# Rheumatoid Arthritis
## Early Diagnosis and Treatment

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**KEYWORDS**

• Early rheumatoid arthritis • Referral • Rheumatoid factor

**KEY POINTS**

- Rheumatoid arthritis is not a laboratory diagnosis.
- Additive, symmetric polyarthritis of small and large joints.
- Do not wait for classicate features (nodules, erosions, deformity).
- Only use corticosteroids as bridge therapy while waiting for DMARDs to be effective.
- Start DMARD therapy and refer as soon as the diagnosis is made.

Rheumatoid arthritis (RA) is a chronic, progressive inflammatory disorder that manifests as a symmetric polyarthritis of small and large joints that may lead to joint and periarticular structural damage and the consequences of systemic inflammation.[1] Recent advances have resulted in better diagnostic criteria, improved serologic testing, novel new drugs, and better guidelines to manage patients with RA. Yet, there are challenges and unmet needs that frustrate patients and physicians alike, including:

- Delays in referral and early diagnosis
- Misuse of serologic testing
- Misconceptions about seronegative RA
- Faulty beliefs that RA drugs are more dangerous than RA itself

RA can be deadly. Many studies have shown that patients with RA live 6 to 11 fewer years than people without RA. This is especially true in women, those with seropositive RA, and those with active or recalcitrant RA. Patients with RA are at greater risk[2,3] to develop the following:

- Functional impairment and disability.
- Serious infections: Pneumonia is the number one cause of infectious death in RA. This risk is largely driven by: (1) the severity of RA, (2) steroid use (glucocorticoids are acutely wonderful, but they are chronically hazardous), (3) breakdown of skin

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(from open ulcers, wounds, and major surgery), and (4) antirheumatic drugs. Although methotrexate (MTX), immunosuppressives, and biologics are often blamed for infectious events, they are only contributory after all of the afore mentioned have upped the risk of infection.

- Lymphoma and cancer: Cancer is one of the top three causes of death in RA. Patients with RA have a higher risk of non-Hodgkin lymphoma, lung cancer, and skin cancers; but have a lower risk of colon and breast cancer. This risk is largely independent of therapies, as and the cancer risk is predominantly driven by chronic inflammation.
- Cardiovascular (CV) death: CV disease is a consequence of chronic uncontrolled inflammation that affects the vasculature and myocardium. The CV risk in RA is further compounded by nonsteroidal anti-inflammatory drug use, weight gain, sedentary lifestyle, and other comorbidities. Control of inflammation and RA activity by prolonged treatment with MTX or other aggressive therapies (eg, biologics) lowers the CV event and death rate in RA.
- Chronic lung disease: Chronic lung disease in RA denotes those who are severe and have a higher mortality risk, especially for lung-related deaths.[4] Up to 20% of patients have chronic interstitial lung disease (ILD) and chronic lung disease is a major risk factor for infections, pneumonia, and death in RA.
- Extra-articular manifestations: These seem to also be a consequence of chronic inflammation and include such manifestations as rheumatoid nodules, Sjögren syndrome (dry eyes, dry mouth), rheumatoid vasculitis, rheumatoid lung, inflammatory eye disease (scleritis), Felty syndrome, amyloidosis, and neuropathy. These occur with more severe disease; seropositivity; and destructive, erosive arthritis.
- Surgery and complications of surgery: In the current era of more aggressive therapy, there has been a steady decline in the need for orthopedic surgery including joint replacements. The risk of surgically related infection or death is low, but does occur. Recent studies have shown that patients with RA undergoing arthroplasty have a low short-term (30 day) mortality risk (same as patients with osteoarthritis; odds ratio, 0.94; 0.38–2.33). Yet RA was associated with a significantly higher long-term mortality from years 1 to 8 after surgery (hazard ratio, 1.22; 1.00–1.49).[5]

## EARLY RHEUMATOID ARTHRITIS

As there is no standard definition of early RA, it is best defined as "the earlier, the better." While the diagnosis of RA can be suspected with as little as 2 to 4 weeks of joint pain, 6 weeks of demonstrable synovitis in multiple joints confirms the "chronicity" required for a confident RA diagnosis (if alternative causes of chronic arthritis are excluded). Early RA clearly begins years to months before it becomes manifest polyarthritis and this is known as "preclinical RA."

