Primary care physicians may contribute to improved outcomes by recognizing the signs and symptoms early on. Part 2 of a Special Report.

Early diagnosis and treatment of rheumatoid arthritis (RA) has been found to lead to long-term improved outcomes in recent years.¹ Primary care physicians (PCPs) may play a key role in attaining these outcomes by recognizing the signs and symptoms early and making timely referrals.

Evaluation of pain in the primary care setting can be complex. But knowing RA classification criteria and identifying several historical, examination, laboratory, and imaging features can help clinicians narrow the differential to inflammatory or autoimmune-based joint pain and, following that, a more specific diagnosis of RA.

**Classification criteria**

Understanding RA classification criteria can help guide the diagnostic evaluation. There are now 2 sets of established criteria: the 1987 American College of Rheumatology (ACR) criteria² and the 2010 ACR/European League Against Rheumatism (EULAR) criteria.³ Each provides valuable understanding of RA and both are appropriate to use in diagnosis, but because the 2010 criteria can identify patients earlier than the 1987 criteria and incorporate newer autoantibody tests, they are becoming increasingly popular in clinical practice.⁴ ⁵

These criteria were developed primarily for research. Although they serve as good guides for clinical diagnosis, patients who do not meet the full criteria may be treated for RA. In addition, patients may meet the criteria and be seronegative for rheumatoid factor (RF) and antibodies to citrullinated protein antigens (ACPA). Because these patients may have other forms of arthritis or autoimmune disease, they are best treated at the discretion of a rheumatologist.

**Next: The Criteria**

Following are the 1987 ACR classification criteria²:

- Morning stiffness > 1 hour
- Arthritis of ≥ 3 joint areas
- Hand arthritis
- Symmetric arthritis
• Nodules
• Elevation of rheumatoid factor
• Radiographic changes

With the 2010 ACR/EULAR classification criteria, 4 or more criteria must be met for diagnosis and findings 1-4 must be present for 6 or more weeks.\(^3\) Arthritis must be observed by a physician. Patients with 1 or more swollen joints consistent with synovitis not better explained by another disease should be tested.

A patient who meets these initial criteria with a score of 6/10 or higher can be classified as having “definite RA”:
• **Joint involvement**: 1 large joint, 0; 2-10 large joints, 1; 1-3 small joints, 2; 4-10 small joints, 3; > 10 joints (at least 1 small), 5
• **Serology** (at least 1 test needed): negative RF and ACPA, 0; low positive RF or ACPA, 2; high positive RF or ACPA, 3
• **Acute-phase reactants** (at least 1 test needed): normal C-reactive protein (CRP) level and erythrocyte sedimentation rate (ESR), 0; abnormal CRP level or ESR, 1
• **Duration of symptoms**: < 6 weeks, 0; ≥ 6 weeks, 1

**Next: The History**

**The diagnostic history and examination for RA**

The key aspects of the diagnostic history and examination for RA allow the physician to differentiate between inflammatory and noninflammatory causes to determine the source of pain or other joint symptoms. Patients with RA typically report pain in and around their joints, often with associated stiffness and self-reported swelling.

Although RA can affect nearly any synovial joint or tendon, typically involved are the proximal interphalangeal (PIP) joints, metacarpophalangeal (MCP) joints (Figure), wrists, and metatarsophalangeal (MTP) joints. Of note, the distal interphalangeal (DIP) joints are associated with osteoarthritis or other forms of inflammatory arthritis (IA), such as psoriatic arthritis, rather than RA. Joint involvement in RA most often is symmetrical, although in early RA the manifestations may be unilateral.

Combined with location, the timing of symptoms—onset as well as duration and variation throughout the day—can provide helpful clues in identifying RA. Patients often describe morning stiffness or increased stiffness after periods of inactivity (“gelling phenomenon”). Although morning stiffness is not included in the 2010 criteria, a duration of morning stiffness of more than 30 to 60 minutes before maximal improvement can be a useful historical point to help identify IA. During the history, a clinician should engage the patient and get him or her to clarify specifically which joints are involved. Recording this information allows for a targeted physical exam and for tracking disease activity over time.

