Diagnosis and differential diagnosis of rheumatoid arthritis

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INTRODUCTION — Rheumatoid arthritis (RA) is a symmetric, peripheral polyarthritis of unknown etiology that, untreated or if unresponsive to therapy, typically leads to deformity and destruction of joints through the erosion of cartilage and bone. This topic will review the diagnosis, diagnostic criteria, and differential diagnosis of this disorder. The clinical features of RA are discussed separately. (See “Clinical features of rheumatoid arthritis“.)

DIAGNOSIS — There is no single clinical, radiologic, or serologic test that enables a diagnosis of RA to be made with certainty. As with other autoimmune rheumatic diseases, the diagnosis depends upon the aggregation of characteristic symptoms, signs, laboratory data, and radiologic findings. The diagnostic value of the following are discussed in more detail below:

- Symmetrical peripheral polyarthritis
- Morning stiffness
- Rheumatoid nodules
- Laboratory features
- Radiographic bone erosions

Symmetric peripheral polyarthritis — Arthritis that affects the metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints of both hands is the single most characteristic clinical feature of RA (picture 1A-C). However, peripheral polyarthritis is also a common feature of other rheumatic diseases such as systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD), systemic sclerosis (scleroderma), psoriatic arthritis, and rheumatic fever. As a result, this finding alone cannot be used to make a diagnosis of RA. On the other hand, symmetric polyarthritis, particularly of the MCP, metatarsophalangeal (MTP), and/or PIP joints, strongly suggests RA. (See “Evaluation of the adult with polyarticular pain“.)

Some patients present with involvement of a single large joint, such as the shoulder or knee. In this setting, the diagnosis depends upon examination of the synovial fluid, additional laboratory tests, and imaging studies. In some cases, further follow-up is required before an accurate diagnosis can be rendered. This is often dependent upon the development of arthritis in the small joints of the hands, the wrist, elbows, or ankle. (See "Evaluation of the adult with monoarticular pain".)
Morning stiffness — Morning stiffness or stiffness after any prolonged period of inactivity occurs in virtually all inflammatory arthropathies and myopathies. However, morning stiffness that lasts more than one hour reflects a severity of joint inflammation that rarely occurs in diseases other than RA.

Rheumatoid nodules — Rheumatoid nodules are typically subcutaneous nodules that vary in size from that of a millet seed to a marble (and occasionally larger). They are free in the subcutaneous tissue, not attached to underlying bone or overlying skin. These nodules are most commonly found over the extensor aspect of the proximal ulna, but may also occur at other pressure locations such as the back of the head, sacrum, Achilles tendon, and tendons of the hand.

Rheumatoid nodules have a high degree of diagnostic specificity for RA. However, their usefulness in practice is limited by the fact that they only occur in about 30 percent of patients; furthermore, they tend to occur later in the course of the disease, by which time the diagnosis is obvious. Thus, the absence of nodules at presentation should not be taken as evidence against the diagnosis of RA.

It is also important to note that not all nodular lesions on the extensor surfaces of the elbow are rheumatoid nodules. Gout, hyperlipidemia, granuloma annulare, Wegener's granulomatosis, the Churg-Strauss syndrome, and other disorders can also cause such lesions. (See "Rheumatoid nodules", section on 'Differential diagnosis'.)

Laboratory features — Rheumatoid factor (RF), antibodies to citrullinated peptides, changes in the serum levels of acute phase reactants, and other laboratory abnormalities are associated with RA. RFs and antibodies to citrullinated proteins and peptides are both useful in diagnosis. Whether both tests should be routinely performed has still not been proven by large population surveys [1], but given the lack of complete overlap between the tests, it is clear that a positive reaction in either increases diagnostic sensitivity and a positive result in both increases specificity. Therefore, in the evaluation of individual patients with a polyarthritis in whom the diagnosis is uncertain, both tests should be performed. Acute phase reactants such as the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are sometimes helpful in the diagnosis of RA, but are of greater use in monitoring disease activity. (See "Acute phase reactants".)

Rheumatoid factors — RFs occur in 70 to 80 percent of patients with RA. Their diagnostic utility is limited because these autoantibodies are also found in virtually all patients with mixed cryoglobulinemia (usually caused by hepatitis C virus infections), approximately 70 percent of patients with Sjögren's syndrome, 20 to 30 percent of those with SLE, and 5 to 10 percent of healthy individuals. The prevalence of RF positivity rises with age. (See "Origin and utility of measurement of rheumatoid factors".)