Preclinical RA, by definition, includes patients who do not meet criteria for RA, but manifest arthralgia (without synovitis), are seropositive, and have a first-degree relative who has RA. A high percentage of these individuals develop increasing joint pain and swelling in the ensuing months to years, particularly in those who are anti–citrullinated protein antibody (ACPA) positive.[6]

Early presentation of inflammatory polyarthritis may also be labeled undifferentiated (inflammatory) polyarthritis or seronegative RA. Both have negative tests for RA but demonstrate the same inflammatory additive polyarthritis as RA. The difference lies with the potential to spontaneously remit. It is estimated that more than half of all patients with early inflammatory polyarthritis have undifferentiated polyarthritis (not

meeting diagnostic criteria) that will go into remission within 3 to 12 months. Those that persist, and are seronegative, are labeled as seronegative RA.

In primary care, new-onset RA is less common than low back pain, osteoarthritis, gout, fibromyalgia, or psoriasis, but is more common than polymyalgia rheumatica (PMR), systemic lupus, or septic arthritis.

In 1994, there were nearly 170,000 new cases of RA in the United States. Population-based incidence rates for early RA range between 5 and 45 cases per 100,000 patients per year (patient-years).[7] Applying a conservative North American incidence rate of 20 cases per 100,000 patient-years, one might anticipate nearly 75,000 new patients with RA in the United States and 7500 in Canada in the next 12 months. This number may be doubled or more by patients who are seronegative, not meeting diagnostic criteria, or having undifferentiated inflammatory polyarthritis.

## ONSET OF RHEUMATOID ARTHRITIS

Onset of RA peaks between 40 and 50 years, but is well described in all ages, including children and adolescents. Moreover, the risk of RA increases considerably after the age of 60 years. Women are affected nearly three times more often than men, but gender differences are less pronounced in older patients.

Certain populations are at greater risk of RA. The Centers for Disease Control and Prevention notes the following to be risk factors for developing RA[8]:

- Age: RA prevalence increases with age.
- Sex: RA is typically three times higher in women than men.
- Genetics: Those with the "shared epitope" have genes conferring a higher risk of developing RA and more severe RA. These genes include HLA class II genotypes (eg, HLA-DR4 or HLA-DR β1 alleles) that become relevant when exposed to environmental triggers, such as smoking or obesity. Nevertheless, these genes are not generally tested for.
- Smoking: Multiple studies show that cigarette smoking increases a person's risk of developing RA and can make the disease worse.
- Obesity: Multiple studies show obesity to be a risk factor for RA onset and also a risk factor for being refractory to standard therapies.
- Being nulliparous: Women who have never given birth may be at greater risk of developing RA.

In about two-thirds of patients, RA has an insidious onset of a symmetric additive polyarthritis. Although constitutional features (ie, malaise, fatigue, low-grade fever) may occur, it is the joint symptoms (pain, swelling, prolonged stiffness) that dominate the clinical picture. Small, medium, and large joints are equally affected. Certain features should argue against RA as a diagnosis, including an acute arthritis onset, monoarthritis, prominent weight loss, rash, or involvement of other organ systems (eg, ocular, neurologic, gastrointestinal).

## DIAGNOSTIC INVESTIGATIONS

Routine laboratory studies may help in confirming the diagnosis and establishing the presence of inflammation, autoantibodies, and the risk for damage or erosions.

