

# Rheumatoid Arthritis

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## Purpose

The purpose of this course is to describe the etiology, pathophysiology, diagnostic criteria, classification systems, deformities, extraarticular manifestations, and treatment options for rheumatoid arthritis.

## Goals

Upon completion of this course, the healthcare provider should be able to:

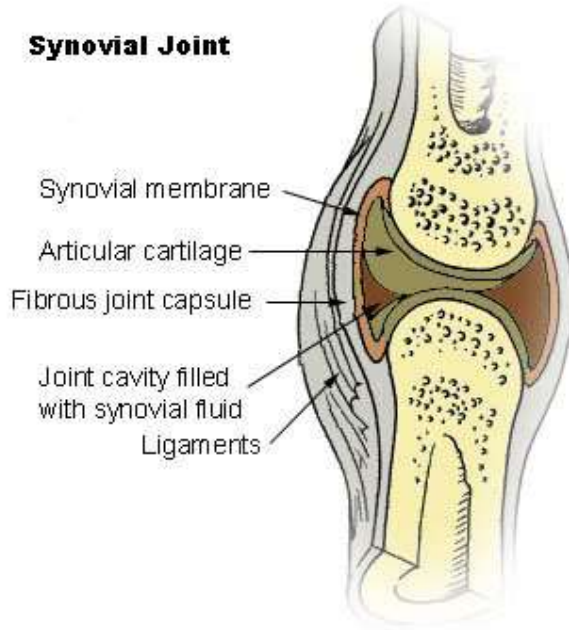
- Describe the normal synovial joint.
- Describe 7 types of synovial joints affected by RA.
- Describe the etiology and pathophysiology of RA.
- Discuss criteria for diagnosis including joint involvement, serological parameters, and acute phase reactants.
- Describe classification systems: stage of RA and functional status.
- Describe 5 common deformities associated with RA.
- Describe 6 extraarticular manifestations of RA.
- List and describe 6 types of exercises used for RA.
- Discuss the use of analgesics, DMARDS, immunomodulators, and corticosteroids.
- Discuss the use of heat and cold.
- Describe 3 types of surgical treatments.
- Discuss complementary therapies.

## Introduction

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder that results in inflammation of connective tissue in synovial (diarthrodial) joints (which are freely movable) and degeneration of cartilage and joint deformity. In addition, almost every body system

can be involved. Extraarticular manifestations include rheumatoid nodules, Sjögren syndrome, and Felty syndrome. RA most commonly affects peripheral joints and the cervical spine.

### Synovial Joint



The articular surfaces (ends) of the bones are covered by hyaline cartilage and separated by a joint cavity, allowing freedom of movement. The joint cavity is lined by a synovial membrane (synovium) and lubricated by viscous synovial fluid. Some joints, such as the knee, contain articular disks or wedges of fibrocartilage between the articular surfaces of the bones.

Approximately 1.3 million American have rheumatoid arthritis, with incidence in females 2.5 times that of males.

Onset of adult RA is most often in middle age, but some people have early onset in their 20s and 30s.

Synovial joints affected by RA	
<b>Plane</b>	Small joints with flat bones that allow sliding or gliding movement, typically found in the wrist, ankles, and vertebrae.
<b>Hinge</b>	Joints that allow movement in only one plane (backward or forward), including the interphalangeal, elbow, knee, and ankle joints.
<b>Pivot</b>	These joints allow rotation about an axis, including the neck and forearm.
<b>Condylloid</b>	These joints allow flexion, extension, adduction, abduction, and circumduction, including wrist, metacarpophalangeal, and metatarsophalangeal joints.
<b>Ellipsoidal</b>	These joints allow movement similar to ball and socket joints but with more restricted movement, including wrist joints.
<b>Saddle</b>	These joints, such as found in the thumbs, allow movement back and forth and up and down but not rotation.

<b>Ball-and-socket</b>	These joints allow twisting and turning movements with one bone having a cup shape and the other rounded, such as in the shoulders and hips.
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## Etiology

While the cause of RA is unclear, it appears from interplay of genetic and environmental factors. Genetic studies show that some may have a genetic predisposition to RA development. For example, 80% of Caucasians with RA express HLA-DRI or -DR4 genetic subtypes. Identical twins have a concordance rate of 30%. Researchers estimate that about 50% of the risk of developing RA is genetic.





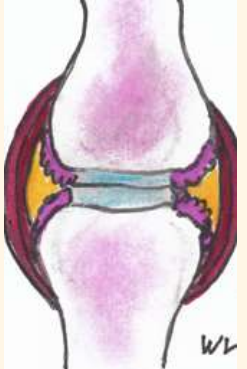

**Smoking** has been linked to both the development of the disease and the severity. A study regarding the relationship of smoking and RA in Sweden involved 1200 patients. Results showed the heaviest smokers had 2.5 times the risk of a positive anti-citrullinated protein antibody (ACPA) test, a marker for RA. The researchers estimated smoking accounted for 35% of ACPA positive RA cases, 50% of cases for those with genetic susceptibility, and 20% of RA cases overall.