Anti-citrullinated peptide antibodies — Antibodies to citrullinated peptides/proteins (ACPA) are usually measured by ELISA using cyclic citrullinated peptides (CCP) as antigen. Anti-CCP has a similar diagnostic sensitivity to rheumatoid factor for RA, but higher specificity [1-4]. Another test, anti-mutated citrullinated vimentin, gives similar results to anti-CCP and is used as an alternative in some laboratories [5]. (See "Clinically useful biologic markers in the diagnosis and assessment of outcome in rheumatoid arthritis", section on 'Anti-citrullinated peptide antibodies'.)

Acute phase reactants — Acute phase reactants, particularly the ESR and CRP, are not
specific for RA. Nevertheless, they are often useful for distinguishing inflammatory conditions, of which RA is one, from noninflammatory disorders that present with musculoskeletal symptoms (eg, osteoarthritis or fibromyalgia). The ESR and CRP response varies between different diseases. For example, whereas both are commonly raised in RA, the CRP is often normal in patients with active SLE. Furthermore, the profile of the acute phase response can vary in individual patients with RA. Monitoring either or both of these acute phase reactants can also be used to assess the activity of the disease.

Other laboratory abnormalities — Other laboratory abnormalities occur among patients with RA, but are also relatively nonspecific. These include:

- Anemia of chronic disease. (See "Hematologic manifestations of rheumatoid arthritis".)
- Thrombocytosis. Platelets are acute phase reactants, and their levels typically rise in a variety of inflammatory conditions. (See "Approach to the patient with thrombocytosis".)
- Leukocytosis — Leukocytosis can be a manifestation of active RA, but infection or treatment with glucocorticoids can also be responsible for this finding.
- Antinuclear antibody — A positive antinuclear antibody test is present in 30 to 40 percent of patients with RA, most commonly those with more severe, chronic disease. (See "Measurement and clinical significance of antinuclear antibodies", section on 'Systemic autoimmune disease'.)
- Inflammatory synovial fluid — Synovial fluid examination typically reveals a leukocytosis with a predominance of polymorphonuclear cells, low glucose, low C3 and C4 complement levels, and protein levels approaching those in serum. Among these different measurements, the total cell count is the most important.
- Hypoalbuminemia — Increased catabolism of albumin contributes to hypoalbuminemia in RA. However, serum albumin concentrations do not correlate well with other measures of disease activity in this condition [6].

Imaging — Erosions of cartilage and bone are among the cardinal features of RA. However, they can also occur in some other forms of inflammatory arthropathy and are therefore not diagnostic of RA in and of themselves (see 'Differential diagnosis' below).

As with other features of RA, the presence of erosions becomes more useful diagnostically with increasing duration of disease. However, with extreme destruction, the severity of erosions may reach a level beyond which further progression cannot be assessed radiographically, despite the presence of ongoing joint damage [7].

In clinical practice, plain film radiography is used most often to assess for the presence of joint damage due to RA. Other imaging techniques such as contrast-enhanced magnetic resonance imaging (MRI) and color Doppler ultrasonography are valuable in research settings. However, the use of MRI or ultrasonography to quantify the amount of synovial tissue or to detect erosions that are not appreciated on plain radiography is not yet a widely accepted surrogate marker of disease activity. MRI and ultrasonography do not yet have an established role in the evaluation of patients with polyarthritis.

Plain film radiography — To be detected by plain radiography, erosions must have eroded through the cortex of the bone around the margins of the joint. MCP and PIP joints
can be identified by plain radiography in 15 to 30 percent of patients in the first year of the disease. By the end of the second year of disease in patients who do not respond to therapy, the cumulative incidence of erosions is 90 percent [8,9].

In some patients, erosions occur first in the ulnar styloid or MTP joints. It is therefore worth evaluating both the hands (including the wrists) and the feet in all patients in whom a diagnosis of RA is suspected.

