

Update in Internal Medicine 2022

Pearls in Rheumatology

Fatemeh Ezzati, MD

Division of Rheumatic Disease, UTSW

Disclosure

- None

Learning Objectives

- Identify when to suspect a diagnosis of inflammatory arthritis
- Select appropriate testing to confirm
- Some pearls about RA and SLE
- Facts about autoimmune disease and Covid vaccination

Case 1

A 53 year-old African American female presents with fatigue, arthralgias, and a rash. She reports that she has been having joint pain with worsened stiffness and swelling in the mornings for the past six months. She has also noted rashes over face and extremities . Rash persists for few days.

Reports some occasional canker ulcer and some hair thinning.

On exam, several MCPs are tender to palpation with trace synovitis, and she has a faint erythematous rash on her cheeks.

Otherwise exam is WNL.

Case 2

A 53 year-old African American female presents with fatigue, arthralgias, and a rash. She reports that she has been having joint pain and muscle pain which is persistent throughout the day and slightly worse at the end of the day for past 6 months.

She has also noted rashes over face and extremities. Rash disappears within few hours. Reports some occasional canker ulcer and some hair thinning. She has brain fog, can not concentrate and can not sleep at nights due to pain.

On exam, she is diffusely tender over joints and muscles with no synovitis and she has a faint erythematous rash on her cheeks.

Otherwise exam is WNL.

What makes these two cases different?

History : Inflammatory versus non-Inflammatory pain (joints versus muscles)

Inflammatory- swelling, redness, better with activity ,ms >1 hour

Non inflammatory- usually no swelling, better with rest, ms <1 hour

Rash – duration, pattern, location

Other associated symptoms : fatigue, sleep disturbance, trouble concentration, brain fog, anxiety, depression

PE: Synovitis

Rash- malar rash versus rosacea or photo eruption rash

Mucocutaneous ulcers

Patchy hair loss

- In which Patient should we order ANA or other tests?
- Why not order it in both cases as screening?

- Why is the ANA not a screening test?
- Present in healthy individuals

- Present in many other diseases
- Autoimmune thyroid disease
- Autoimmune liver disease
- Primary pulmonary hypertension
- Multiple sclerosis
- Malignancy (lymphoma)
- Chronic infection

▪ What is the significance of the tests ordered in making the diagnosis of SLE?

- SLE is diagnosed based on both **clinical and laboratory features**.
- Immunologic criteria play a significant role in the diagnosis of SLE.
- ANA positivity is found in almost all patients with SLE; while the ANA is very sensitive for the diagnosis of SLE (>99%), it is not specific.
- Other autoantibodies frequently seen in patients with SLE are the following:
 - anti-dsDNA (40%)
 - anti-Smith (30%)
 - anti-RNP (30%)
 - anti-SSA/Ro (35%)
 - anti-SSB/La (15%)
 - antiphospholipid antibodies (30%)

- Typical features in Lupus patients besides joint pain
- Fatigue is very common in SLE (80-100%) but **non-specific**
- Other etiologies should also be considered.
- Mucocutaneous lesions occur in 80% of patients, including acute cutaneous lupus (particularly malar rash), chronic cutaneous lupus most commonly discoid lupus erythematosus, oral ulcers, and non-scarring alopecia.
- Cytopenias are common, particularly lymphopenia.
- Renal involvement occurs in > 50% of patients. Diagnostic clues include proteinuria, hematuria, and RBC casts, as evident in this patient.