### *Acute Phase Reactants*

The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) provide surrogate evidence of inflammation. However, these may be elevated with infection; other rheumatologic disorders; malignancy; pregnancy; and chronic renal, liver, or lung

disease. Moreover, in active RA, the ESR or CRP may be elevated only in 60% of patients. Thus, when elevated, these biomarkers may support an RA diagnosis, but their predictive value (positive and negative) is limited. Other laboratory studies may also indicate chronic inflammation, including an anemia of chronic disease; thrombocytosis; hypoalbuminemia; hypergammaglobulinemia; or elevated levels of ferritin, haptoglobin, or complement.

### *Serologic Tests*

Autoantibodies have been used to guide the diagnosis of various autoimmune diseases. Testing for serologic markers may tilt the diagnostic probabilities or add prognostic value to the evaluation of inflammatory polyarthritis. The presence of RF and antinuclear antibodies is nonspecific and is found in patients with infection, malignancy, and rheumatologic diseases. These autoantibodies are present in other diseases, including viral hepatitis, systemic lupus erythematosus, cryoglobulinemia, Sjögrens syndrome, paraproteinemias, bacterial endocarditis, mycobacterial diseases, syphilis, leprosy, chronic interstitial lung disease, parasitic infections, and malignancies.

Serum rheumatoid factor (RF) is closely associated with RA and may confirm a clinically suspected diagnosis or characterize the severity of disease. RF is usually measured as an IgM antibody that binds to the Fc part of IgG. RF is found in up to 80% of established patients with RA, but may only be found in 50% of patients in the first 6 months of symptoms. RF is not specific to RA, because it is seen in 5% of the general population and up to 15% of elderly persons. RF is also positive in numerous other conditions including Sjögren syndrome, cryoglobulinemia, systemic lupus erythematosus, sarcoidosis, Waldenstrom macroglobulinemia, bacterial endocarditis, mycobacterial disease, hepatitis, chronic liver disease, leprosy, syphilis, parasitic diseases (eg, leishmaniasis), chronic interstitial lung disease, and lymphoproliferative malignancies. RF (and cyclic citrullinated peptides [CCP]/ACPA) should not be used as a screening tool, but should be ordered intelligently, in the setting of undiagnosed poly arthritis with swollen joints. Although it is true that higher titers RF (>100 IU/mL) are more likely to be RA, RF levels do not correlate with disease activity. High titers are associated with more severe RA and risk for extra-articular manifestations.[9] Lastly, other than the first 6 months, repeated or serial measurement of RF levels is rarely indicated or helpful.

Antibodies against CCP (also called ACPA) have also proven to be a useful diagnostic and staging tool, especially in early patients with RA. ACPA are nearly as sensitive as serum RF (70% CCP+ in RA of <2 years duration); But CCP antibodies are far more specific for RA (>90%+).[10] For example, although RF is often found with hepatitis C infection, ACPA is usually absent.

The presence of ACPA has been correlated with early RA, aggressive RA, radiographic damage, and shared epitope (genotype associated with RA). Moreover patients with high titers of ACPA (>250 IU/mL) or those who are double positive for RF and ACPA have a poorer prognosis.

## CINCHING THE DIAGNOSIS OF RHEUMATOID ARTHRITIS

An early diagnosis requires access to medical and diagnostic services, suspicion based on onset features, and judicious use of serologic testing. RA is a clinical, and not a laboratory diagnosis. RA should be considered in the following scenarios:

- Pain, swelling, and stiffness in multiple joints going on for 12 weeks or more

- First-degree relative of a patient with RA with chronic joint symptoms (but not the lower spine or distal interphalangeal [DIP] joints)
- New-onset carpal tunnel syndrome with wrist swelling and inflammation
- Those with chronic, additive, symmetric polyarthritis affecting the proximal interphalangeal (PIP), metacarpophalangeal, wrist, and metatarsophalangeal joints
- Those meeting criteria for the diagnosis

