

Diagnosing Rheumatoid Arthritis

In order to properly make a diagnosis of rheumatoid arthritis (RA) you really need to someone who is very familiar with the disease. Why? Well, it's because the diagnosis of RA is really a clinical diagnosis. By this we mean that the doctor has to take a good history and perform a thorough physical examination. Following this the doctor will be able to determine if you have arthritis and if the arthritis is caused by your immune system (inflammatory arthritis).

Believe it or not RA cannot be reliably diagnosed by a blood test or by using diagnostic criteria. Why? Well, let's take a look ...

The Rheumatoid Factor (RF)

As I said above, RA is diagnosed primarily through a clinical assessment. A negative rheumatoid factor does not mean you don't have RA. I'll repeat, a negative rheumatoid factor does not mean you don't have RA. There are many people with a clinical diagnosis of rheumatoid arthritis who don't have a positive rheumatoid factor.

A positive rheumatoid factor doesn't mean that you have RA? What?? A positive rheumatoid factor doesn't mean that you have RA. Why?

- A rheumatoid factor can be caused by other diseases such as chronic infections with hepatitis B or C. A rheumatoid factor can also be seen with other rheumatic diseases.
- A very high titre (level) of rheumatoid factor (in the 100's or 1000's) makes it more likely that you have RA.
- A rheumatoid factor can be present years before the onset of rheumatoid arthritis. You haven't developed it yet.
- A very low titre (level) of rheumatoid factor doesn't mean that you have RA.

Antibodies to Anti-Cyclic Citrullinated Peptides (ACPA)

These antibodies (anti-CCP) have been around since the mid 2000's. They are useful in that they aren't usually found in diseases other than RA. So if you have a positive anti-CCP then chances are you're dealing with RA. The presence of these antibodies may predict the development of RA and can be detected in healthy individuals years before the onset of clinical RA. They are also a marker for more severe disease. The problem is that these antibodies aren't found in everyone with RA.

I know it sounds really confusing and it can be. That is why we have specialists called rheumatologists to help sort this type of thing out.

Diagnostic Criteria

We have many students and residents coming through the clinic and all are eager to use diagnostic criteria. The problem with the diagnostic criteria is they are really used for studies so we know all of the participants in a study met certain criteria. However, they aren't really that useful to make a diagnosis clinically. The criteria are not intended for the diagnosis for routine clinical care; they were primarily intended to categorize research (classification criteria).

Let's look at the earliest criteria

Rheumatoid Arthritis: 1987 Revised Classification Criteria

Adapted from: Arnett FC, Edworthy SM, Bloch DA, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum. 1988;31:315-324.

Requirements: A patient shall be said to have rheumatoid arthritis if he/she has satisfied **at least four of these seven criteria**. Criteria (1)-(4) must have been present for at least 6 weeks. Patients with two clinical diagnoses are not excluded. Designation as classic, definite, or probable rheumatoid arthritis is not to be made.

1. **Morning Stiffness:** Morning stiffness in and around the joints, lasting at least 1 hour before maximal improvement;
2. **Arthritis of 3 or more joint areas:** At least three joint areas simultaneously have had soft tissue swelling or fluid (not bony overgrowth alone) observed by a physician. The 14 possible areas are right or left proximal interphalangeal (PIP), MCP, wrist, elbow, knee, ankle, and MTP joints.
3. **Arthritis of the hand joints:** At least one area swollen (as defined above) in a wrist, MCP, or PIP joint.
4. **Symmetric arthritis:** Simultaneous involvement of the same joint areas [as defined in (2)] on both sides of the body (bilateral involvement of PIPs, MCPs, or MTPs is acceptable without absolute symmetry).
5. **Rheumatoid nodules:** Subcutaneous nodules, over bony prominences, or extensor surfaces, or in juxta-articular regions, observed by a physician.
6. **Serum rheumatoid factor:** Demonstration of abnormal amounts of serum rheumatoid factor by any method for which the result has been positive in <5% of normal subjects.
7. **Radiographic changes:** Radiographic changes typical of rheumatoid arthritis on posteroanterior hand and wrist radiographs, which must include erosions or unequivocal bony decalcification localized in or most marked adjacent to the involved joints (osteoarthritis changes alone do not qualify).

Ok, so let's think about someone with early rheumatoid arthritis (just started 2 months ago) and see how the criteria fall apart:

1. **Morning Stiffness:** Arguably many patients are stiff and sore in the morning so many patients would meet this criteria. However, not all.
2. **Arthritis of 3 or more joint areas:** RA has to start somewhere and most often it creeps up on you. So in the early phases many people have arthritis in only a few areas and don't meet this criteria.
3. **Arthritis of the hand joints:** Many patients start with RA in their feet or other joints. They would not satisfy this criteria.
4. **Symmetric arthritis:** Often times the arthritis doesn't start out symmetrically. Strike this one down.
5. **Rheumatoid nodules:** Only happen in people who have a positive rheumatoid factor and usually years down the road (unless really severe).
6. **Serum rheumatoid factor:** Not everyone has this. Perhaps only 30-50% with early RA will have this.
7. **Radiographic changes:** Often times in early disease this criteria will not be met.