While other environmental factors may be at play, the results suggest that people with risk factor for RA (such as familial disease) should avoid or stop smoking. While risks decreased with smoking cessation, risks still remained relatively high even 20 years after cessation.

While there is some evidence that an infective process may lead to RA, no study has been able to prove this conclusively or to identify causative agents. However, in some cases, initial symptoms of RA are preceded by a flu-like illness, arthritis has been induced in animal studies with bacteria, bacterial products are present in RA patients' joints, and many disease-modifying drugs have antibacterial properties.

Some studies suggest that drinking more than 3 cups of decaffeinated coffee daily may increase but drinking tea may decrease risks. Those taking oral contraceptives have decreased risk. Additionally, women who are pregnant often have significant decrease in symptoms, suggesting hormones may play a role in the disease.

## Pathophysiology

	<p><b>The normal joint:</b></p> <ul style="list-style-type: none"> <li>• Cartilage is intact.</li> <li>• Synovial fluid is clear.</li> <li>• Synovial membrane is not inflamed.</li> <li>• Joint is normal in size.</li> <li>• Mobility is not impaired.</li> <li>• Joint is pain free.</li> </ul>
	<p><b>Early inflammation:</b></p> <ul style="list-style-type: none"> <li>• Autoimmune reaction occurs in synovial tissue with production of autoantibodies (rheumatoid factor).</li> <li>• T and B cells proliferate with angiogenesis in synovial lining.</li> <li>• Activated CD4 cells stimulate monocytes, macrophages, and synovial fibroblasts to secrete proinflammatory cytokines (interleukin-1, interleukin-6, and necrosis tumor factor), which drive inflammatory response and contribute to cartilage destruction.</li> <li>• Synovium becomes inflamed and thickens.</li> <li>• Soft tissue edema is evident.</li> </ul>
	<p><b>Chronic inflammation:</b></p> <ul style="list-style-type: none"> <li>• Phagocytosis produces proteolytic enzymes that break down collagen, damaging cartilage.</li> <li>• Synovitis is present with increasing inflammation.</li> <li>• Early pannus (highly vascular granulation tissue) forms and begins to destroy cartilage at the joint periphery.</li> <li>• Rheumatoid nodules may occur.</li> </ul>
	<p><b>Advanced disease:</b></p> <ul style="list-style-type: none"> <li>• Pannus causes increasing destruction of cartilage and subchondral bone erosion.</li> <li>• Pannus scars and damages supporting structures (ligaments and tendons).</li> <li>• Joint deformity is evident.</li> <li>• Joint laxity, subluxation, and contractures may occur and cause joint instability and decreased ROM.</li> <li>• Synovitis may increase.</li> <li>• Soft tissue swelling is evident.</li> </ul>

	<ul style="list-style-type: none"> <li>• Osteophytes may form.</li> <li>• Systemic complications may occur.</li> </ul>
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## Criteria for diagnosis

Until 2010, diagnosis focused on evidence of joint destruction, but new criteria developed by the American College of Rheumatology and the European League against Rheumatism focus on identifying and treating early RA in order to prevent joint destruction.

Criteria for RA (Total of 6 points = positive diagnosis)	
<b>Joint involvement</b>	<p><b>Small joints:</b> Metacarpophalangeal joints (MCP), proximal interphalangeal (PIP) joints, and interphalangeal joint of the thumb, second through third metatarsophalangeal joint, and wrist.</p> <p><b>Large joints:</b> Elbows, hips, and knees:</p> <ul style="list-style-type: none"> <li>▪ Involvement of 1 large joint = 0 points.</li> <li>▪ Involvement of 2-10 large joints = 1 point.</li> <li>▪ Involvement of 1-3 small joints (with or without involvement of large joints) = 2 points.</li> <li>▪ Involvement of 4-10 small joints (with or without involvement of large joints) = 3 points.</li> <li>▪ Involvement of more than 10 joints (with involvement of at least 1 small joint) = 5 points.</li> <li>▪</li> </ul>
<b>Serological parameters</b>	<p><b>Include:</b> Rheumatoid factor (RF) and anti-citrullinated protein antibody (ACPA):</p> <ul style="list-style-type: none"> <li>▪ Negative RF <i>and</i> negative ACPA = 0 points.</li> <li>▪ Low-positive RF <i>or</i> low-positive ACPA = 2 points.</li> <li>▪ High-positive RF <i>or</i> high-positive ACPA = 3 points.</li> </ul>
<b>Acute phase reactants</b>	<p><b>Include:</b> Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).</p> <ul style="list-style-type: none"> <li>• Elevated ESR = 1 point.</li> <li>• Elevated CRP = 1 point</li> </ul>

While the new criteria are useful for classifying the disease for research purposes, identifying patients prior to onset of symptoms does not always occur. For clinical practice, then, the following criteria are commonly used with  $\geq 4$  out of 7 symptoms considered positive for RA:

1. Stiffness upon arising in the morning persisting >1 hour.
2.  $\geq 2$  joint involvement.
3. Wrist, PIP, or MCP joint involvement persisting >6 weeks.
4. Symmetrical, bilateral joint involvement.
5. Positive RF or positive ACPA.
6. Presence of subcutaneous rheumatoid nodule over extensor surface.
7. Radiographic evidence of joint destruction.