Requisite features begin with joint pain and stiffness that improve with activity. Hallmark findings include joint swelling or effusion, and possibly warmth or erythema. **Table 1** lists the 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for the diagnosis of RA.[11] Inherent to these criteria are inflammatory features and serologies that allow for an earlier diagnosis. This contrasts older criteria that relied heavily on long-standing, established disease features, such as chronicity, rheumatoid nodules, and radiographic erosions. The 2010 American College of Rheumatology/European League Against Rheumatism criteria are weighted in favor of more joints, higher titers of RF and ACPA (or CCP antibodies); and less so for acute phase reactants (ESR or CRP), duration, and large joints only. Six points or more one necesiary to diagnose RA.

## DIFFERENTIAL DIAGNOSIS: OTHER CONSIDERATIONS

When patients fail to meet criteria or have atypical features, other diagnostic considerations should be considered (**Box 1**). Early RA is often confused with other

**Table 1**
**2010 American College of Rheumatology/European League Against Rheumatism classification criteria for RA**

| Joint Distribution | Score |
|---|---|
| 1 large joint | 0 |
| 2–10 large joints | 1 |
| 1–3 small joints (large joints excluded) | 2 |
| 4–10 small joints (large joints excluded) | 3 |
| >10 joints (at least 1 small joint) | 5 |
| Serology | |
| Negative RF and negative ACPA | 0 |
| Low positive RF or ACPA ($\leq 3 \times$ ULN) | 2 |
| High positive RF or ACPA ($>3 \times$ ULN) | 3 |
| Symptom duration | |
| <6 wk | 0 |
| $\geq$6 wk | 1 |
| Acute-phase reactants | |
| Normal CRP and ESR | 0 |
| Abnormal CRP or ESR | 1 |

To be considered, the patient must: (1) have at least 1 joint with definite clinical synovitis (swelling), and (2) synovitis not better explained by another disease.

A score of $\geq$6 is required to have RA.

*Adapted from* Aletaha D, Neogi T, Silman AJ, et al. 2010 Rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum 2010;62(9):2574; with permission.

**Box 1**
**Differential diagnosis of early rheumatoid arthritis**

Infection-related
- Reactive arthritis
- Viral arthritis
  - Parvovirus B19
  - Hepatitis B
  - Hepatitis C
  - Alpha viruses: chikungunya or Zika virus (mosquito-borne)

Elder onset
- Calcium pyrophosphate deposition disease rheumatoid-like arthritis
- Polymyalgia rheumatica
- Inflammatory osteoarthritis

Rheumatoid-related
- Seronegative RA
- Palindromic rheumatism
- Undifferentiated inflammatory polyarthritis
- Adult-onset Still disease, systemic lupus erythematosus

Spondylarthritis-related
- Psoriatic arthritis
- Enteropathic arthritis

conditions that are typically polyarticular, especially infection-related arthritides, such as reactive arthritis or viral arthritis caused by parvovirus B19, hepatitis B, hepatitis C, chikungunya virus, or Zika virus.[12] Other considerations are discussed below.

### *Polymyalgia Rheumatica*

In the elderly (>60 years), early RA may be confused with calcium pyrophosphate deposition disease (CPPD), inflammatory osteoarthritis, and PMR. Although RA and PMR have prolonged morning stiffness, high acute phase reactants, and joint pains, PMR is distinguished from RA with prominence of limb girdle (shoulders, hips) myalgic stiffness or soreness and a lack of RF or ACPA antibodies. Yet there are patients with PMR that may resemble RA with synovitis and swelling of the hands or wrists.

### *Calcium Pyrophosphate Deposition Disease*

CPPD and chondrocalcinosis are common in the elderly. CPPD may manifest as pseudogout attacks (involving the knee, wrist, or feet) or as chondrocalcinosis with osteoarthritis accompanied by calcification of cartilage and occasionally as chronic, somewhat inflammatory symmetric polyarthritis that resembles RA. CPPD is confirmed by arthrocentesis, identification of calcium pyrophosphate crystals, radiographic chondrocalcinosis, and negative serologic tests for RF or ACPA, although elderly patients often have a positive RF.

