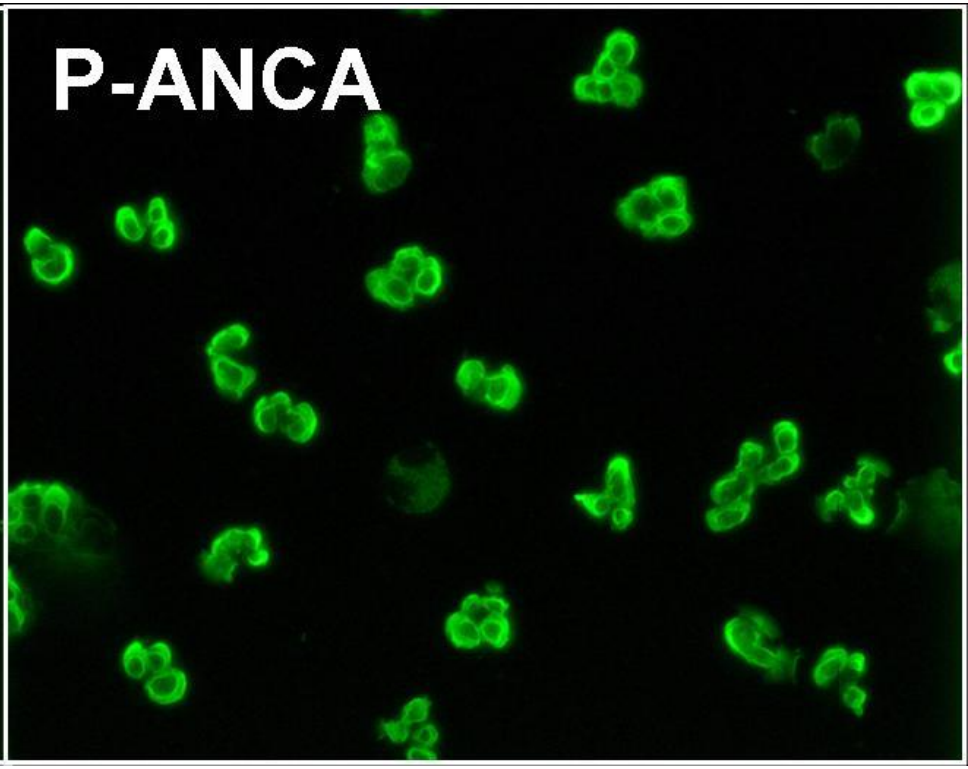
Antineutrophil-cytoplasmic antibodies (ANCA)





Antigen = Proteinase-3 (PR3)

Antigen = Myeloperoxidase (MPO)

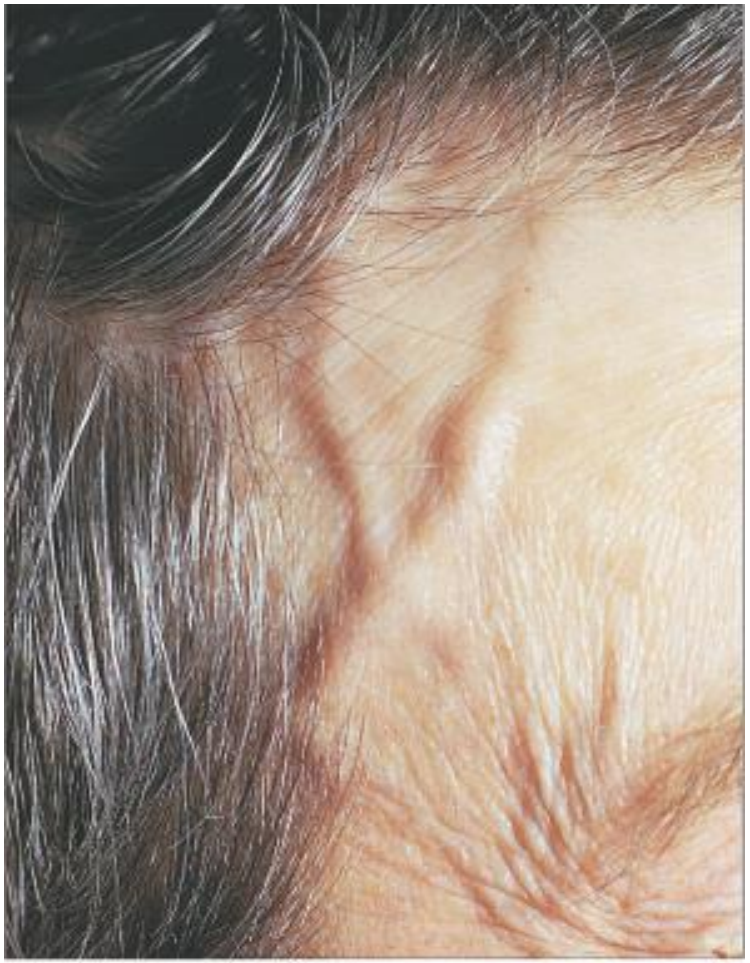
ANCA-associated vasculitis: clinical and laboratory features

