CME

# Diagnosing and managing patients with rheumatoid arthritis

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## ABSTRACT

Rheumatoid arthritis (RA) is a chronic, progressive, inflammatory condition that affects about 1% of the world's population. The multifactorial nature of RA has created continuous research discoveries leading to improved identification of specific pathways for the pathogenesis of RA. Improved understanding of the pathways has allowed the development of new targeted drugs. Clinicians must understand the most common pathways for pathogenesis of RA, proper diagnostic techniques, and the appropriate management of this disease given the many possible options at their disposal.


**Keywords:** rheumatoid arthritis, autoimmune, ACR, EULAR, pharmacologic therapy, nonpharmacologic therapy

## Learning objectives

- Compare and contrast the presentation of RA with other common joint diseases.
- Analyze the most appropriate tests for diagnostic workup of RA.
- Summarize and recommend treatments for RA based on patient needs.

A 30-year-old woman presents to the clinic due to worsening joint pain. She states that her pain and stiffness have been present for about 7 months and are no longer responsive to treatment with acetaminophen. The pain and stiffness are limited to her hands. Her arthralgias are worse in the morning but are improved by taking a warm shower or holding a hot cup of coffee. Even with these accommodations, it takes about 45 minutes to an hour each morning before she can finally get her day started. On further review of symptoms, she admits to generalized fatigue but denies fever, night sweats, weight loss, or stiffness in her back.

On physical examination, she has swollen and tender metacarpophalangeal (MCP) joints and proximal interphalangeal (PIP) joints bilaterally, for a total of 14 affected joints (see **Figure 1** for an example in a different patient).

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## CLINICAL PRESENTATION

The most likely diagnosis for this patient is rheumatoid arthritis (RA), a chronic, systemic, autoimmune inflammatory disease affecting more than 1% of the world's population.[1,2] Patients with RA can present at any time in life; the peak incidence is between ages 35 and 50 years.[3] Women are more frequently affected than men at a ratio of 3:1.[3] Patients typically present with prolonged morning stiffness, joint pain, and symmetric swelling of the wrists and the MCP, PIP, and metatarsophalangeal (MTP) joints.[4] As the disease progresses, larger joints become affected, predominantly knees and elbows. Rarely, patients can develop neck pain and stiffness due to tenosynovitis of the transverse ligament at C1; this usually occurs in patients who have had the disease for more than 10 years.[5] Systemic symptoms such as fatigue and other constitutional signs are common in patients with RA. Patients also may demonstrate extra-articular manifestations at the time of presentation, most commonly rheumatoid nodules, secondary Sjögren syndrome, and pulmonary fibrosis.[1,4,6] Patients also are at increased risk of premature immunosenescence, leading to early cognitive impairment,

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DOI:10.1097/01.JAA.0000742944.34230.87

## Key points

- RA classically presents with symmetric inflammation of the small joints of the hands and feet, prolonged morning stiffness, and constitutional signs such as fatigue and fever.
- Many genes have been linked to the development of RA, including HLA DR beta 1 alleles, which drive production of a shared epitope linked to autoantibody production and citrullination of proteins leading to joint destruction.
- The ACR/EULAR criteria for diagnosis require 6 out of 10 points based on the type and number of joints affected, serology, and duration of symptoms.
- The ACR and EULAR recommend that DMARD monotherapy be started as soon as a diagnosis is made with a stepped approach to additional therapy and a treat-to-target goal of complete remission or low disease activity.

malignancies, accelerated atherosclerosis, and cardiovascular disease.[1]

On physical examination of patients with early RA, palpation of the joint line will reveal swelling and bogginess. As the disease progresses, the clinician may appreciate warmth and mild erythema, decreased range of motion, and deformities of the joint, particularly ulnar deviation of the fingers (**Figure 2**), swan neck deformity (hyperextension), and boutonniere deformity (hyperflexion).[7] Joint deformities associated with RA need to be differentiated from Heberden nodes (affecting the DIP) and Bouchard nodes (affecting the PIP) that are found in patients with osteoarthritis. Complications of joint deformities of RA include compressive ulnar neuropathy, carpal tunnel syndrome, and the formation of Baker cysts.[7]

## DIFFERENTIAL DIAGNOSIS

Several arthritic disorders may be confused with RA, including osteoarthritis (OA), psoriatic arthritis, other rheumatologic disorders, and infectious causes of joint disease such as septic arthritis. OA typically presents later in life, predominantly in weight-bearing joints, and does not present with systemic symptoms.[4] Furthermore, patients with OA typically describe pain and stiffness with activity. Although they may have morning stiffness, it is shorter in duration than the stiffness experienced by patients with RA. One way to remember the difference in clinical manifestations between RA and OA are the four S's for RA (symmetrical, small joints, synovitis, and systemic) compared with LOAD for OA (large joints, oligoarticular, asymmetric, and degenerative).