**Radiography** Plain radiography (X-ray) remains the most commonly used imaging procedure and provides differentiation between osteoarthritis and RA.

However, x-ray does not show early cartilage damage or synovitis, so CT scan, MRI, and ultrasound may also be used for diagnosis and monitoring.

**Lab tests** Numerous blood tests may be done during diagnosis, sometimes to rule out other disorders. For example, blood counts may show anemia and increased white blood counts, which often occur with RA. However, the primary tests for diagnosis of RA include:

<b>Laboratory tests for RA</b>	
<b>Rheumatoid factor (RF)</b>	Indicates presence of a macroglobulin type antibody that occurs in connective tissue disease, so it is not specific to RA but is often used for diagnosis with other indications. Normal value 0-20 IU/mL.
<b>Anti-citrullinated protein antibody (ACPA):</b>	Indicates the presence of autoantibodies against citrullinated proteins. Sensitivity may vary from one type of detection kit to another, but people with RA react to a number of different citrullinated antigens. Sensitivity is comparable to RF testing. Normal values: <ul style="list-style-type: none"> <li>• Negative: &lt;20.</li> <li>• Weakly positive: 20-39.</li> <li>• Moderately positive: 40-59.</li> <li>• Strongly positive: &gt;60.</li> </ul>
<b>Erythrocyte sedimentation rate (ESR):</b>	Indicates inflammation, resulting in increased globulins or fibrinogens, which cause the red blood cells to clump and fall to the bottom of a test tube when held vertically. ESR is nonspecific and usually used along with other tests. ESR is less sensitive to changes than CRP. A rising ESR rate may indicate

	<p>increasing inflammation or a poor response to treatment. Normal values:</p> <ul style="list-style-type: none"> <li>• &lt; Age 50: 0-15 mm/h males and 0-25 females.</li> <li>• &gt; Age 50: 0-20 mm/h males and 0-30 females.</li> </ul>
<b>C-reactive protein (CRP):</b>	<p>Indicates presence of abnormal glycoproteins, produced by the liver in response to an active inflammatory process. CRP is sensitive and rises and falls quickly in response to inflammation, but it is non-specific and does not indicate the type of inflammation.</p> <p>Normal value &lt;1 mg/dL.</p>

Based on clinical indications and diagnostic studies, RA may be classified according to the stage of the disease.

<b>Stages of RA</b>	
<b>1</b>	While slight bone thinning may be evident, no joint damage is evident on X-ray.
<b>2</b>	Bone thinning is evident about the joint with or without slight damage to bone. There may be slight damage to cartilage, atrophy of adjacent muscles and limited joint mobility, but no joint deformities are seen. Soft tissue abnormalities (nodules) about the joint may occur.
<b>3</b>	Cartilage damage, bone damage, and bone thinning about joint are evident on X-ray, and there is extensive muscle atrophy, and joint deformity (such as subluxation, ulnar deviation, or hyperextension) , but no permanent stiffening or ankylosis. Abnormalities of soft tissue (nodules, tenosynovitis) about the joint may occur.
<b>4</b>	Cartilage damage, bone damage, and osteoporosis about the joint are evident on X-ray as well as extensive muscle atrophy with permanent stiffening or joint ankylosis. Abnormalities of soft tissue around the joint may occur.

People with RA are also classified according to functional status:

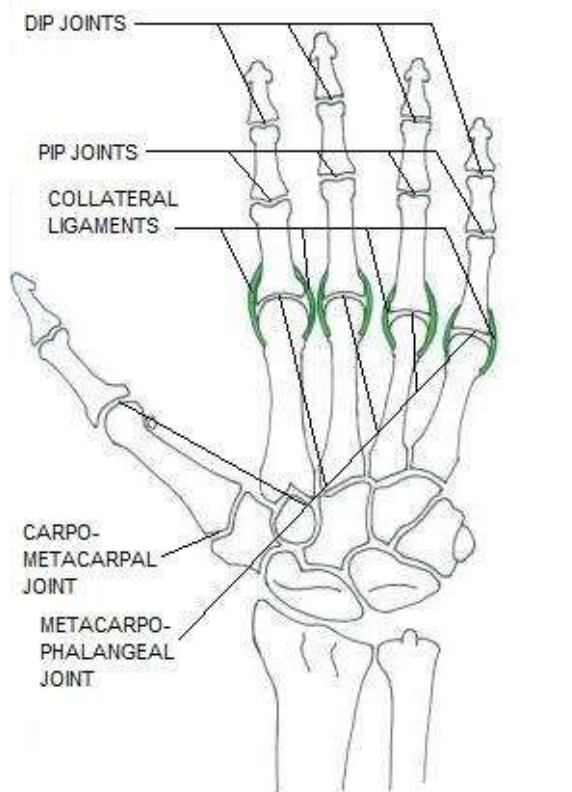
<b>Functional status</b>	
<b>Class 1</b>	Able to independently perform activities of daily living.
<b>Class 2</b>	Able to perform usual activities involving self care and work but limited in other activities, such as engaging in sports and doing household chores.
<b>Class 3</b>	Able to perform usual activities involving self care but

	limited in work and other activities.
<b>Class 4</b>	Limited in ability to perform all usual activities involving self care, work, and other activities.