Pearls in SLE

- If a photosensitive rash develops, review the medication list
- HCTZ and NSAIDs can contribute to photosensitivity
- PABA sunscreens can as well (use PABA-free formulas)

- LUPUS rash is not transient, if transient think something else

Pearls in SLE

- ANA titer is more important than pattern
- High titer is usually associated with some autoimmune disease.
- Always order ENA panel if high titer ANA (in the presence of clinical picture)
- Do not repeat ANA
- DsDNA and C3, C4 are the only markers we recheck for lupus activity monitoring

Pearls in SLE

- Do we have ANA negative lupus
- Rare
- ANA as an entry criteria in new ACR/Eular classification criteria (2019) for SLE

Pearls in SLE

- Given the increase risk of early atherosclerosis in SLE, patients with SLE should have annual evaluation of modifiable cardiovascular risk factors and appropriate intervention when indicated
- Appropriate testing includes the following:
 - blood pressure assessment, fasting lipid panel, blood sugar and/or hemoglobin A1C, BMI calculation, and query about tobacco use.

Case 3

- A 25 year-old female presents with 3 months history of pain and stiffness in the MCPs and wrists. The symptoms are worse in the morning, lasting for 1 hour and improve with activity . On exam the wrists are slightly swollen and tender and MCPs are tender but not swollen
- ESR is 52
- X-rays show peri-articular osteopenia but no erosions.

Case 4

- A 52 y/o female presents with 6 months history of pain and swelling in her hands mainly PIP and DIPs. Pain is persistent throughout the day and slightly worse with use . She has morning stiffness of about 30 minutes.
- In exam she has extensive synovitis involving PIP and DIP joints, otherwise normal exam.
- Xray shows evidence of erosion in multiple PIP and DIP joints with no involvement of MCP or wrist.

- What makes these two cases different?
- What other labs to check?

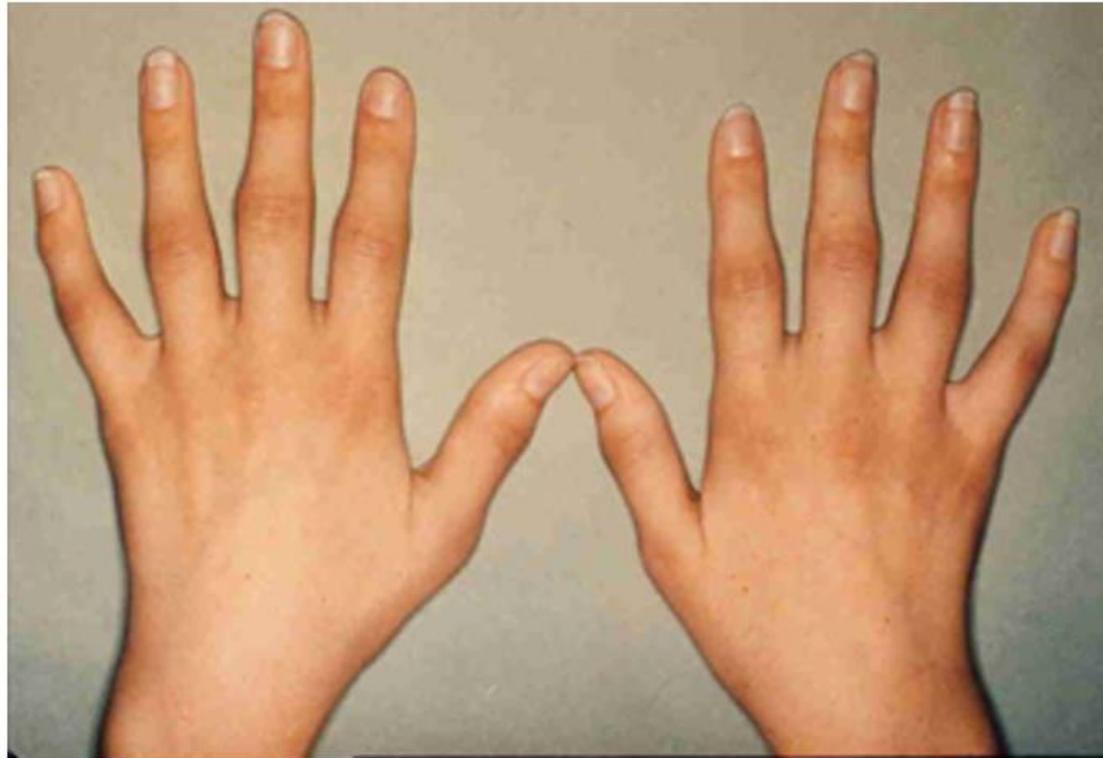
- Location of pain MCP/PIP and wrist versus PIP/DIP

- What conditions involve DIP?