Patients with psoriatic arthritis typically have a history of a psoriatic rash (erythematous plaques with silvery-white scale on the extensor surfaces). Most of the time the rash appears before the joint symptoms manifest; however, patients can present with joint symptoms before or in conjunction with rash onset. On physical examination, a patient with psoriatic arthritis also may present with nail pitting or dactylitis (sausage digits); these patients also have an increased risk of spinal joint involvement.[8]

Other rheumatologic disorders with joint pain to consider in the differential diagnosis include systemic lupus erythematosus, systemic sclerosis, polymyalgia rheumatica, and fibromyalgia.[9,10] Lupus and systemic sclerosis have associated skin findings; polymyalgia rheumatica and fibromyalgia present with myofascial pain. Septic arthritis is most often monoarticular, caused by Gram-positive cocci, and occurs in older adults with underlying health issues.[9,10] Gonococcal joint disease presents as a

**FIGURE 1.** Inflammation of the MCP and PIP joints in a different patient

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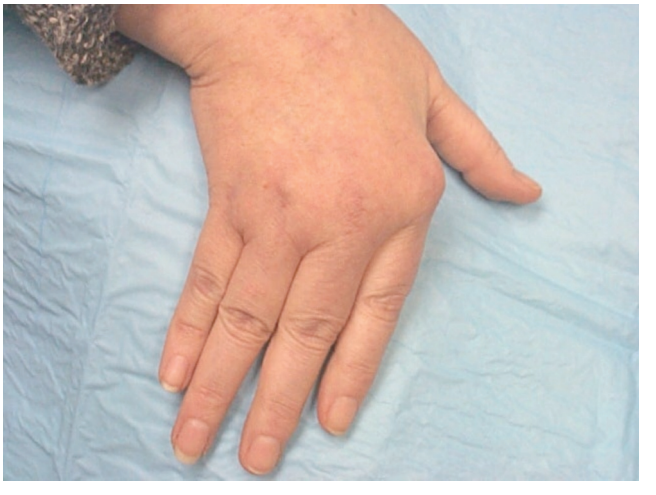

**FIGURE 2.** Inflammation of MCP joints with ulnar deviation

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monoarticular arthritis in young healthy adults.[9,10] Viruses such as parvovirus B19 or hepatitis C present as a polyarthritis. Parvovirus-induced arthritis generally is short-lived (weeks to months), resolves spontaneously, and usually is associated with exposure to a child with fifth disease (erythema infectiosum).[11] Patients with hepatitis C with cryoglobulinemia may present with positive rheumatoid factor; therefore, consider potential hepatitis C risk factors. Patients with tickborne illnesses, Rocky Mountain spotted fever, or Lyme disease can present with joint pain, but frequently demonstrate a characteristic rash, fever, and history of tick bite.[9,10] In patients with an oligo- or monoarthritic presentation, the diagnosis would be more likely due to crystalline arthropathies (such as gout or pseudogout), septic arthritis, or spondyloarthropathies associated with human leukocyte antigen (HLA)-B27.[9]

## PATHOPHYSIOLOGY

RA is an autoimmune condition with a multifactorial cause, including genetic and environmental factors. A strong association exists between patients with HLA DR beta 1 alleles and the development of RA. Patients with these alleles code for an amino acid sequence known as the shared epitope.[10,12] Although the exact mechanism is still unknown, theories propose that the presence of the shared epitope allows more efficient recognition by, or differentiation of, T cells that lead to the production of autoantibodies. In addition, the presence of the shared epitope increases citrullination of proteins (conversion of the amino acid arginine into citrulline). Common proteins in the synovium that are at risk for citrullination include fibrin, fibrinogen, and vimentin; these citrullinated proteins can be readily attacked by the immune system, leading to the development of anti-cyclic citrullinated proteins (anti-CCP or ACPA).[1,2,10]

Tobacco smoke is a major environmental trigger and has been shown to increase citrullination of proteins and either trigger the onset of RA or exacerbate existing disease.[1,10]