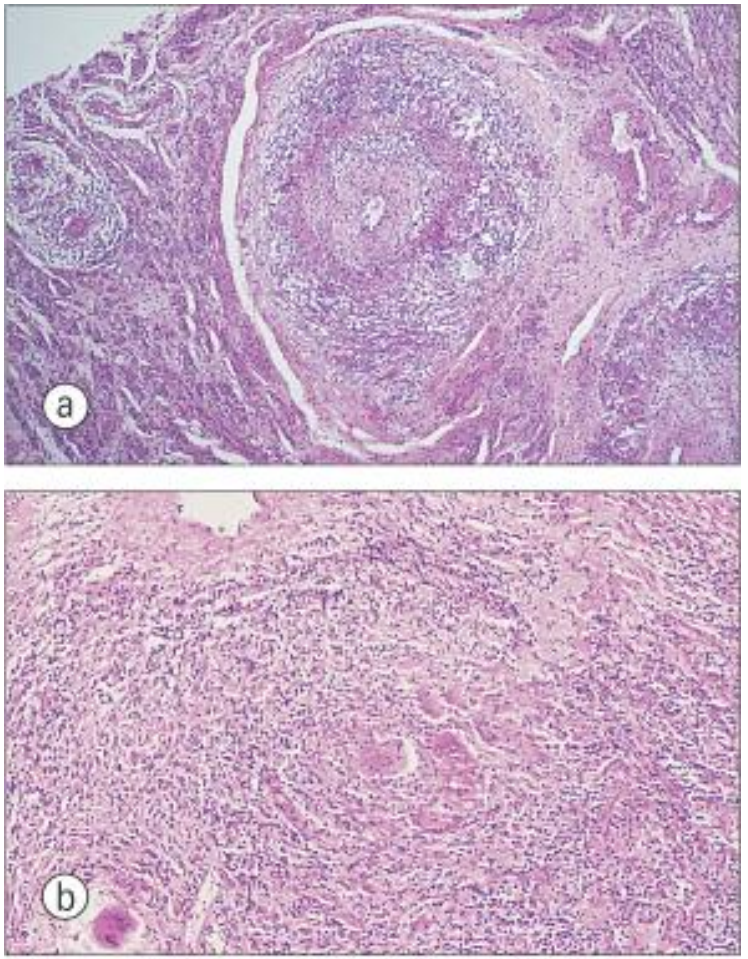
- **Microscopic polyangiitis (MPA)**
  - Small-vessel necrotizing vasculitis
  - Associated with **MPO-ANCA >90%**

- **Granulomatosis with polyangiitis (GPA, Wegener's)**
  - Small-vessel necrotizing vasculitis
  - Additional features of **necrotizing granulomatous inflammation** in upper airway, lungs, skin, elsewhere
  - Associated with **PR3-ANCA ~80%, MPO-ANCA 10%**