- RA- MCP, PIP, Wrist
- OA- DIP and PIP
- Psoriatic arthritis- Different forms:
 - DIP
 - Mimics RA- wrist, MCP and PIP

- Two most common condition involving DIP:
- OA and psoriatic arthritis
- DIP is never involved in RA unless concomitant with OA

Inflammatory synovitis

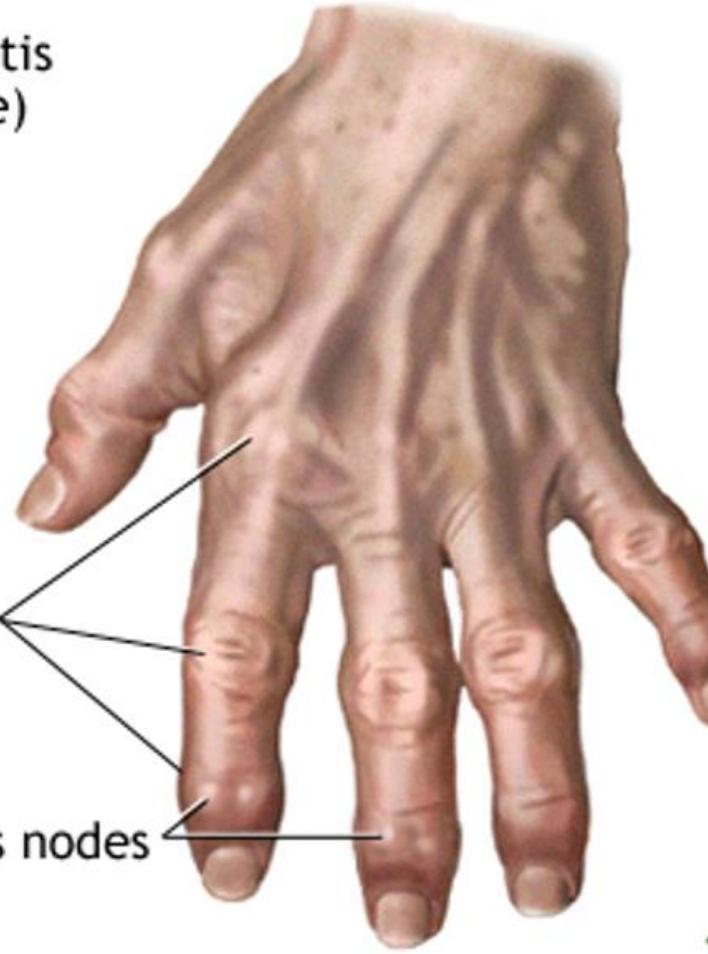




Osteoarthritis
(late stage)

Fusiform
swelling
of joints

Heberden's nodes



- Antibodies commonly checked when RA is suspected include rheumatoid factor (RF) and anti-cyclic citrullinated peptide (CCP) antibody.
- Presence of these antibodies is predictive of **more aggressive disease** and may prompt more aggressive treatment.
- **Anti-CCP is more specific** for RA than RF.
- **RA is a clinical diagnosis** and antibody positivity is not necessary in order to make a diagnosis. This is called "seronegative RA"

- How about ESR or CRP?
- Non-specific and can be seen in other conditions.
- Patients can have signs of active inflammation and a normal ESR. However, a high ESR is a marker for systemic inflammation and is probably indicative of an overall worse prognosis.