**MR imaging** — Magnetic resonance imaging (MRI) is a more sensitive technique than plain radiography for identifying bone erosions. When radiography and MRI were compared in a group of 55 patients with early arthritis, MRI identified seven times as many erosions in the metacarpophalangeal and proximal interphalangeal joints than plain radiographs [10]. MRI also may detect bone erosions earlier in the course of the disease than is possible with plain films [11]. As an example, approximately 45 percent of patients with symptoms for only four months were found to have erosions detected by this method [12]. Decreased signal from the bone marrow on T1-weighted images and enhancement of the marrow with gadolinium administration is interpreted as bone marrow edema. The presence of marrow edema on MRI is predictive of later development of erosive disease [13]. A similarly increased sensitivity of MRI has also been noted for early RA of the forefoot [14].

Because of an apparent association between administration of gadolinium-containing MRI contrast agents and the development of systemic nephrogenic fibrosis in patients with severely impaired renal function (eg, estimated glomerular filtration rate <15 to 30 mL/min) use of these agents should be avoided in such patients. (See "Nephrogenic systemic fibrosis/nephrogenic fibrosing dermopathy in advanced renal failure", section on 'If gadolinium must be given'.)

It is also possible to identify and estimate the quantity of hypertrophic synovial tissue using MRI. The presence of MRI-detected synovial proliferation correlates with the later development of bone erosions [15]. Use of this imaging technique outside of research settings may be hastened by the development of MRI scanners that are designed specifically for imaging the extremities [16,17].

**Ultrasonography** — Ultrasonography is another alternative for estimating the degree of inflammation and the volume of inflamed tissue. Direct comparison of color Doppler ultrasonography and contrast enhanced MRI in one study of 29 patients demonstrated agreement regarding the presence or absence of inflammation between the two techniques in 75 percent of the joints of the hands and wrists that were examined [18]. Both imaging modalities found features of inflammation in joints that were neither tender nor swollen on physical examination. Ultrasonography can also be used to assess the MTP joints [19].

**Classification criteria** — Criteria have been developed for the classification of patients with RA for the purpose of epidemiologic studies and clinical trials, not primarily for clinical diagnosis. Nevertheless the same features that are of value in classification tend to be useful for the purpose of diagnosis in clinical practice.

The classification criteria are those developed and validated by the American College of Rheumatology (table 1) [20]. A patient can be classified as having RA if at least four of these criteria are satisfied; four of the criteria must be present for at least six weeks: morning stiffness, arthritis of three or more joint areas, arthritis of the hands, and
symmetric arthritis.

These criteria are primarily used for those with established disease. They may not be satisfied early in the course of disease in some patients who subsequently develop typical RA [21]. On the other hand, patients who initially fulfill the diagnostic criteria occasionally evolve into other diagnoses, particularly systemic lupus erythematosus (SLE), Sjögren's syndrome, scleroderma, mixed connective tissue disease, psoriatic arthritis, and crystalline arthritis.

**DIFFERENTIAL DIAGNOSIS** — A variety of other conditions must be considered in the differential diagnosis of RA. Features of some disorders that are included in the differential diagnosis of RA are shown in the table (table 2A-B). (See "Evaluation of the adult with polyarticular pain").

**Acute viral polyarthritis** — Viral infections such as rubella [22], parvovirus [23], and hepatitis B can cause an acute polyarthritis syndrome that lasts from a few days to several weeks, although rarely beyond six weeks. Hepatitis C can cause a polyarthritis or oligoarthritis in a minority of patients, but is more commonly associated with arthralgias. (See "Specific viruses that cause arthritis").

A large joint arthritis has also been reported in association with human T lymphotropic virus type 1 (HTLV-I) [24]. These infections are sometimes associated with the presence of RFs (usually in low titer), antinuclear antibodies, and elevated acute phase reactants. HTLV-I infections can generally be distinguished from RA by the presence of a rash (atypical of early RA), the finding of IgM antiviral antibodies, and the typically self-limited nature of arthritis associated with HTLV-I.

**Connective tissue diseases and sarcoidosis** — For the reasons noted above, early RA may be difficult to distinguish from the arthritis of SLE, Sjögren's syndrome, overlap syndromes, and sarcoidosis. In long-standing disease, however, morning stiffness, symmetric arthritis, subcutaneous nodules, and the deformities characteristic of RA do not develop in these other disorders. There are two potential exceptions to this statement:

- An erosive arthritis has been described in some overlap syndromes, particularly those associated with anti-tRNA synthetases and anti-U1 RNP antibodies [25]. (See "Clinical manifestations of mixed connective tissue disease").