Another gene with a strong association in the development of RA is protein tyrosine phosphatase N22 (PTPN22), which regulates T and B cells and also is associated with other autoimmune disorders, including type 1 diabetes, lupus, and Hashimoto disease.[12] The presence of the PTPN22 gene increases citrullination of proteins as well as reactivity of T and B cells.[1] Hyperreactive T and B cells activate proinflammatory mediators (tumor necrosis factor [TNF], interleukin [IL]-1, IL-6, and metalloproteinases, among others) that lead to the synovial inflammation seen in patients with RA.[1,2,13] Synovial hyperplasia leads to recruitment of lymphocytes and neutrophils that release cytokines and proteinases that promote joint destruction.[1,13] Many other notable genes have been implicated in the development of RA, including the signal transducer and activator of transcription 4 (STAT4), TNF–receptor 1 and C5 complement component (TRAF1-C5 locus), peptidyl arginine deiminase 4 (PADI-4), and cytotoxic T-lymphocyte associated protein 4 (CTLA-4) genes.[1,13]

## DIAGNOSIS

In 2010, the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) updated the criteria for diagnosis of RA.[14] That update specifies that patients must have at least one joint involved with definitive synovitis, no other explanation for the symptoms, and a minimum of six points out of a possible 10 to confer a diagnosis of RA. Points are calculated based on the type and number of joints affected, serology, duration of symptoms, and presence of acute phase reactants (**Table 1**).[6,14] The patient described in our clinical scenario meets the ACR/EULAR criteria with more than 10 small joints involved (5 points) and symptoms for longer than 6 weeks (1 point).[6,14]

When evaluating a patient with suspected RA based on history and physical examination, the clinician should order an erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP), anti-CCP antibody, rheumatoid factor, complete blood cell (CBC) count, and hepatic and renal function tests. The inflammatory markers such as the ESR or CRP are nonspecific for RA. Despite their lack of specificity, these laboratory values can be used to calculate disease severity and response to therapy using an RA clinical activity instrument such as the DAS28 (Disease Activity Score with 28 joints).[15] Radiographs of the hands and feet provide a baseline determination of the extent of joint damage (**Figure 3**).[4] High-frequency ultrasound and MRI also have been helpful in early detection of synovial inflammation and erosive joint damage.[4,6,16] Anti-CCP and rheumatoid factor are diagnostic markers for RA. Anti-CCP has an equivalent sensitivity, but is more specific for RA than rheumatoid factor and has been found to predict erosive joint disease.[4,6,14,16] In patients with early disease both tests should be used rather than just one, so that additional cases can be recognized.[15] The 2010 ACR/EULAR criteria use serology (rheumatoid factor and anti-CCP) and acute phase reactants (ESR or CRP) in the diagnosis of RA (**Table 1**).[4,6,14]

Baseline liver tests are appropriate if therapy with methotrexate or sulfasalazine is being considered, because these drugs are potentially hepatotoxic. Baseline renal function tests also are appropriate if therapy with methotrexate is being considered, because it is contraindicated in patients with an estimated glomerular filtration rate (eGFR) of less than 30 mL/min. Additionally, patients with RA are at risk of anemia. Patients most commonly present with a normochromic, normocytic anemia (anemia of chronic disease); however, menstruating women

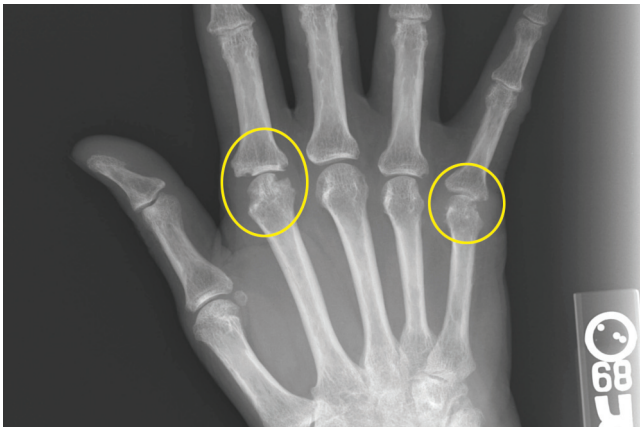

**FIGURE 3.** Radiograph of a hand with early erosions related to RA

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and patients with gastrointestinal bleeding from nonsteroidal anti-inflammatory drug (NSAID) use may have concomitant iron-deficiency anemia.[10] A CBC count will help identify an underlying anemia, although additional studies may be required to follow up abnormal findings. Rule out pregnancy in women of childbearing potential because many of the disease-modifying antirheumatic drugs (DMARDs) have teratogenic effects.