Pearls in RA

- Xrays are usually normal in the early stage of RA
- Magnetic resonance imaging (MRI) and ultrasonography are useful in early disease before radiographic evidence of bone erosion occurs
- MRI can also reveal synovial thickening, which has been shown to predict the future presence of bony erosions

Pearls in RA

- Methotrexate is the initial drug of choice for patients with RA.
- The recommended treatment plan recommends an initial dose of 15 mg/week

Inflammatory (erosive OA)

- Evidence of PIP and DIP involvement
- Normal MCP and wrist (other than CMC arthritis)
- Pain is worse with use
- NO specific tx to avoid progression of disease
- Conservative tx with NSAIDs, topicals, paraffin bath, OT
- No benefit with DMARDs

Case 5

- 25 year-old female with hx of SLE currently on Methotrexate is presenting for follow up. She has had three Covid vaccination within last year with the third dose 6 months ago. She tested positive for Covid 1 month ago , had only mild symptoms and is doing well now. Is she eligible to get the booster? If yes, does she need to hold her Methotrexate for the vaccine?

General Considerations Related to COVID-19 Vaccination in Rheumatic and Musculoskeletal Disease Patient

AIIRD(autoimmune and inflammatory rheumatic disease) patients are at higher risk for hospitalized COVID-19 and worse outcomes compared to the general population.

Beyond known allergies to vaccine components, there are **no known additional contraindications** to COVID-19 vaccination for AIIRD patients

The expected response to COVID-19 vaccination for many AIIRD patients on systemic immunomodulatory therapies is **blunted** in its magnitude and duration compared to the general population

A theoretical risk exists for **AIIRD flare or disease worsening** following COVID-19 vaccination. However, the benefit of COVID-19 vaccination for RMD patients outweighs the potential risk for new onset autoimmunity.

Recommendations for Primary and Supplemental Dosing of the COVID-19 Vaccine in RMD Patients

- For AIIRD patients not yet vaccinated, either of the mRNA vaccines is recommended over the J&J vaccine. There is no recommendation for one mRNA vaccine over another.
- AIIRD patients who completed the **primary COVID vaccine series** and are expected to have mounted an inadequate vaccine response should receive a **supplemental dose (e.g., a 3rd dose)** as recommended by the CDC for immunocompromised individuals
- RMD patients who have completed a primary COVID vaccine series, and any supplemental doses for which they qualify, should receive **booster dose(s)** as recommended by the CDC for immunocompromised individuals
- The timing of booster shot intervals is vaccine dependent. For both the Moderna and Pfizer mRNA vaccines, a booster shot is recommended **at least 5 months** after completion of the primary vaccine series. The recommended interval for those having received the J&J vaccine is at least **2 months**

Recommendations for Primary and Supplemental Dosing of the COVID-19 Vaccine in RMD Patients

- Healthcare providers should not routinely order any lab testing (e.g., antibody tests for IgM and/or IgG to spike or nucleocapsid proteins) to assess immunity to COVID-19 post-vaccination, nor to assess the need for vaccination
- COVID vaccination should occur as soon as possible for those for whom it is being recommended, irrespective of disease activity and severity in a yet-unvaccinated person

Rheum meds and Covid vaccine

Do we need to hold them?

How long?

What to expect if disease flares?

Guidance Related to the Use and Timing of Vaccine Dosing and Immunomodulatory Therapy in Relation to COVID-19 Vaccination in RMD Patients