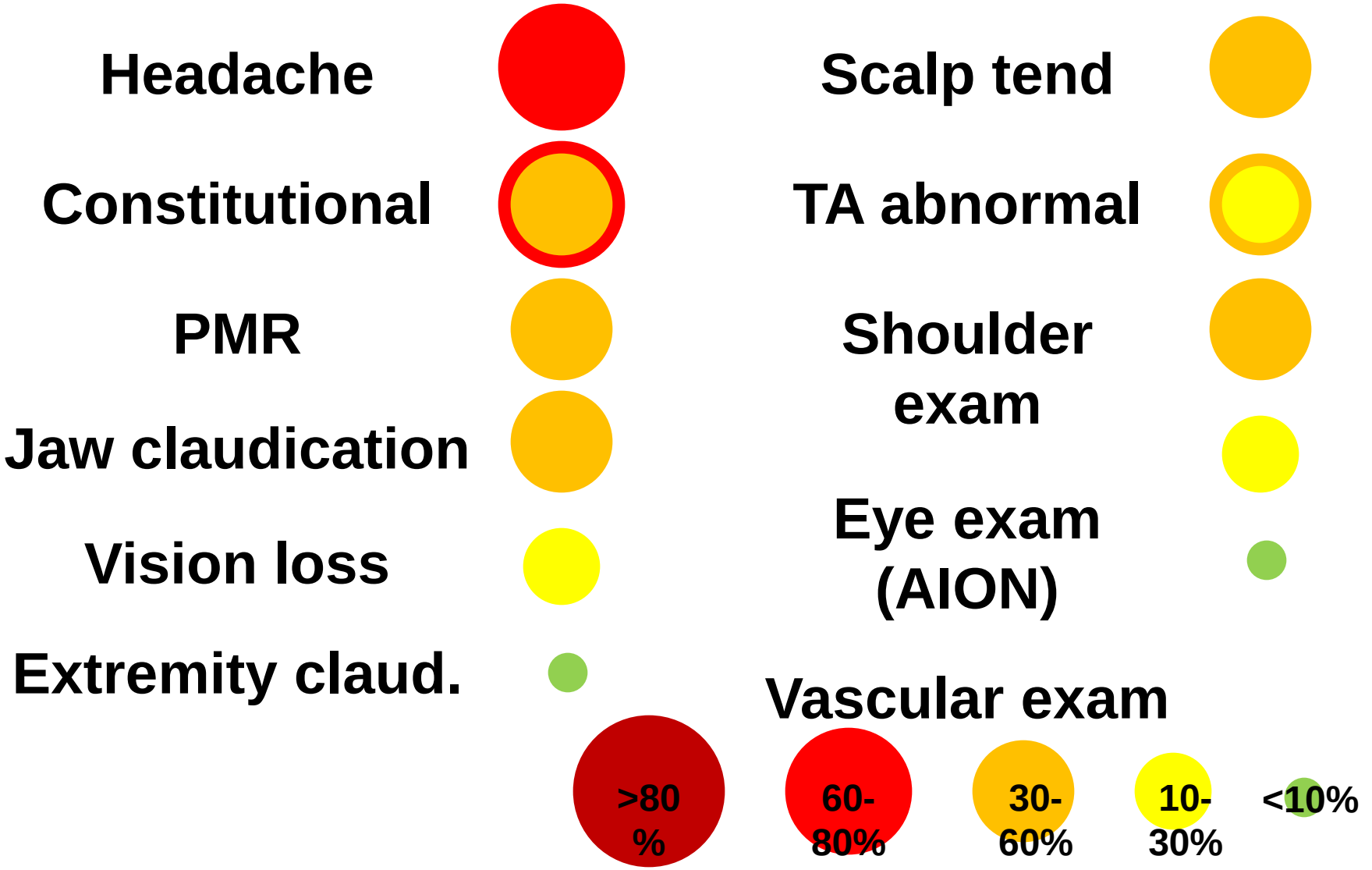
- **Eosinophilic granulomatosis with polyangiitis (EGPA, Churg-Strauss)**
  - Small-vessel necrotizing vasculitis
  - **Hyper eosinophilia, asthma**, eosinophilic inflammation
  - Associated with **MPO-ANCA 40%**