## PHARMACOLOGIC TREATMENT

The ACR treatment guidelines for RA were developed in 2008, with updates in 2012 and 2015.[17,18] The ACR recommendations are divided into two categories: DMARD-naïve early RA and DMARD-naïve established RA, with treatment guidelines that require assessment of high-risk conditions including heart failure, hepatitis B, hepatitis C, history of treated or untreated malignancy, and previous serious infection before initiating therapy.[18]

The EULAR treatment guidelines were developed in 2010, with updates in 2016 and most recently in 2019.[19] They do not differentiate between early or established RA, but provide recommendations from the time of diagnosis.[19]

Both guidelines are similar in their stepped approach to therapy and in their treat-to-target goal of clinical remission or, if not possible, low disease activity.[18,19] Both the ACR and EULAR recommend that DMARD monotherapy (preferably with methotrexate) should begin as soon as the diagnosis is determined. Other DMARDs include the following categories: conventional synthetic (csDMARDs); targeted synthetic (tsDMARDs), biological originator (bDMARDs), and biosimilar (bsDMARDs) (**Table 2**).[18,19] Both guidelines note that glucocorticoids should be used only for short-term control (less than 3 months) for patients with flares, or when initiating or changing DMARDs.[6,18,19]

A main difference between the two guidelines is that the ACR takes disease activity into account when initiating treatment, but EULAR initiates early treatment with methotrexate unless contraindicated, and assesses patient response at 3 and 6 months.[18,19] If improvement does not occur at 3 months, or target is not achieved at 6 months, EULAR guidelines then assess disease activity, referred to collectively as *poor prognostic factors*, to determine the next steps in treatment.[18,19] **Table 3** compares the guidelines for the ACR and EULAR criteria.[18,19]

Before starting therapy, obtain baseline laboratory testing including CBC, ESR, CRP, renal and liver panels, screening for hepatitis B and C, and tuberculosis. If hydroxychloroquine is being considered, it is important to obtain a baseline retinal examination.[18,19]

As previously noted, the choice of medication depends on the stage and severity of RA at the time of diagnosis; however, a csDMARD, usually methotrexate, generally is recommended as the first-line medication unless contraindicated, in which case leflunomide or sulfasalazine are the initial choices.[18,19] In a woman with RA who is planning to become pregnant, the goal is to initiate a DMARD that is not teratogenic and that will allow her to safely become pregnant. For this reason, therapy would be initiated with sulfasalazine, a sulfapyridine linked with 5-aminosalicylic acid (5-ASA) (pregnancy category B).

**TABLE 1.** 2010 ACR/EULAR criteria

A score of 6 or more is consistent with a definitive diagnosis of RA.

| **Affected joints** | **Points** |
|---|---|
| 1 large joint | 0 |
| 2-10 large joints | 1 |
| 1-3 small joints (large joints not counted) | 2 |
| 4-10 small joints (large joints not counted) | 3 |
| >10 joints (at least one small joint) | 5 |
| **Serology** | **Points** |
| Negative rheumatoid factor AND negative anti-CCP | 0 |
| Low positive rheumatoid factor OR low positive anti-CCP | 2 |
| High positive rheumatoid factor OR high positive anti-CCP | 3 |
| **Duration of symptoms** | **Points** |
| <6 weeks | 0 |
| ≥6 weeks | 1 |
| **Acute phase reactants** | **Points** |
| Normal CRP and ESR | 0 |
| Abnormal CRP or ESR | 1 |

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**TABLE 2.** DMARDs[18,19,23]