Medication	Timing Considerations for Immunomodulatory Therapy and Vaccination	Level of Task Force Consensus
	(applies to both primary vaccination and supplemental [booster] dosing)	
Abatacept IV	Time vaccination so that it occurs one week prior to the next dose of IV abatacept	Moderate
Abatacept SQ	Hold for one to two weeks (as disease activity allows) after each COVID vaccine dose	Moderate
Acetaminophen, NSAIDs	Assuming that disease is stable, hold for 24 hours prior to vaccination. No restrictions on use post vaccination once symptoms develop.	Moderate
Belimumab SQ	Hold for one to two weeks (as disease activity allows) after each COVID vaccine dose	Moderate
TNFi, IL-6R, IL-1R, IL-17, IL12/23, IL-23, and other cytokine inhibitors†	The Task Force failed to reach consensus on whether or not to temporarily interrupt these following each COVID vaccine dose, including both primary vaccination and supplemental (booster) dosing	Moderate
Cyclophosphamide IV	Time CYC administration so that it will occur approximately 1 week after each vaccine dose, when feasible	Moderate
Hydroxychloroquine, IVIG	No modifications to either immunomodulatory therapy or vaccination timing	Strong (HCQ), Moderate (IVIG)
Rituximab or other anti-CD20 B-cell depleting agents	Discuss the optimal timing of dosing and vaccination with the rheumatology provider before proceeding‡	Moderate
All other conventional and targeted immunomodulatory or immunosuppressive medications (e.g., JAKi, MMF) except those listed above§	Hold for one to two weeks (as disease activity allows) after each COVID vaccine dose	Moderate

Note: individual medications that were specifically voted on by the task force are listed on separate rows and were not collapsed, even if the resulting recommendation was similar to others.

* RMD = rheumatic and musculoskeletal disease; IVIG = intravenous immunoglobulin; TNFi = tumor necrosis factor inhibitor; IL = interleukin; JAKi = janus kinase inhibitor; CYC = cyclophosphamide; RTX = rituximab; IV = intravenous; SQ = subcutaneous; NSAID = non-steroidal anti-inflammatory drugs; MMF = mycophenolate mofetil; **JAKi = baricitinib, tofacitinib, upadacitinib**

† Examples of specific cytokine inhibitors are as follows: IL-6R = sarilumab; tocilizumab; IL-1R = anakinra, canakinumab; IL-17 = ixekizumab, secukinumab; IL-12/23 = ustekinumab; IL-23 = guselkumab, risankizumab

‡ Some practitioners measure CD19 B cells as a tool with which to time the booster and subsequent rituximab dosing. For those who elect to dose without such information, or for whom such measurement is not available or feasible, provide a supplemental dose 2-4 weeks before next anticipated rituximab dose (e.g., at month 5.0 or 5.5 for patients on an every 6 month rituximab dosing schedule)

§ Includes apremilast; azathioprine; calcineurin inhibitors; cyclophosphamide (oral); IVIG; leflunomide; methotrexate, janus kinase inhibitors [JAKi] (baricitinib, tofacitinib, upadacitinib), mycophenolate; sulfasalazine

Case 6

- A 36 y/o female with hx of RA is presenting for follow up. She is not taking any medication for RA due to concern for side effects.
- She is asking about anti- inflammatory diet and exercise .
- Does this help?
- Does this replace medication

Inflammatory /autoimmune disease and diet

- No specific diet
- Stay a healthy weight (Excess weight can make some specialist medications ineffective, may increase disease activity and delay remission)
- **Eat more oily fish** Fish such as sardines, mackerel, herring, salmon, and snapper have a darker flesh which is rich in omega-3 polyunsaturated fats. In addition to their heart-health benefits, fish oils have been shown to help dampen general inflammation and may help to reduce joint pain and stiffness
- **Fish oils** . High-dose fish oil supplements have been shown to reduce symptoms of RA, such as the duration of morning stiffness, the number of swollen and tender joints and joint pain. Fish oil supplements should have 500-1000mg of EPA and DHA (omega-3 fats) per capsule
- **Follow a Mediterranean diet** This type of diet includes poultry, fish, and less lean red meat than a typical UK diet, plenty of vegetables (fresh, frozen or canned), fresh fruit, olive oil, wholegrain cereals, peas and beans and nuts and seeds. This means saturated fats are reduced and replaced by unsaturated fats including omega-3
- **Eat iron-rich foods** lean red meat, eggs, green leafy vegetables, peas, beans and lentils, and fortified breakfast cereals

- Thank you!