## Clinical indications

The primary symptom that brings people to the attention of healthcare providers is usually pain. If the joint is inflamed, people may guard the joint by immobilizing it, limiting mobility and leading to contractures. Symptoms may vary considerably, depending on the degree or stage of the disease. Classic symptoms of RA include joint pain, swelling, erythema, and calor (warmth). Joints often feel spongy on palpation.

Symptoms are slow and insidious in most people, typically beginning with the smaller joints—hands, wrists, and feet—and then progressing over time to larger joints, such as the hips, knees, shoulders, cervical spine, jaw (temporomandibular), and ankles. General systemic symptoms, such as fever, malaise, arthralgia, and weakness may occur prior to obvious joint inflammation and swelling. Some people (about 10%) have rapid onset of disease.



JOINTS OF THE FINGERS AND HAND

The **joints of the hand** are frequently the first sites of deformity in RA:

- Distal interphalangeal (DIP).
- Proximal interphalangeal (PIP).
- Carpometacarpal (CMC).
- Metacarpophalangeal (MCP).

With normal joints in the hand, a person can generally either extend the joints of a finger or flex them, but both extension and flexion cannot occur at the same time. With RA, damage to the joints and the extensor and flexor tendons disrupt this normal pattern.



## Deformities associated with RA

### Ulnar deviation/drift



One of the most characteristic signs of RA is ulnar deviation of the fingers, especially at the metacarpophalangeal joint. Ulnar deviation may occur in all fingers, but the 4<sup>th</sup> and 5<sup>th</sup> metacarpals are especially at risk.

This deformity is also often associated with other deformities, such as elbow pronation and flexion or ulnar wrist flexion. In many cases, the wrist tends to deviate toward the thumb, resulting in a "Z" deformity.

Ulnar deviation may occur slowly, most noticeable on flexion. The ability to grab or pinch diminishes and the hands weaken.

Splinting, especially in early stages, may provide some increase in strength and hand function, but splinting and joint protection strategies do not appear to alter the progression.

### Hallux valgus

Hallux valgus (commonly referred to as a bunion) is medial deviation of the first metatarsal and lateral deviation and/or rotation of the hallux (great toe), with or without medial soft-tissue enlargement of the first metatarsal head.



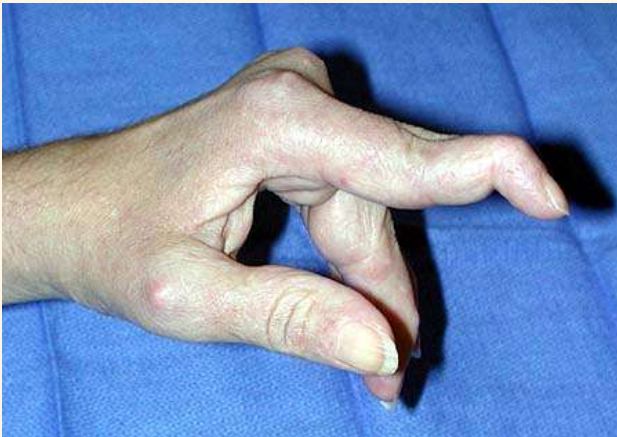
### **Boutonniere**



With boutonniere deformity, the proximal interphalangeal (PIP) finger joint is hyperflexed, and the distal interphalangeal (DIP) joint is hyperextended.



### **Swan-neck**



This deformity is characterized by hyperextension of the PIP and hyperflexion of the DIP. A similar condition in the thumb if referred to as "duckbill" thumb (because the thumb has fewer joints), but involvement of the thumb is more common in osteoarthritis.