- Jaccoud's arthropathy occurs in 5 to 10 percent of patients with Sjögren's syndrome or SLE, and can also occur in sarcoidosis [26]. (See "Musculoskeletal manifestations of systemic lupus erythematosus" and "Sarcoid arthropathy").

The joint deformities of Jaccoud's arthropathy are not caused by destruction of joints, but by loosening and lengthening of periarticular structures and tendons. The ulnar drift or swan neck deformities caused by this disorder resemble RA superficially, but can be distinguished by the fact that they are "correctable" on physical examination: fingers with these deformities can be moved manually back into normal alignment. In addition, radiographs in Jaccoud's arthropathy rarely reveal the cartilage loss, erosions, or cysts that are typical of longstanding RA.

**Hypermobility syndrome and fibromyalgia** — Pain rather than stiffness or swelling is the dominant symptom of the two common disorders: hypermobility syndrome and
fibromyalgia [27,28]. Although the hypermobility syndrome and fibromyalgia can both bear superficial resemblances to RA, there are important distinguishing features:

- The hypermobility syndrome is associated with hyperextendable joints. (See "Clinical manifestations and treatment of the hypermobility syndrome".)

- Fibromyalgia is associated with tender points at nonarticular sites such as the medial portions of the elbows, across the trapezius muscle, and down the spine. (See "Clinical manifestations and diagnosis of fibromyalgia in adults".)

- Neither the hypermobility syndrome nor fibromyalgia is associated with true arthritis, significant titers of RF or anti-CCP antibodies, or elevated levels of acute phase reactants.

Although RA is normally not difficult to distinguish from fibromyalgia, it is important to note that many patients with RA develop secondary fibromyalgia. Complaints in such patients may relate more to their fibromyalgia than to their RA.

**Reactive arthritis** — RA may present as monoarthritis in large joints such as the knees. In that setting, reactive arthritis is high on the differential [29]. The physical signs of both reactive arthritis and RA can be identical in the knees. However, the following findings on history, physical examination, or other assessments are more consistent with reactive arthritis:

- History of recent urethritis or enteric infection

- Asymmetric pattern of joint involvement

- Symptoms or signs of enthesopathy (inflammation at the site where a tendon inserts into a bone, eg, the insertion point of the Achilles tendon into the heel)

- Keratoderma blennorrhagica or circinate balanitis (see "Reactive arthritis (formerly Reiter syndrome")

- Radiologic evidence of sacroiliitis and/or spondylitis

- The presence of HLA-B27

Involvement of the hands in reactive arthritis does not pose as great a diagnostic dilemma as the knees. Hand arthritis is more commonly asymmetric than in RA. Furthermore, reactive arthritis will involve not only the joint, but also the fascial layers of the digit, giving rise to a characteristic "sausage" swelling of the fingers (or toes if the feet are involved) (picture 2).

The arthritis associated with inflammatory bowel disease may also be part of the differential diagnosis. This disorder may be missed if abdominal symptoms are not prominent, or not specifically asked for in the history. (See "Arthritis associated with gastrointestinal disease".)

**Psoriatic arthritis** — Psoriatic arthritis may resemble rheumatoid arthritis closely. The two disorders are virtually indistinguishable in some patients in the absence of RF or antibodies to CCP (seronegative RA) [30]. The distinction between these two conditions is complicated further by the fact that the joint symptoms of psoriatic arthritis may precede the onset of skin disease by many years.

http://www.uptodate.com/online/content/topic.do?topicKey=rheumart/4741&view=print 8/16/2010
Thus, in some patients, the only clue to the diagnosis of psoriatic arthritis is a family history of psoriasis. However, in the majority, the findings of skin psoriasis, nail changes (onychodystrophy), sausage toes or fingers, spinal involvement, and/or arthritis mutilans helps distinguish the two entities. (See “Clinical manifestations and diagnosis of psoriatic arthritis”.)

**Crystalline arthritis** — Crystalline arthritis (gout and pseudogout) can become chronic and even assume a polyarticular distribution. The diagnosis is established by the finding of urate or calcium pyrophosphate crystals in synovial fluids. The presence of tophi on physical examination, the detection of serological markers of RA, and the characteristic appearance of gouty erosions are also useful in parsing these two conditions. (See “Clinical manifestations and diagnosis of gout” and “Clinical manifestations and diagnosis of calcium pyrophosphate crystal deposition disease”.)