| Drug and routes of administration | Required baseline and/or monitoring tests | Major considerations |
|---|---|---|
| ***csDMARDs*** | | |
| Methotrexate (oral, SC, IM) | • CBC count, liver function tests, creatinine at baseline and every month for 3 months, then every 3 months thereafter<br>• Pregnancy test for women | • Contraindicated in pregnancy (category X)<br>• Folic acid supplementation recommended (1 mg/d)<br>• Avoid alcohol use<br>• Avoid with chronic liver disease<br>• Avoid with preexisting blood dyscrasias<br>• Contraindicated in patients with eGFR less than 30 mL/min |
| Leflunomide (oral) | • CBC count, liver function tests, creatinine at baseline and every month for 3 months, then every 3 months thereafter<br>• Pregnancy test for women | • Contraindicated in pregnancy (category X)<br>• May require cholestyramine washout when discontinuing treatment for patients planning on pregnancy<br>• Risk of severe hepatic impairment |
| Sulfasalazine (oral) | • CBC count, liver function tests, creatinine at baseline and every month for 3 months, then every 3 months thereafter and after increasing the dose<br>• Screen for G6PD deficiency at baseline if at risk | • Can be used in pregnancy (category B)<br>• Folic acid supplementation recommended<br>• Caution in hepatic and renal impairment<br>• Caution with blood dyscrasias<br>• Monitor for agranulocytosis<br>• Avoid in patients with hypersensitivity to sulfonamides or salicylates |
| Hydroxychloroquine (oral) | • Baseline and annual retinal eye examination | • Pregnancy use if necessary (category not assigned)<br>• Risk of retinal toxicity<br>• Risk of cardiomyopathy and conduction disorders |
| ***tsDMARDs (JAKis)*** | | |
| Baricitinib, tofacitinib, upadacitinib (all oral) | • Baseline TB testing and annually while on therapy<br>• CBC count, liver function tests, creatinine at baseline and every month for 3 months, then every 3 months thereafter | • Avoid use in pregnancy due to insufficient data<br>• Boxed warning for risk of serious infections (TB, zoster, invasive fungal, and other opportunistic infections)<br>• Malignancy<br>• VTE (DVT, PE, and other arterial thromboses) |
| ***bDMARDs: TNF inhibitors*** | | |
| Adalimumab (SC)<br>Certolizumab (SC)<br>Etanercept (SC)<br>Golimumab (SC, IV)<br>Infliximab (IV) | • Baseline TB testing and annually while on therapy<br>• Hepatitis B, hepatitis C<br>• CBC count, liver function tests, creatinine at baseline and every month for 3 months, then every 3 months thereafter | • Use in pregnancy: adalimumab (category B), certolizumab (category B), golimumab (IV category B, SC category not assigned), etanercept (category not assigned), infliximab (category not assigned)<br>• Neonates/infants considered immunosuppressed 1-3 months after in utero exposure and live vaccines should be avoided up to 6 months of age<br>• Boxed warning for risk of serious infections (TB, zoster, invasive fungal, and other opportunistic infections)<br>• Malignancy<br>• Hepatitis B reactivation<br>• Anaphylaxis<br>• Risk of demyelinating disorders<br>• Worsening and new-onset heart failure (infliximab contraindicated in class III/IV heart failure above doses of 5 mg/kg) |
| ***bDMARDs: IL-6R inhibitors*** | | |
| Sarilumab (SC)<br>Tocilizumab (SC, IV) | • Baseline TB testing and annually while on therapy<br>• Hepatitis B, hepatitis C<br>• CBC count, liver function tests, creatinine at baseline and every month for 3 months, then every 3 months thereafter<br>• Lipid profile at baseline and every 6 months while on therapy | • Use in pregnancy: Not recommended due to insufficient data<br>• Neonates/infants considered immunosuppressed 1-3 months after in utero exposure and live vaccines should be avoided up to 6 months of age<br>• Boxed warning for risk of serious infections (TB, zoster, invasive fungal, and other opportunistic infections<br>• Elevated transaminases<br>• Hepatitis B reactivation<br>• Hyperlipidemia<br>• IV tocilizumab—risk of infusion reaction, SJS |