### *Inflammatory Osteoarthritis*

Osteoarthritis and seropositivity increases with age. Coincident seropositivity in the presence of DIP and PIP osteoarthritic changes (Heberden and Bouchard nodes) is not uncommon, but is still just osteoarthritis with a positive RF or ACPA such is an example of the limited value of RF or ACPA in establishing a diagnosis of RA, especially at low titers. Nonetheless a minority of osteoarthritis manifests inflammatory osteoarthritis, distinguished by having inflammatory synovitis and erosive changes

in multiple PIP and DIP joints of the hands. Such patients are usually seronegative and the radiograph erosions of inflammatory OA are distinctly different ("gullwing" central erosions) from that seen in RA.

#### *Other Autoimmune Conditions*

Uncommonly, other autoimmune disorders (eg, lupus, polymyositis, scleroderma) may have a polyarticular onset. Time and disease evolution will distinguish these from RA.

#### *Spondylarthritis*

Psoriatic arthritis and inflammatory bowel disease (enteropathic) arthritis may present as either an asymmetric, oligoarticular (three joints or fewer) chronic arthritis or with RA-like symmetric polyarthritis. Aside from their diagnosis affirming skin (psoriasis) or gut (Crohn) disease, they may have associated features of dactylitis, enthesitis (eg, heel pain), or sacroiliitis or spondylitis, that sets them apart from RA.

#### *Undifferentiated polyarthritis*

Studies from early arthritis clinics have shown that most new-onset, inflammatory oligoarthritis or polyarthritis will not meet criteria for the diagnosis of RA. Yet their joint involvement may have an RA-like distribution, and are distinguished from early RA by being seronegative and often go will into remission. This subset is more prevalent than early RA, and only a minority ($\leq$20%) of these patients with undifferentiated polyarthritis progress to RA. These patients are often labeled as having inflammatory arthritis, undifferentiated polyarthritis, or mistakenly as early RA. Regardless of diagnostic label, treatment of early RA and undifferentiated polyarthritis should match the degree and duration of synovitis and not be dictated by the diagnostic criteria.

#### *Palindromic rheumatism*

Palindromic rheumatism is an uncommon disorder linked to RA because occasionally patients with RA initially present with a palindromic pattern. It is characterized by recurrent, afebrile attacks of monoarthritis or tendonitis, occasionally polyarthritis, usually lasting hours to days. Pain, swelling, and redness occur in typical RA joints (eg, wrists, shoulders, ankles, knees, metatarsophalangeal, and fingers). Less than half of patients are seropositive and seropositivity increases the odds of evolving into chronic RA. Nearly half of affected patients experience chronic, intermittent palindromic attacks; in 30% to 40% the condition evolves into RA; and up to 15% go into clinical remission. Palindromic rheumatism needs to be distinguished from early RA, and other recurrent arthropathies, such as crystalline arthritis, Behçet disease, or familial Mediterranean fever. Patients with recurrent attacks may benefit from intra-articular or oral corticosteroids, antimalarial drugs, or disease-modifying antirheumatic drug (DMARD) therapy.

#### *Adult-onset Still disease*

Still disease is a variant of juvenile idiopathic arthritis (previously called juvenile RA). Adult-onset Still disease is a febrile inflammatory disorder of young adults with hallmark features of quotidian fevers, evanescent rashes, and polyarthritis.[13] Although polyarthritis is seen in up to 80% of patients with adult-onset Still disease, nearly 30% develop an erosive, RA-like arthritis that often requires treatment with DMARDs or biologics.

### NOT RHEUMATOID ARTHRITIS!

There are several scenarios that should not be confused with early RA, but often are, usually because of overinterpretation of polyarthralgias and rheumatoid serologies.