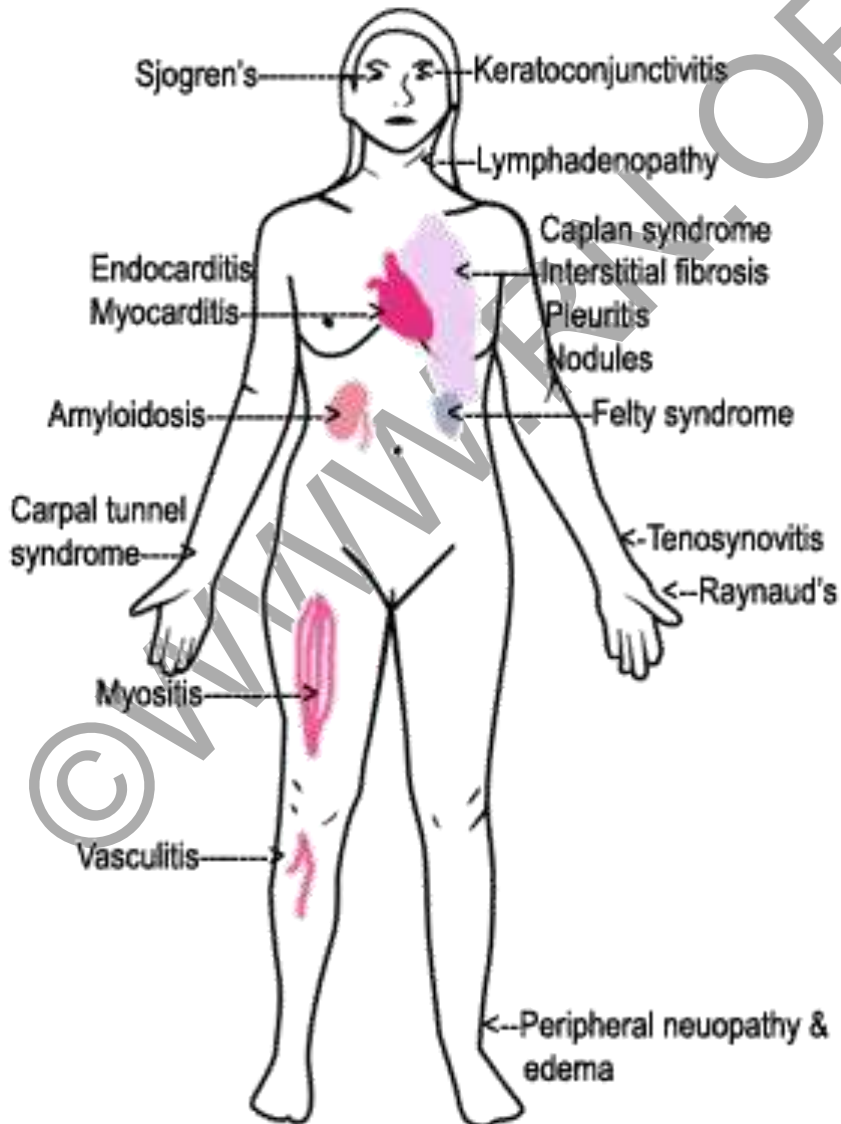


## Ankylosis



With destruction of the joint and loss of cartilage, the bones may fuse, resulting in complete loss of joint mobility. This most commonly occurs in the hands/fingers and cervical vertebrae but can affect other joints, such as the temporomandibular and cricoarytenoid joints.

## Extraarticular manifestations of RA



**Nodules** Soft tissue nodules occur in approximately 30% of those with RA and are most common near joints or pressure areas, such as the elbow, back of the head, and back of the ankle. The nodules themselves usually do not cause symptoms but may become inflamed if injured and may ulcerate. Nodules are usually non-tender, moveable, and may disappear spontaneously.

In some cases, nodule form on vocal chords, resulting in hoarseness. Nodules occurring in vertebral bodies may cause bone destruction. They are associated only with increased RF. Nodules often indicate a more destructive and rapidly progressive form of RA.



Nodules may occur on the sclera of the eyes as well, resulting in development of cataracts and loss of vision. Complications of nodules can include pain, decreased mobility, neuropathy, ulceration, infection, and fistula formation. While nodules can be surgically removed, they often recur. Corticosteroid injections into nodules may decrease size.

**Sjogren's syndrome** Sjogren's syndrome occurs in 10 to 15% of those with RA. Sjogren's is an autoimmune arthritic disorder in which antibodies primarily attack lacrimal and salivary glands, causing inflammation:

- Lacrimal: Dry eyes, irritation, infection, and corneal abrasion.
- Salivary: Mouth dryness, dysphagia, infection of parotid glands, dental decay, periodontitis, and dry lips.

In some cases, other glands are also affected, including those lining the breathing passages of the lungs, resulting in lung infection, and the vagina, resulting in painful intercourse. Other symptoms can include vasculitis, which can lead to tissue damage.

**Raynaud's disease** Raynaud's disease is a disorder involving intermittent digital vasoconstriction of the hands and feet, especially in response to cold

or stress. Secondary RD, such as that caused by RA, is usually more severe and resultant impairment of circulation may cause ulcerations or gangrene.



**Raynaud's phenomenon** refers specifically to the vasoconstriction of arterioles of the hands and/or feet, causing pallor and/or cyanosis (white phase and blue phase). A recovery phase results in hyperemia or rubor (red phase). Thus, symptoms are described as a progression from white to blue to red. Hands are more often affected than feet. Usually, at the onset of disease, just one or two fingertips are involved, but with progression of the disease, the entire fingers to the distal palm are affected. With secondary RD, symptoms may be unilateral or bilateral.