Of note, most of the historical evaluation for the presence of IA and in particular RA is focused on the patient’s current history. However, various epidemiologic, familial, and genetic factors can affect RA risk. In particular, RA is more likely to develop in women than in men, the risk in families is increased 5- to 7-fold, and tobacco use increases risk.\(^1\)

Assessing these factors may be useful, but their effect on the pretest probability for RA is largely unknown. As such, the diagnosis of RA relies on the joint symptom history and the physical examination, laboratory, and imaging findings. Other historical features (fatigue, general malaise) may be reported and should be assessed, but they are less specific for a diagnosis of RA.
Next: The Physical Exam

Physical examination: The “gold standard”

Imaging with ultrasound or MRI is being used increasingly in managing many forms of IA, including RA, but the “gold standard” in clinic for identifying the synovitis of RA is currently the physical examination. Although identifying joint findings of synovitis can be difficult without extensive training, the examiner should evaluate joints carefully for the objective signs of warmth, swelling, and effusion that can represent underlying synovitis, as well as tenderness. About 4 kg/cm² of pressure applied by the examiner’s fingertips—typically the amount of pressure required to blanch the nailbed—is recommended. Swelling can range from as subtle as loss of feeling in a sharp joint line at the MCPs to an obviously spongy or boggy feeling. For an examiner who is not highly trained to identify synovitis, perhaps the most important aspect of the examination is a thorough evaluation of not just symptomatic joints but also the joints typically involved in RA (PIPs, MCPs, wrists, and MTPs). Recording tenderness and swelling in these joints can help demonstrate to a rheumatologist that RA is suspected and can be useful in monitoring response to therapy and disease activity. According to the 1987 ACR criteria, the presence of rheumatoid nodules also supports the diagnosis. Often found on extensor surfaces, nodules can vary in size and may feel, to the examiner, like a firm lump under the skin. Because nodules usually are later manifestations of RA, they typically are not useful in early diagnosis.

Next: Lab Testing

Laboratory testing in the initial evaluation

Extensive testing may be needed in the initial evaluation of IA, but here we focus on tests useful in RA. RF and ACPA are the autoantibody tests in the 2010 criteria. In most clinical settings in the United States, ACPA is assessed by the commercial assay anti-cyclic citrullinated peptide (anti-CCP) antibody. Both RF and CCP are about 80% sensitive for RA, although specificity of RF is 80% for RA and more than 95% for anti-CCP. Several healthy patients have positive RF, and RF can be elevated in diseases like hepatitis C, Sjogren syndrome, and systemic lupus erythematosus. ACPAs as a class have had a large impact on the diagnosis of RA because of their high specificity for RA. Although there is an argument that anti-CCP testing should replace RF testing in RA, at this time testing for both RF and anti-CCP offers increased sensitivity for RA and maintains high specificity. Other lab tests in RA include inflammation tests, such as the CRP level and the ESR. These should be assessed if RA is suspected because, according to the 2010 criteria, they can assist in diagnosis. They also provide some prognostic information because higher levels portend worse outcomes. Periodic assessment is appropriate to gauge response to therapy. Additional biomarker assays being used in RA management include the Multiple Biomarker Disease Activity assay. These types of assays have shown some efficacy in monitoring disease activity, but their role in the initial diagnosis of RA is not yet clear. At the time of diagnostic evaluation, routine testing for a complete blood cell count, liver injury, and renal function is important to understand a patient’s general health and to help guide initial therapy (eg, methotrexate or MTX may be contraindicated in renal failure). Identifying other comorbidities that could affect therapy, such as infection with hepatitis B and C, HIV, and tuberculosis, at baseline is also important. In symmetric arthritis, joint aspiration typically is not needed to make a diagnosis. However, it can be a critical diagnostic procedure in cases where only a single joint is inflamed, crystalline disease is suspected, there are additional symptoms (eg, rapid onset of arthritis or fever suggesting infection), or there is other diagnostic uncertainty. If joint fluid is obtained, assessment of total white blood cell count and differential, crystals, and a gram stain or culture should be sufficient to make most diagnoses.

Next: Imaging

Imaging techniques for identifying synovitis

Synovitis or joint damage characteristic of RA may be identified with a variety of imaging techniques, including plain radiography, ultrasound, and MRI. For a primary care physician, plain radiography of symptomatic joints is an acceptable starting point in the initial diagnostic workup. When a patient is suspected of having RA, plain radiography (including 2 views of the hands, wrists, and feet) can help identify the bone damage and erosions that are typical for RA and that, if present, indicate more severe disease—further emphasizing the need for timely initiation of appropriate therapy. Of note, having a patient who is referred to rheumatology bring the actual images to the
consultation allows the rheumatologist to review them personally.

• Click here to go to the next installment in this Special Report, Changing the RA Referral Paradigm.

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