**Infectious arthritis** — Infectious arthritis is usually monoarticular, but polyarthritis can occur. The diagnosis is established by culturing the pathogen from the synovial fluid or from the blood. Patients with septic arthritis may or may not appear toxic on examination, depending upon the stage of their infection, the presence of medications that can mask infection (eg, glucocorticoids), and other clinical variables. Peripheral blood leukocytosis with a left shift is common, but not invariably present.

A low threshold for suspecting infection is required, particularly in compromised hosts. Patients with RA are at increased risk for joint infections because a damaged joint can serve as a nidus of infection. Synovial fluid leukocyte counts and glucose levels are similar to those seen in RA. (See “Septic arthritis in adults”.)

**Osteoarthritis** — Osteoarthritis (OA) can be confused with RA in the middle aged or elderly patient when the small joints of the hands are involved. However, different patterns of clinical involvement usually permit the correct diagnosis (table 3).

- OA of the fingers typically affects the distal interphalangeal joints and is frequently associated with Heberden's nodes in this area.
- In contrast, RA typically affects the MCP and PIP joints and is not associated with Heberden's nodes.
- The carpometacarpal joint of the thumb is typically involved in OA.
- Swelling of the joints is hard and bony in OA. In contrast, soft, warm, boggy, and tender joints are typical of RA.
- Stiffness of the joint is a very common feature of RA, but is relatively rare in OA. Furthermore, the stiffness of RA is characteristicly worse after resting the joint (eg, morning stiffness), while the stiffness of OA (if present) is typically worse after any effort and is often described as evening stiffness.
- Radiographs also help distinguish RA from OA. OA is characterized by narrowing of the joint space due to cartilage loss and osteophytes due to bone remodeling, but not erosions or cysts.
- OA is classically associated with the absence of RFs and normal levels of acute phase
reactants. However, RFs may be present, usually in low titer, consistent with the patient's (older) age.

**Paraneoplastic disease** — Joint pain or frank polyarthritis can occur in association with cancer. The following are some examples:

- **Myelodysplasia** — Patients with myelodysplastic syndrome sometimes develop polyarthritis that mimics seronegative RA. In a cohort study of 87 patients with myelodysplastic syndrome, five had inflammatory arthritis that resembled RA [31]. (See "Treatment and prognosis of the myelodysplastic syndromes".)

- **Hypertrophic pulmonary osteoarthropathy** — Patients with hypertrophic pulmonary osteoarthropathy typically demonstrate clubbing of the digits, joint pain, and periosteal new bone formation. Joint effusions may occur. (See "Malignancy and rheumatic disorders", section on 'Hypertrophic osteoarthropathy'.)

**Multicentric reticulohistiocytosis** — Multicentric reticulohistiocytosis is a rare but highly destructive form of arthritis. The rapid joint destruction of multicentric reticulohistiocytosis resembles the arthritis mutilans occasionally observed in RA. Multiple smooth, shiny erythematous nodules located in the periungual region suggest multicentric reticulohistiocytosis. Binucleated or multinucleated foreign body type giant cells are present on skin or synovial biopsies in multicentric reticulohistiocytosis [32,33].

Multicentric reticulohistiocytosis is relatively resistant to glucocorticoids and to DMARDs such as methotrexate and hydroxychloroquine. However, there are case reports of response to tumor necrosis factor-alpha inhibition [34,35] and to parenteral administration of an aminobisphosphonate [36,37].

**Fibroblastic rheumatism** — Fibroblastic rheumatism is a rare disease of unknown etiology. Fibroblastic rheumatism shares the features of arthralgia, arthritis, and nodules with RA [38-40]. Flexion contractures of the fingers occur in most patients, while thickened palmar fascia is noted in about one half of reported cases. Biopsy of a nodule or thickened skin typically reveals increased thickness of collagen fibers and fibroblastic proliferation. Decreased elastic fibers, and the presence of myofibroblasts are noted in approximately 50 percent. Radiographic findings are variable, but periarticular osteopenia and erosions may be noted.

Due to the rarity of fibroblastic rheumatism there is no well established treatment. Progressive disease may lead to sclerodactyly and ankylosis of affected joints.