Triggers include exposure to cold, vasoconstrictive medications, and cigarette smoking. Treatment involves avoiding triggers, calcium channel blockers (nifedipine), or sympathectomy (for severe cases). People must be advised that smoking poses grave danger of their developing gangrene, so smokers should be enrolled in smoking cessation programs.

**Felty syndrome** Felty syndrome affects only about 1% of those with RA. Felty syndrome is characterized by splenomegaly and leukopenia (primarily neutropenia). The bone marrow appears to normally produce white blood cells, but the number of neutrophils circulating is low, perhaps because excessive amounts are stored in the spleen, causing it to enlarge. The reason some people get Felty syndrome is not clear, but it is associated with the presence of rheumatoid factor.

Neutropenia results in depressed immune response, putting people with Felty syndrome at increased risk of infection, such as pneumonia and skin infections. Those with ulcerations, especially, may develop skin infections.

Treatment depends on the severity of the illness. If mild no particular treatment other than standard treatment for RA is indicated, but with more severe symptoms, patients may receive weekly injections of

granulocyte stimulating factor/GSF to increase production of white blood cells.

**Caplan syndrome** Caplan syndrome, also referred to as rheumatoid pneumoconiosis, is a combination of RA and pneumoconiosis and occurs in people with RA who have been exposed to mining dust, such as coal, silica, or asbestos. Intrapulmonary nodules form, further interfering with breathing.

The nodules may appear in the lungs before other symptoms of RA. Multiple round (0.5 to 2.0 cm) nodules are usually present, typically at the lung peripheries. The nodules may form in groups, sometimes coalescing to form a large nodule. The nodules may cavitate and resemble tuberculosis.



People exhibit both restrictive and obstructive ventilatory defect with decreased lung volume. Symptoms include cough and dyspnea. The condition may have sudden onset and may be fairly mild or progress to severe fibrosis. Early treatment with standard RA drugs as well as corticosteroids is indicated. Smoking cessation is also essential, so people may need referrals to smoking cessation programs.

**Amyloidosis** Amyloidosis secondary to RA is associated with deposits of an abnormal protein (AA) in organs, such as the heart, kidneys, liver, intestines, nerves, joints, and lungs, with symptoms depending upon the organs involved. Amyloidosis of the kidneys can result in nephrotic syndrome and end-stage renal disease. Kidney failure is, in fact, the most common cause of death with systemic amyloidosis. Treatment of RA may be used prophylactically and therapeutically to prevent further deterioration. Renal dialysis and/or kidney transplantation may be indicated.

## Treatment options

There is no cure for RA, but treatment may help to delay progress of the disease, reduce joint destruction, and maximize mobility.

Treatment is individualized according to the clinical presentation, person's age, and person's occupation. Treatment usually includes some combination of a variety of different treatment options:

- Strengthening exercises.
- Rest.
- Joint protection.
- Medications.
- Education.
- Physical therapy and occupational therapy.

**Exercise** Exercise plays a critical role in RA therapy because they can help to reduce pain and improve mobility and overall functional ability.

Exercises for RA	
<b>Aquatic</b>	Exercises are done in warm (84-94°F) water with the person wearing non-slip footwear. Water should be deep enough to minimize compression on joints, usually 3.5 to 4 feet. The buoyancy lessens stress on the joints aids in performance of dynamic and aerobic exercises and facilitates ROM exercises. Water also provides gentle two-way resistance to aid in developing muscle strength.
<b>Aerobic</b>	Exercises should begin slowly and progress to tolerance, optimally to 20-30 minutes 3-5 days per week in order to improve endurance and cardiovascular health. Exercises should be of moderate intensity and may be modified for the individual. Studies show that people with RA who engage in aerobic exercises have increased functional ability and decreased joint pain. Typical aerobic exercises include walking and swimming. High impact aerobic exercises (such as running) are usually avoided.
<b>Dynamic</b>	Exercises increase strength and endurance as well as increase flow to joints and increase strength of bone and cartilage. Care should be exercised with unstable joints as strengthening exercises may increase biomechanical stress. Exercises usually begin with repetitions against gravity progressing to repetitions against resistance using weights, machines, body weight, rubber bands, or water.
<b>Isometric</b>	Exercises increase muscle tone and may be used prior to

	beginning dynamic and weight-bearing exercises. Exercises include tightening and relaxing muscles and should be done at 70% of maximum contraction daily. Blood pressure and circulation should be monitored as isometric exercises can restrict blood flow to muscles.
<b>ROM</b>	Exercises maintain flexibility and may involve stretching to increase joint mobility. Exercises may need to be limited if inflammation is present. Active and active/self-assisted exercises should be done daily.

### Medications

Medications are used to control pain and inflammation and to slow progression of the disease. Identifying RA in the initial stages and beginning therapy early, within the first 12 weeks, may help to suppress or reverse the disease process. Many studies are being conducted to determine the optimal course of treatment for people with RA, and most studies seem to indicate that early combined therapy is more effective for most people than monotherapy. However, treatment depends on individual risk assessment, clinical presentation, and age.