So you can now see that in early rheumatoid arthritis the 1987 criteria fall apart. These criteria are good for those who have had RA for a few years – so called established RA. Fair enough.

In the late 1990's and through the last decade we realized that treating RA earlier led to much better outcomes. However, researchers found that most patients with early RA didn't meet the 1987 criteria. Therefore new criteria needed to be developed to study the disease and ensure all patients entering research studies met some form of preliminary criteria. Hence the 2010 criteria are born!

I encourage you to read at least the introduction of the [2010 Criteria Paper](#) as you'll understand why these were developed

As you go through the criteria, imagine you have 3 swollen joints in your hand for more than 6 weeks and a low positive RF. You would score 5 points. However, most rheumatologists would think that you likely have early RA and would initiate therapy. But don't you need to score 6 or more to diagnose RA?? Nope, not clinically!

The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for rheumatoid arthritis

Adapted from: ARTHRITIS & RHEUMATISM, Vol. 62, No. 9, September 2010, pp 2569–2581

Target population (Who should be tested?): Patients who

1. have at least 1 joint with definite clinical synovitis (swelling)*
2. with the synovitis not better explained by another disease†

Classification criteria for RA (score-based algorithm: add score of categories A–D; a score of $\geq 6/10$ is needed for classification of a patient as having definite RA) ‡

A. Joint involvement§	Score
1 large joint¶	0
2-10 large joints	1
1-3 small joints (with or without involvement of large joints)	2
4-10 small joints (with or without involvement of large joints)	3
> 10 joints (at least 1 small joint)	5
 B. Serology (at least 1 test result is needed for classification)††	
Negative RF and negative ACPA	0
Low-positive RF or low-positive ACPA	2
High-positive RF or high-positive ACPA	3
 C. Acute-phase reactants (at least 1 test result is needed for classification)‡‡	
Normal CRP and normal ESR	0
Abnormal CRP or abnormal ESR	1
 D. Duration of symptoms§§	
< 6 weeks	0
≥ 6 weeks	1

* The criteria are aimed at classification of newly presenting patients. In addition, patients with erosive disease typical of rheumatoid arthritis (RA) with a history compatible with prior fulfillment of the 2010 criteria should be classified as having RA. Patients with longstanding disease, including those whose disease is inactive (with or without treatment) who, based on retrospectively available data, have previously fulfilled the 2010 criteria should be classified as having RA.

† Differential diagnoses vary among patients with different presentations, but may include conditions such as systemic lupus erythematosus, psoriatic arthritis, and gout. If it is unclear about the relevant differential diagnoses to consider, an expert rheumatologist should be consulted.

‡ Although patients with a score of $< 6/10$ are not classifiable as having RA, their status can be reassessed and the criteria might be fulfilled cumulatively over time.

§ Joint involvement refers to any swollen or tender joint on examination, which may be confirmed by imaging evidence

of synovitis. Distal interphalangeal joints, first carpometacarpal joints, and first metatarsophalangeal joints are excluded from assessment. Categories of joint distribution are classified according to the location and number of involved joints, with placement into the highest category possible based on the pattern of joint involvement.

¶ “Large joints” refers to shoulders, elbows, hips, knees, and ankles.

“Small joints” refers to the metacarpophalangeal joints, proximal interphalangeal joints, second through fifth metatarsophalangeal joints, thumb interphalangeal joints, and wrists.

** In this category, at least 1 of the involved joints must be a small joint; the other joints can include any combination of large and additional small joints, as well as other joints not specifically listed elsewhere (e.g., temporomandibular, acromioclavicular, sternoclavicular, etc.).

†† Negative refers to IU values that are less than or equal to the upper limit of normal (ULN) for the

laboratory and assay; low-positive refers to IU values that are higher than the ULN but ≤ 3 times the ULN for the laboratory and assay; high-positive refers to IU values that are >3 times the ULN for the laboratory and assay. Where rheumatoid factor (RF) information is only available as positive or negative,

a positive result should be scored as low-positive for RF. ACPA = anti-citrullinated protein antibody.

‡‡ Normal/abnormal is determined by local laboratory standards. CRP = C-reactive protein; ESR = erythrocyte sedimentation rate.

§§ Duration of symptoms refers to patient self-report of the duration of signs or symptoms of synovitis (e.g., pain, swelling, tenderness) of joints that are clinically involved at the time of assessment, regardless of treatment status.

Concluding thoughts

So you can see that the diagnosis of RA can be challenging. You really need to see an expert in arthritis care (a rheumatologist) to make the diagnosis and get you started on treatment.