Critical to the RA diagnosis is the objective finding of swollen, inflamed joints. It should be noted that RA is not:

- Induced by trauma.
- Caused or cured by diet alone.
- Arthralgia (joint pain): one needs to demonstrate synovitis or swollen joints to consider RA.
- Hand deformity: hand deformities do occur in RA, but also osteoarthritis, psoriatic arthritis, gout, and other autoimmune diseases.
- Low back or DIP joint arthritis.
- Widespread pain with fatigue: such patients are more likely to have fibromyalgia.
- Lyme disease: RA should not be confused with Lyme arthritis. The latter only occurs in those who live in or travel to Lyme disease–endemic areas and who usually had demonstrated the bulls-eye rash called erythema chronicum migrans. Serologic testing for Lyme disease is far less predictive than these clinical requirements for the diagnosis. Lyme arthritis is a late manifestation of Lyme disease and usually presents as intermittent or persistent inflammatory arthritis in a few large joints, especially the knee, shoulder, ankle, elbow, or wrist. It does not appear as a chronic, additive, symmetric polyarthritis of large and small joints, typical of RA.

## RULES FOR REFERRAL

Once the diagnosis of RA is suspected or confirmed, the primary care or diagnosing physician should develop a treatment plan, initiate therapy, and consider referral. The goal is to reduce the time from symptom onset to diagnosis, and to reduce the time from diagnosis to the initiation DMARD therapy.

Early referral is necessary as MRI studies have shown articular erosions are seen as early as 12 to 16 weeks from the onset. Within the first 3 years, nearly 70% of patients have radiographic damage. These data underscore the need for prompt diagnosis, treatment, and referral. Referral is necessary to confirm the RA diagnosis and initiate prompt DMARD therapy. A recent UK National Health Service study of 822 patients with RA showed the median time between symptom onset and rheumatology consult was 27.2 weeks and that only 20% of patients were seen within the first 3 months of symptom onset.[14]

Ideally, all patients with recent-onset RA or inflammatory arthritis should be evaluated by a rheumatologist. Diagnostic certainty may be fleeting in early disease because the symptoms are not fully developed, seropositivity is lower in the first 6 months, and outcomes of new-onset polyarthritis vary.[15]

Emery and colleagues[16] have developed rules for early arthritis referral to a rheumatologist:

1. Three or more swollen joints
2. A positive metacarpophalangeal or metatarsophalangeal squeeze test to elicit pain
3. Morning stiffness of 30 minutes or more in relevant joints
4. Joint symptoms of greater than 6 weeks but less than 6 months
5. An abnormal serologic test (RF, CCP) or elevated ESR or CRP

## TREATMENT CHOICES IN EARLY RHEUMATOID ARTHRITIS

It is the clinician's task to address the patient's pain, swelling, and stiffness with effective interventions. There are three modalities that every clinician should address in early RA: (1) analgesics, (2) corticosteroids, and (3) DMARDs.

### *Analgesics*

The initial goal is to minimize pain, inflammation, and functional impairment. Analgesic therapy, splinting, and physical therapy should be liberally prescribed soon after onset and used until a diagnosis is established. Analgesic agents include acetaminophen, tramadol, nonacetylated salicylates, nonsteroidal anti-inflammatory drugs, or low-dose prednisone. These can be used at the lowest effective dose. For instance, a patient with new-onset RA with swollen PIPs and knees could be given any of the following (noting limits imposed by comorbidities and contraindications):

- Extended-release acetaminophen, 650 mg, two tablets twice daily
- Meloxicam, 7.5 mg daily or twice daily (with meals)
- Tramadol, 50 mg twice or three times daily as needed
- Prednisone, 5 mg daily

Pain is a prevalent feature in early RA and is most often related to inflammation, rather than damage. Thus, strong narcotic or addictive analgesics should be avoided and prohibited in patients with early RA.