<b>Medications for RA</b>	
<b>Analgesics</b>	<p>These are often first-line therapy for mild or initial disease to help control pain, fever, and inflammation. They should be given with meals and monitored for adverse effects.</p> <ul style="list-style-type: none"> <li>• <b>Salicylates:</b> Adverse effects include tinnitus, gastric irritation and bleeding, and purpura.</li> <li>• <b>NSAIDs:</b> Adverse effects include GI disturbance (gas, nausea, vomiting, heartburn, constipation, diarrhea), rash, and confusion (in the elderly). NSAIDs should not be taken with salicylates. NSAIDs are usually given in conjunction with DMARDs.</li> <li>• <b>Topical capsaicin (Zostrix®):</b> Adverse effects may include local skin irritation and burning.</li> </ul>
<b>DMARDs</b>	<p>Disease-modifying antirheumatic drugs are generally considered second-line therapy although many studies now recommend early treatment with DMARDs to prevent progression of RA:</p> <ul style="list-style-type: none"> <li>• <b>Antimalarials (hydroxychloroquine, chloroquine):</b> Usually given with NSAIDs and have anti-inflammatory effect but are slow acting with onset of action in 2-4 months. Adverse effects include</li> </ul>



rash, visual changes, GI upset, photosensitivity, beeching of hair. Requires eye exam every 6-12 months.

- **Gold compounds** (aurothioglucose, gold sodium thiomalate, auranofin): Inhibit T- and B-cell activity and reduce synovitis in active stage of RA but are slow acting with onset of action at 3-6 months. Usually taken IM weekly for 6 months and then every 2-4 weeks. Usually given with NSAIDs. Adverse effects include stomatitis, dermatitis, diarrhea, hematuria, bone marrow suppression (neutropenia and thrombocytopenia)
- **Sulfasalazine**: Usually administered with NSAIDs for anti-inflammatory effect as well as reducing lymphocyte response and inhibiting angiogenesis. Requires adequate fluid intake. Adverse effects include rash, GI upset, headache, liver function abnormalities, and anemia. Contraindicated in those with allergies to sulfa drugs or salicylates.
- **Penicillamine**: Usually given with NSAIDs for anti-inflammatory effect as well as inhibiting T-cell function and impairment of antigen presentation. Action is slow with onset of action in 2-3 months. Adverse effects include GI upset, decreased sense of taste, rash, pruritis, bone marrow suppression, proteinuria. Requires CBS and urinalysis every 2-4 weeks.
- **Immunosuppressives** (methotrexate, azathioprine, cyclophosphamide): Drugs affect DNA synthesis and suppress the immune system but have teratogenic potential. Methotrexate is most commonly used but azathioprine and cyclophosphamide are used for more aggressive disease that is not responsive to other drugs. Adverse effects include bone marrow suppression, GI ulcerations, alopecia, nausea, vomiting, rash, increased infection, and bladder toxicity. Drugs are teratogenic, so women of child-bearing age must use adequate birth control.
- **Cyclosporine**: Suppresses immune response by inhibiting T-cells and is used for severe RA that does not respond to other DMARDs. May be given in conjunction with methotrexate. Dosage is increased slowly, observing for toxicity. Adverse effects include bleeding gums, edema, excessive hair

	<p>growth, and tremors. Creatinine is monitored every 2 weeks until stable.</p>
<p><b>Immuno-modulators (Biologics)</b></p>	<p>Some studies suggest that immunomodulators, such as tumor necrosis factor (TNF) blocking agents or abatacept, should be used early as part of combined therapy. These medications are injectable, generally sc or IV:</p> <ul style="list-style-type: none"> <li> <p>• <b>Pyrimidine synthesis inhibitor</b> (leflunomide): Used for antiproliferative and antiinflammatory effects for moderate to severe RA, either alone or in combination with other DMARDS (but not with methotrexate). Requires loading dose and then daily dosage. Adverse effects include diarrhea, alopecia, rash, and stomatitis. Liver function tests must be monitored.</p> </li> <li> <p>• <b>TNF blocking agents</b> (adalimumab, etanercept, infliximab): Used for antiinflammatory and immunologic response for moderate to severe RA that does not respond to methotrexate or other DMARDS. Requires testing for TB prior to administration. Adverse effects include increased risk of infection. Medication must be withheld with fever.</p> </li> <li> <p>• <b>Interleukin-1 receptor antagonist</b> (anakinra): Used for antinflammatory and immunologic response for moderate to severe RA that does not respond to methotrexate. May be combined with methotrexate, other DMARDS, or other TNF-blocking agents. Adverse effects include increased risk of infections. Medication must be withheld with fever.</p> </li> <li> <p>• <b>Abatacept</b> (Orencia®). Used for moderate to severe RA to prevent progression of the disease either as monotherapy or in conjunction with methotrexate but should not be used with TNF blocking agents or other biologics, such as anakinra. Adverse effects include increased risk of infection, such as upper respiratory infections, urinary infections, pneumonia, cellulites, diverticuliti, and acute pyelonephritis.</p> </li> </ul>
<p><b>Cortico-steroids</b></p>	<p>Because of severe side effects, corticosteroids should be used for the shortest possible duration at lowest effective dose. Medications include prednisone, prednisolone, and hydrocortisone Used for anti-</p>

	inflammatory action. Onset is rapid, within days. May be used for intraarticular injections to relieve pain and stiffness of joints although repeated injections may result in damage to the joint. Adverse effects include cataracts, GI irritation, Cushinoid syndrome, hyperglycemia, hypertension, osteoporosis, avascular necrosis, hirsuitism, and pscyhosis.
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### Joint protection