Giant cell arteritis (GCA)

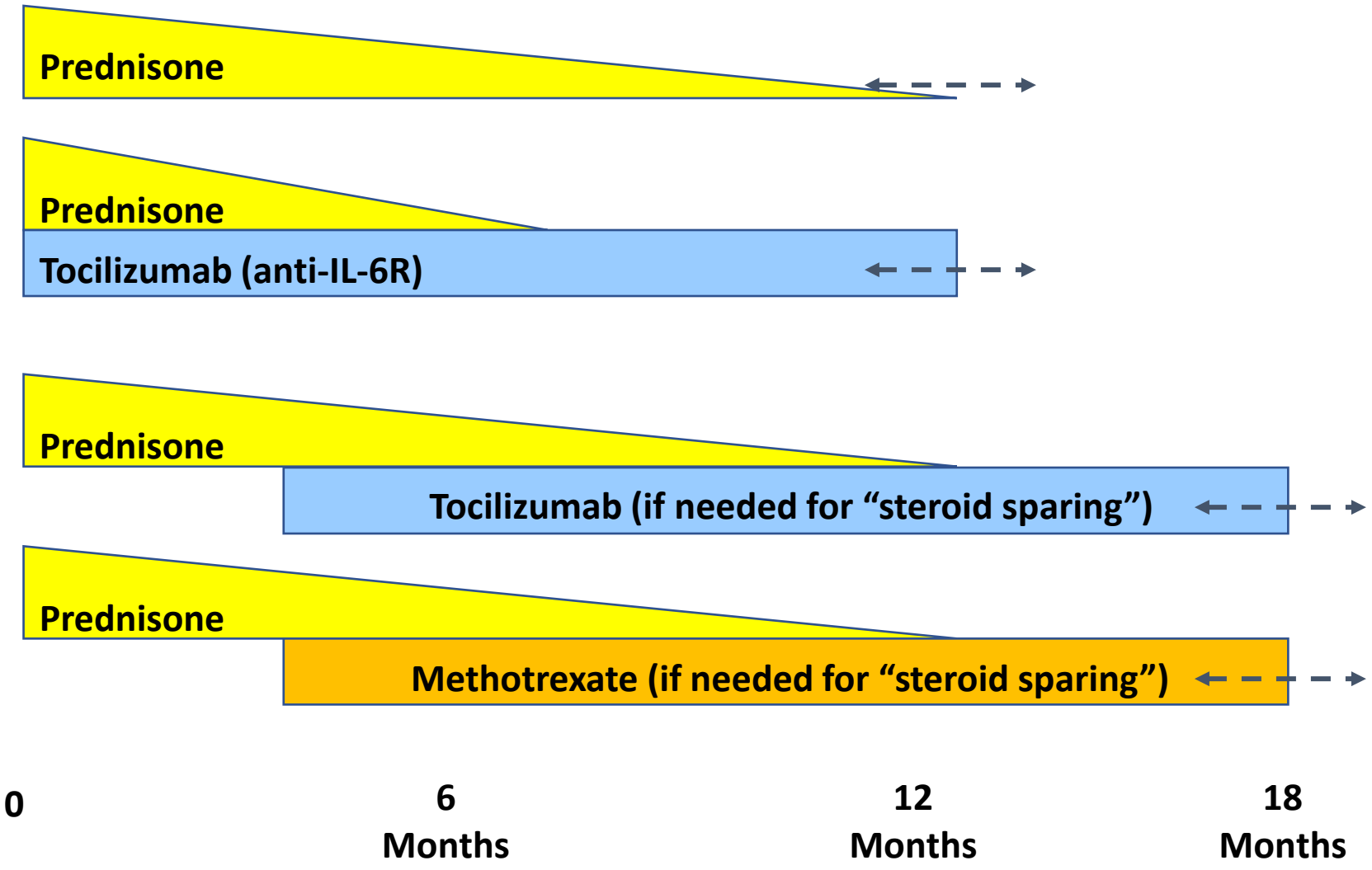




Symptoms and signs in GCA



Common Approaches to GCA

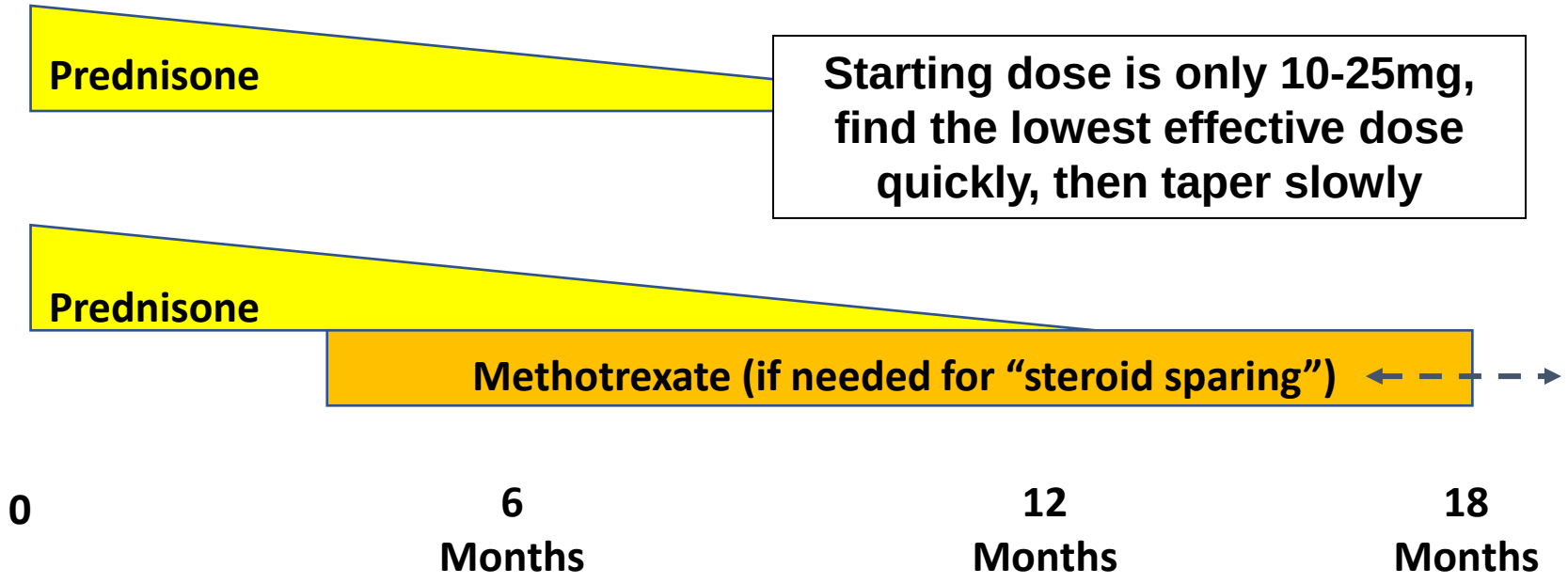


Polymyalgia rheumatica

- **Inflammatory arthritis, bursitis, and tenosynovitis** (usually a combination)
  - Negative for RF and CCP antibodies
  - No specific lab or imaging finding, just inflammation

- **Clinical syndrome**
  - Bilateral shoulder pain in great majority
  - Hip girdle > neck > widespread pain common
  - Peripheral arthritis in 10%
    - Peripheral arthritis without shoulder pain is not PMR
  - Constitutional symptoms common

Common Approaches to PMR



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Thank you !