**INFORMATION FOR PATIENTS** — Educational materials on this topic are available for patients. (See "Patient information: Rheumatoid arthritis symptoms and diagnosis" and "Patient information: Rheumatoid arthritis treatment" and "Patient information: Complementary therapies for rheumatoid arthritis".) We encourage you to print or e-mail these topics, or to refer patients to our public web site, www.uptodate.com/patients, which includes these and other topics.

**SUMMARY AND RECOMMENDATIONS** — No single clinical manifestation, laboratory test, or imaging study result allows the diagnosis of rheumatoid arthritis (RA) to be made with certainty. The diagnosis of RA is based upon both a constellation of compatible features and the exclusion of other diseases. (See 'Differential diagnosis' above.)
We find the following components of the medical evaluation helpful in making a clinical diagnosis of RA:

- We perform a thorough medical history, with particular attention to joint pain, stiffness, and associated functional difficulties.

- A complete physical examination is indicated to assess for synovitis, limited joint motion, extraarticular disease manifestations, and signs of diseases included in differential diagnosis.

- We suggest selected laboratory testing, including assays for acute phase reactants (erythrocyte sedimentation rate and C-reactive protein), rheumatoid factor, anti-cyclic citrullinated peptide antibodies, and antinuclear antibodies. If suspected clinically, we obtain tests for the presence of active viral infections (hepatitis B virus, hepatitis C virus, and parvovirus B19). (See 'Laboratory features' above.)

- Selected imaging studies are indicated, including bilateral radiographs of the hands, wrists, and feet. Although plain radiographs are unlikely to reveal joint space narrowing or erosive disease in the first few weeks to months of disease, such studies establish a baseline and help exclude other causes of joint dysfunction. Magnetic resonance imaging studies and ultrasonography remain most appropriate for research settings. (See 'Imaging' above.)

- If a joint effusion is present, particularly in the setting a monoarthritis, oligoarthritis, or asymmetric joint inflammation, aspiration and examination of the fluid is needed for the diagnosis or exclusion of gout, pseudogout, or an infectious cause of arthritis. The critical tests to analyze on the synovial fluid are the cell count and differential, crystals, and culture.

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REFERENCES


Synovial thickening of the metacarpophalangeal joint

Bilateral swelling of the MCP joints is evident in this patient with rheumatoid arthritis. Note also the mild swan neck deformities present in several fingers, particularly the left middle and fifth fingers. Courtesy of Patrick J Venables, MD.
Swelling of the metacarpophalangeal joints of the right hand

Swelling of the MCP joints, moderate MCP flexion, and swan neck deformities are evident in this patient with rheumatoid arthritis. *Courtesy of Patrick J Venables, MD.*
Joint deformity in MCTD

Deforming arthritis in mixed connective tissue disease characterized by ulnar deviation and swan neck deformities. These abnormalities are also seen in rheumatoid arthritis. *Courtesy of Robert M Bennett, MD.*
# American Rheumatism Association Revised Criteria for Rheumatoid Arthritis Classification

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>Morning stiffness</td>
<td>Morning stiffness in and around the joints, lasting at least one hour before maximal improvement.</td>
</tr>
<tr>
<td>Arthritis of 3 or more joint areas</td>
<td>At least 3 joint areas (out of 14 possible areas; right or left PIP, MCP, wrist, elbow, knee, ankle, MTP joints) simultaneously have had soft-tissue swelling or fluid (not bony overgrowth alone) as observed by a physician.</td>
</tr>
<tr>
<td>Arthritis of hand joints</td>
<td>At least one area swollen (as defined above) in a wrist, MCP, or PIP joint.</td>
</tr>
<tr>
<td>Symmetric arthritis</td>
<td>Simultaneous involvement of the same joint areas (as defined above) on both sides of the body (bilateral involvement of PIPs, MCPs, or MTPs, without absolute symmetry is acceptable).</td>
</tr>
<tr>
<td>Rheumatoid nodules</td>
<td>Subcutaneous nodules over bony prominences or extensor surfaces, or in juxta-articular regions as observed by a physician.</td>
</tr>
<tr>
<td>Serum rheumatoid factor</td>
<td>Demonstration of abnormal amounts of serum rheumatoid factor by any method for which the result has been positive in less than 5% of normal control subjects.</td>
</tr>
<tr>
<td>Radiographic changes</td>
<td>Radiographic changes typical of rheumatoid arthritis on posteroanterior hand or wrist radiographs, which must include erosions or unequivocal bony decalcification localised in, or most marked adjacent to, the involved joints (osteoarthritis changes alone do not qualify).</td>
</tr>
</tbody>
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Note: For classification purposes, a patient has RA if at least four of these criteria are satisfied (the first four must have been present for at least six weeks).
## Confirming a diagnosis of rheumatoid arthritis (RA)*