People with moderate (erosive) RA need to learn joint protective measures, usually through working with a physical and/or occupation therapist who can design measures specific to the person's needs.

Basic techniques include:

- Use proper body mechanics, especially for lifting and working.
- Do daily ROM to maintain joint flexibility.
- Avoid activities that increase pain.
- Avoid prolonged or forceful gripping or pinching.
- Use assistive devices, such as handles for items such as keys and toothbrush, lid openers, electric can openers, and grabbers/reachers.
  - Avoid making a tight fist.
  - Hold items with the hands flat instead of pinching to hold.
  - Pick items up from the floor by bending the knees and squatting or by sitting on a chair and leaning down.
  - Use angled reading, writing desk.
  - Slide items rather than lifting them.
- Prevent stiffness by stopping activities to rest and exercise joints.
- Rest joints before they become fatigued and painful.
- Avoid repeatedly going up and down stairs.
- Schedule regular rest periods.
- Use lightweight splints occasionally during acute inflammation.
- Use the strongest joint available for any tasks; for example, use palms instead of fingers or forearms instead of hands.
- Avoid repetitious movements.
- Sit to work when possible instead of standing.



### Heat and cold

Both heat and cold applications may be used to relieve pain and swelling. Ice packs are usually applied to relieve discomfort associated with inflammation and are especially helpful with initial inflammation, but cold can increase stiffness. Heat is applied to relieve stiffness.

Many people use both: heat in the morning to relieve stiffness that is common on arising and cold to joints in the evening that are painful from inflammation resulting from use. Heat, such as soaking in a warm bath, may be helpful before engaging in exercise to relax muscles and decrease stiffness, followed by ice packs to joints after exercise.

**Surgical treatment** As people become experience more pain and increased limitation in movement and ability to carry out activities, a number of surgical treatments may be considered.

<b>Surgical treatments for RA</b>	
<b>Synovectomy</b>	With RA, the synovium becomes inflamed and clogged with inflammatory debris and cells, thickening and producing enzymes that damage the cartilage; so the lining may be removed surgically, usually arthroscopically.
<b>Joint replacement</b>	Total joint replacement may be necessary when joints become so damaged that mobility is severely impaired because of pain or stiffness. As part of this process, some bone is resected and replaced with prosthetic parts. Total joint replacements may include: <ul style="list-style-type: none"> <li>• Knee.</li> <li>• Hip.</li> <li>• Ankle.</li> <li>• Shoulder.</li> </ul>
<b>Other joint repair</b>	A number of procedures are available for treatment of smaller joints, such as in the fingers. Procedures include removing the synovial lining, joint replacements, and joint fusions. The choice of procedure depends on a number of factors, such as the joint involved, the degree of damage, and the condition of the supporting structures about the joint.  A bunionectomy may be performed to correct hallux valgus. Surgeons may use a variety of different procedures, depending on the degree and angle of deformity. In some cases, only soft tissue is removed, but in most cases an osteotomy (bone repositioning) is performed. With severe deformity, the entire joint may be removed and replaced with a

prosthetic joint.
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### **Complementary therapies**

Many different complementary therapies are used by people with chronic pain, including those with RA.

Some, such as copper bracelets and magnets are dubious at best, but other therapies, such as acupuncture, relaxation and visualization, biofeedback, and Tai Chi are reported to help some people.

Most complementary therapies pose little or no risk to people, and a placebo affect may help people to perceive that they have less pain even if a therapy has no value (copper bracelet); however, they should be cautioned that there is no evidence that these therapies can slow the progression of the disease, so they should also take standard treatments as well.

### **Conclusion**

Despite advances in the treatment of RA, it remains a chronic debilitating disease. Medications that help to control progression of the disease have many adverse side effects, and people, especially in later stages of the disease, often have to modify their activities and deal with chronic pain. Healthcare providers must be on the alert for depression in those with RA. People with RA are twice as likely to suffer depression than others, but they often remain untreated because they are reluctant to discuss this issue with healthcare providers. Depression often results in reduced activity, resulting in reduced mobility as joints stiffen.

The elderly with RA face particular challenges because metabolic and physical changes may increase their sensitivity to drugs used to manage RA. People with RA should be made aware of community resources available to them, such as meals-on-wheels programs and public transportation options for the disabled.

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