### *Corticosteroids*

Patients with slowly progressive or aggressive RA may achieve short-term benefits from injectable or low-dose oral corticosteroids while waiting for DMARD therapies (MTX, hydroxychloroquine [HCQ], or sulfasalazine [SSZ]) to be in effect. It is paramount to note that steroids are acutely wonderful and chronically dangerous. Even low doses of prednisone (5 mg per day) carry a significantly increased risk of serious or hospitalizeable infections, and higher rated of CV events and comorbidities (diabetes, osteoporosis) with doses greater than 5 mg daily. Dosing steroids in early RA should be at the lowest dose effective and possible (2.5 mg is preferred over 5 mg or 7.5 mg daily) and only until DMARD or biologic therapies have controlled the synovitis. Hence, most patients only need to be on low-dose oral corticosteroids for less than 4 months. Lastly, intra-articular corticosteroids usually used in the knee and shoulder can provide effective short-term relief in those patients with disproportionate symptoms from one or a few joints.

### *Disease-Modifying Therapy*

DMARDs include conventional synthetic DMARDs (eg, MTX, HCQ, SSZ, and leflunomide) and biologic DMARDs (eg, etanercept, adalimumab, abatacept, and tocilizumab). Currently there are numerous Food and Drug Administration approved DMARDs for use in RA: 6 conventional DMARDs (eg, MTX, SSZ, HCQ), 9 biologic DMARDs, and 13 biosimilar DMARDs (copies of etanercept, adalimumab, infliximab, or rituximab).

The primary care physician should start conventional DMARD therapy soon after the diagnosis, with either HCQ or MTX, while referring the patient to the rheumatologist for ongoing DMARD management. HCQ tends to have far less side effects than MTX, but does not have the overall efficacy of MTX. Starting doses for these agents are:

- HCQ, 200 mg: one or two tablets per day (dosed as 4–5 mg/kg/d)
- MTX, 2.5 mg: four tablets given once a week (eg, every Friday) along with daily folic acid, 2 mg per day

Patients taking HCQ require little monitoring but do need a baseline eye examination soon after starting HCQ therapy. Patients taking MTX should be tested for hepatitis

before use and have laboratory studies at 1 month and 3 months after starting and then every 3 months to monitor for cytopenia or hepatotoxicity.

With referral, to the rheumatologist confirms the diagnosis; fine tunes the use of analgesics, steroids, and DMARD therapy; and involves adjunctive providers (physical therapy, orthopedists) when needed. Moreover, rheumatologic services can further advise the patient on numerous issues including lifestyle issues (weight loss, smoking cessation), future pregnancies, vaccination safety CV risks associated with RA, work and ergonomic adjustments, and future prognosis.

## CONSEQUENCES OF DELAYED INTERVENTION

Numerous studies have demonstrated the advantage of early and aggressive treatment, even with older DMARDs, such as gold and HCQ.[17] Numerous treatment options exist for patients with early RA. Early institution of appropriately aggressive treatment can dramatically improve the patient's synovitis, quality of life, and lessen joint destruction and the future need for hospitalization and orthopedic surgery. Thus, there is a critical window of opportunity to diagnose and treat early RA as soon as possible.[18] Early recognition, diagnosis, DMARD initiation, and partnering with a rheumatologist is a proven formula, wherein, patients captured in the first 3 to 12 months of their disease can manage their disease and optimize long-term outcomes.

## CLINICS CARE POINTS

- RA is not a laboratory diagnosis; up to 20% of patients are seronegative.
- Polyarthritis lasting more than 6 weeks is required.
- An additive, symmetric polyarthritis of small and large joints is evident at disease onset.
- Do not wait for classic features (nodules, erosions, deformity) because they are seen late.
- Only use corticosteroids as bridge therapy while waiting for DMARDs to be effective.
- Start DMARD therapy and refer as soon as the diagnosis is made.

## DISCLOSURE

None.

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