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Sex</th>
<th>Age</th>
<th>Lab tests</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Undifferentiated seronegative polyarthritis</td>
<td>F &gt; M</td>
<td>35-65</td>
<td>10-15 percent RF+</td>
<td>Chronic seronegative inflammatory polyarthritis, atypical of RA or fails to meet classification criteria for RA. Up to 20 percent of cases may evolve into RA, nearly 50 percent will go into remission.</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>M = F</td>
<td>30-55</td>
<td>&lt;20 percent RF+</td>
<td>10 percent of those with psoriatic arthritis will have an RA-like distribution (MCPs, PIPs, wrists). Cutaneous psoriasis will be evident in the vast majority of cases.</td>
</tr>
<tr>
<td>Tophaceous gout</td>
<td>M &gt; F, M &lt; 45</td>
<td>25-70</td>
<td>95 percent RF-</td>
<td>Intermittent inflammatory arthritis during the onset, with evolution of tophi and chronic inflammatory polyarthritis. Elevated serum urate and tophi help distinguish from RA.</td>
</tr>
<tr>
<td>Erosive inflammatory OA</td>
<td>F &gt; M</td>
<td>&gt;60</td>
<td>RF- (or normal for age)</td>
<td>Chronic polyarthritis with intermittent or sustained inflammation affecting PIP and DIP joints. Radiographs demonstrate distinctive erosions and evidence of OA.</td>
</tr>
<tr>
<td>Pseudogout</td>
<td>F = M</td>
<td>&gt;60</td>
<td>5-10 percent RF+</td>
<td>5 percent of patients will have &quot;rheumatoid-like&quot; inflammatory arthritis with stiffness, fatigue, synovitis, and elevated ESR, often lasting 4 weeks to several months.</td>
</tr>
<tr>
<td>Reactive arthritis (formerly known as Reiter's syndrome)</td>
<td>M &gt; F</td>
<td>16-50</td>
<td>95 percent RF--; 50-80 percent HLA-B27+</td>
<td>See criteria for spondyloarthropathies; often associated with low back pain, ocular, genitourinary, or GI symptomatology and enthesitis (heel pain).</td>
</tr>
<tr>
<td>Enteropathic arthritis</td>
<td>M = F</td>
<td>All ages</td>
<td>95 percent RF-</td>
<td>20 percent of patients with Crohn's disease or ulcerative colitis will develop peripheral arthritis. Diagnosis may be difficult until GI involvement becomes apparent. Associated with oral ulcerations, GI symptoms or other features of spondyloarthropathy</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>F &gt; M</td>
<td>15-40</td>
<td>10-15 percent RF+; usually ANA+</td>
<td>Chronic nondeforming inflammatory polyarthritis associated with ANA positivity and other features of SLE.</td>
</tr>
</tbody>
</table>
1. RA often begins insidiously with vague constitutional and musculoskeletal symptoms that may last for weeks or months before synovitis becomes apparent.
2. During the first 6 months of RA, <50 percent of patients will be RF-positive, and the sensitivity of the 1987 ACR criteria is reduced.
3. A variety of less common chronic inflammatory seronegative articular conditions may clinically resemble early RA. It may be necessary to observe and evaluate the patient repeatedly for evolution of the disorder and manifestation of features that will distinguish them from RA. The above disorders can mimic RA. Data from Lipsky, P. Algorithms for the diagnosis and management of musculoskeletal complaints: A new tool for the primary-care provider, (See www.swmed.edu/home_pages/cme/endurmat/lipsky/index.html).
## Confirming a diagnosis of rheumatoid arthritis*