*(Continues)*

**TABLE 2.** DMARDs[18,19,23] *(Continued)*

| | | |
|---|---|---|
| ***bDMARDs: costimulation inhibitors*** | | |
| Abatacept (SC, IV) | • Baseline TB testing and annually while on therapy<br>• Hepatitis B, hepatitis C<br>• CBC count, liver function tests, creatinine at baseline and every month for 3 months, then every 3 months thereafter<br>• Monitor blood glucose with IV formulation | • Use in pregnancy: not recommended due to insufficient data<br>• Risk of serious infections (TB, zoster, invasive fungal, and other opportunistic infections)<br>• Malignancy<br>• Hepatitis B reactivation<br>• Anaphylaxis<br>• In IV formulation, elevated blood glucose due to maltose in solution; not a problem with SC formulation<br>• Use with caution in patients with COPD due to increased dyspnea and adverse reactions |
| ***bDMARDs: anti-B cell (CD20 inhibitors)*** | | |
| Rituximab (IV) | • Baseline TB testing and annually while on therapy<br>• HBV, HCV<br>• CBC, liver function tests, creatinine at baseline and every month for 3 months, then every 3 months thereafter | • Use in pregnancy: Not recommended due to B-cell depletion in neonates<br>• Boxed warning for risk of hepatitis B reactivation, mucocutaneous reactions such as SJS, infusion reactions, progressive multifocal leukoencephalopathy<br>• Risk of increase in opportunistic infections<br>• Risk of cardiac conduction disorders |
| ***bsDMARDS*** | | |
| Adalimumab, etanercept, infliximab, and rituximab have biosimilar medications available | See drug details above | See drug details above |

Methotrexate is a folate antagonist and is teratogenic (pregnancy category X).[6] Leflunomide (pregnancy category X) also is teratogenic, is a pyrimidine synthesis inhibitor, essentially inhibiting rapidly dividing cells, in particular lymphocytes.[6]

If the patient fails to improve, presents or remains with moderate to high disease activity, fails to achieve the target of remission or low disease activity, additional DMARDs should be added to the therapeutic regimen.[18,19] Under the ACR guidelines, the decision as to which category of medication to choose depends on moderate to high disease activity. EULAR guidelines are dependent on the presence or absence of poor prognostic factors, such as moderate to high disease activity as determined by the DAS28; high ESR or CRP; high swollen joint count; positive rheumatoid factor or ACPA; early erosions on radiography; and failure of two or more csDMARDs.[15,18,19] In patients with moderate to high disease activity and no response to DMARD monotherapy for early RA, the ACR recommends the following therapeutic options: combination csDMARDs; TNF inhibitor bDMARDs +/- methotrexate; or non-TNF inhibitor bDMARDs; all of the choices can add short-term glucocorticoids.[18] The ACR makes the same recommendation for patients with established RA, but adds the option of a Janus kinase inhibitor (JAKi).[18] The EULAR criteria offer slightly different recommendations. In the absence of poor prognostic factors, the recommendation is to change or add another csDMARD.[18] If poor prognostic factors are present, a switch to a bDMARD or JAKi is recommended.[19]

Failure to achieve remission on this new protocol requires a change to a new bDMARD or JAKi.[19] Both guidelines recommend that even if patients fail one medication in a class, clinicians should try prescribing different drugs in the same class, because response varies across patients. Although the preferred goal is remission, studies have shown only 10% to 50% of patients achieve sustained remission.[10] Remission is defined as greater than 6 months in which all the following criteria are met:

- one or no tender joints
- one or no swollen joints
- CRP of 1 mg/dL or less
- patient global assessment of 1 or less (range, 0-10).[18-20]

Some authors suggest that dose reduction may be attempted in patients with sustained remission; however, if the patient has a disease flare, clinicians must be ready to increase medications promptly.[11,19] The ACR strongly encourages against discontinuing all RA medications even in patients in sustained remission.[18] The goal of treatment for RA is to reduce disease activity and the rate of joint destruction. The mainstay of pharmacologic therapy is early intervention with use of nonbiologic and biologic DMARDs together with adjunctive medications such as NSAIDs, oral and intra-articular corticosteroids, and analgesic medications, including opioids.