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<tr>
<td>Polymyositis/dermatomyositis</td>
<td>F &gt; M</td>
<td>30-60</td>
<td>95 percent RF; 50 percent ANA; 70 percent CK</td>
<td>Chronic inflammatory arthritis uncommonly occurs early in course of PM/DM. Features of proximal muscle weakness, bulbar dysphagia, muscle enzyme elevation or skin involvement (ie, Gottron's papules) should be sought.</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>F &gt; M</td>
<td>30-50</td>
<td>95 percent RF; &gt;90 percent ANA+</td>
<td>Chronic inflammatory polyarthritis may predominate over skin changes early in the disease. Associated with Raynaud's phenomenon, sclerodactyly, dysphagia, hypertension, or renal abnormalities.</td>
</tr>
<tr>
<td>Sarcoid arthritis</td>
<td>F &gt; M</td>
<td>20-40</td>
<td>25 percent RF+</td>
<td>15 percent of patients with sarcoidosis will develop arthritis. Early in the disease a chronic inflammatory oligo or polyarthritis lasting weeks to months may develop and typically involve the ankles and knees. Other features of sarcoidosis (ie, erythema nodosum, hilar adenopathy) are usually apparent.</td>
</tr>
<tr>
<td>Parvovirus B19-associated arthritis</td>
<td>F &gt; M</td>
<td>Any age</td>
<td>&lt;10 percent RF+; &gt;80 percent anti-B19 IgM antibodies (acutely)</td>
<td>Adults manifest a flu-like picture, seldom develop the &quot;slapped-cheek&quot; rash and arthralgias are more common than arthritis. Arthritis is an acute inflammatory polyarthritis with an RA-like distribution lasting 2 weeks. Less than 10 percent develop a chronic inflammatory arthritis.</td>
</tr>
<tr>
<td>Polymyalgia rheumatica</td>
<td>F &gt; M</td>
<td>&gt;50</td>
<td>90 percent RF; &gt;95 percent ESR</td>
<td>Proximal girdle pain and stiffness without synovitis.</td>
</tr>
</tbody>
</table>

* 1. RA often begins insidiously with vague constitutional and musculoskeletal symptoms that may last for weeks or months before synovitis becomes apparent.
2. During the first 6 months of RA, <50 percent of patients will be RF-positive, and the sensitivity of the 1987 ACR criteria is reduced.
3. A variety of less common chronic inflammatory seronegative arthritic conditions may clinically resemble early RA. It may be necessary to observe and evaluate the patient repeatedly for evolution of the disorder and manifestation of features that will distinguish them from RA. The above disorders can mimic RA. Data from Lipsky, P. Algorithms for the diagnosis and management of musculoskeletal complaints: A new tool for the primary-care provider, (See www.swmed.edu/home_pages/cme/endurmat/lipsky/index.html).
Sausage toe in reactive arthritis

Sausage toe (with diffuse swelling) of the second digit and mild keratoderma blennorrhagica on the dorsum of the foot in a man with reactive arthritis (formerly Reiter's syndrome). Courtesy of Craig Wiesenhutter, MD and David Yu, MD.
### Distinction between rheumatoid arthritis and osteoarthritis

<table>
<thead>
<tr>
<th>Feature</th>
<th>Rheumatoid arthritis</th>
<th>Osteoarthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary joints affected</td>
<td>Metacarpophalangeal</td>
<td>Distal interphalangeal</td>
</tr>
<tr>
<td></td>
<td>Proximal interphalangeal</td>
<td>Carpometacarpal</td>
</tr>
<tr>
<td>Heberden's nodes</td>
<td>Absent</td>
<td>Frequently present</td>
</tr>
<tr>
<td>Joint characteristics</td>
<td>Soft, warm, and tender</td>
<td>Hard and bony</td>
</tr>
<tr>
<td>Stiffness</td>
<td>Worse after resting (eg, morning stiffness)</td>
<td>If present, worse after effort, may be described as evening stiffness</td>
</tr>
<tr>
<td>Laboratory findings</td>
<td>Positive rheumatoid factor</td>
<td>Rheumatoid factor negative</td>
</tr>
<tr>
<td></td>
<td>Positive anti-CCP antibody</td>
<td>Anti-CCP antibody negative</td>
</tr>
<tr>
<td></td>
<td>Elevated ESR and C reactive protein</td>
<td>Normal ESR and C reactive protein</td>
</tr>
</tbody>
</table>

CCP: cyclic citrullinated peptide