**TABLE 3.** Comparing the ACR and EULAR guidelines[18,19]

| Disease activity | ACR guideline | | Poor prognostic factors | EULAR |
|---|---|---|---|---|
| | Early RA | Established RA | | |
| Initial diagnosis: low disease activity | DMARD monotherapy (methotrexate preferred) +/- short-term glucocorticoids | DMARD monotherapy (methotrexate preferred) +/- short-term glucocorticoids | Initial diagnosis: No contraindications for methotrexate | Methotrexate +/- short-term glucocorticoids |
| Initial diagnosis: moderate to high disease activity | DMARD monotherapy (methotrexate preferred) +/- short-term glucocorticoids | DMARD monotherapy (methotrexate preferred) +/- short-term glucocorticoids | Initial diagnosis: Contraindications for methotrexate | Leflunomide or sulfasalazine +/- short-term glucocorticoids |
| **Symptoms improved at 3 months and achieved target at 6 months: continue on regimen** | | | | |
| **If symptoms NOT improved at 3 months or target NOT achieved at 6 months, see below** | | | | |
| Moderate to high disease activity | Choose from:<br>• Combination csDMARDs<br>OR<br>• TNF inhibitor bDMARDs +/- methotrexate<br>OR | Choose from:<br>• Combination csDMARDs<br>OR<br>• TNF inhibitor bDMARDs +/- methotrexate<br>OR | NO Poor prognostic factors | Change to or add:<br>• Leflunomide or sulfasalazine alone<br>OR<br>• csDMARD combination* |
| | • non-TNF inhibitor bDMARDs +/- methotrexate | • non-TNF inhibitor bDMARDs** +/- methotrexate<br>OR<br>• JAKi +/- methotrexate | Poor Prognostic Factors Present | Add to current regimen: |
| | +/- short-term glucocorticoid with any regimen | +/- short-term glucocorticoid with any regimen | | • bDMARD<br>OR<br>• JAKi |
| **Symptoms improved at 3 months and achieved target at 6 months: continue on regimen** | | | | |
| **If symptoms NOT improved at 3 months or target NOT achieved at 6 months, see below** | | | | |
| Moderate to high disease activity | | • Switch to a different medication in the same class (TNF inhibitor bDMARD or non-TNF inhibitor bDMARD) +/- methotrexate<br>OR<br>• Switch to a medication in a different class (TNF inhibitor bDMARD or non-TNF inhibitor bDMARD first before JAKi) +/- methotrexate | | • Change the bDMARD<br>OR<br>• Change the JAKi<br>OR<br>• Change to a different class of medication |

*Most frequently used csDMARD combination is methotrexate, sulfasalazine, and hydroxychloroquine
**Non-TNF inhibitor drugs include IL-6R inhibitors, costimulation inhibitors, and anti-B cell (CD20 inhibitors)

## NONPHARMACOLOGIC TREATMENT

Nonpharmacologic intervention also is important for patients with RA to improve or maintain mobility, strength, and endurance. A significant aspect of treatment is proper patient education about the disease, treatment, and health maintenance so patients can be better involved in the management of their disease. Consultations with physiatry and occupational and physical therapies are invaluable because they provide assistance with splints and orthotic devices, exercise programs, education on joint protection, adaptive equipment use and training, and methods to conserve energy.[21] Consultation with a nutritionist also can be beneficial, especially for patients with severe RA, who frequently suffer from malnutrition or anorexia. Patients with obesity would also benefit from consultation with a nutritionist to help modify their eating habits; excess weight puts stress on joints. Heat and cold therapies also may provide relief of joint pain. When joint deformity becomes severe, surgical intervention can provide pain relief and improve joint function.

Patients with RA should have regularly scheduled appointments with their primary care provider to monitor their general health, paying particular attention to their cardiovascular health. Patients with RA have an increased risk of coronary artery disease and should be counseled about cardiovascular risk factors and started on statins or other medications if they are at higher risk.[1,22] In addition, before starting therapy, the ACR recommends that patients have the pneumococcal, hepatitis B, influenza, human papillomavirus, and zoster virus vaccines.[18] If biologic DMARDs are initiated before appropriate vaccination, the patient cannot receive live vaccines. Patients may be given inactivated vaccines following special protocols.

## CONCLUSION

The case patient was started on oral methotrexate therapy for her RA, but was switched to parenteral dosing due to gastrointestinal intolerance. She experienced remission on this regimen and after 1 year, attempted a dose reduction. The reduction led to a flare of her RA. She was returned to her original dose of subcutaneous methotrexate in addition to a short course of glucocorticoids with subsequent resolution of her flare. The patient was counseled that if she desires pregnancy in the future, she will need to be transitioned to sulfasalazine and to establish care with high-risk obstetrics. The patient expressed understanding and agreement with the plan.

RA is a chronic, systemic, autoimmune, inflammatory disease characterized by prolonged morning stiffness, symmetric swelling and pain typically of the wrists, MCP, PIP, and MTP joints. Early recognition and diagnosis of RA may allow intervention with appropriate DMARDs with a decrease in the destructive arthropathy that can occur with this disorder. The ultimate goal of therapy is prolonged remission or low-disease activity, a decrease in joint destruction, and improved quality of life. Pharmacologic and nonpharmacologic therapy require a multidisciplinary team approach with appropriate referrals to rheumatology, physiatry, OT, PT, nutrition, and, in women wishing to become pregnant, high-risk obstetrics. **JAAPA**

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