Rheumatoid arthritis (RA) is a chronic degenerative inflammatory disease of the joints. More than two million Americans have the condition; about 70% of them are women.

RA has long frustrated patients and doctors. It has widely varying effects, its course is unpredictable, its causes are unknown, and no cure is in sight. In recent years, however, medical science has made striking progress in treating the condition. In some people, early and aggressive therapy can halt joint damage and reduce long-term disability.

Symptoms and causes
The affected joints feel warm, swollen, and tender. They may be stiff when you wake up and ache after you rest. Rheumatoid arthritis often strikes the wrists and the upper part of the fingers. The neck, shoulders, hips, knees, ankles, and feet may also be affected. Unlike other types of arthritis, RA tends to have a symmetrical pattern: When the right knee is affected, the left usually is as well.

Rheumatoid arthritis can also attack tissues in addition to the joints, causing further symptoms. Fatigue and fever are common. Lymph nodes may swell. Some people develop nodules (lumps of tissue) beneath the skin near the joints, or in bony areas often exposed to pressure, such as the elbow and the forearm. In about 40% of RA cases, the pericardium — the tissue sac that encircles the heart — becomes inflamed. Inflammation may also occur in the lining of the lungs (pleuritis) or in the tear ducts and salivary glands, resulting in dry eyes and mouth. Some people develop anemia (a low red blood cell count).

The course of the disease is varied and unpredictable. For some women, symptoms come and go over a few months and then disappear without producing any noticeable damage. Others have moderate symptoms for a lifetime, with acute phases during which more severe symptoms, called flares, alternate with remissions. Still others have severe, unremitting disease that continues for decades and causes debilitating joint damage.

It’s likely that many factors — genetic, environmental, and hormonal — interact to trigger the immune system’s attack on the body. Mounting evidence suggests that infectious agents, such as viruses or bacteria, may unleash the disease in genetically susceptible people. The symptoms tend to go away during pregnancy and return after the baby is born, so scientists suspect that estrogen and other sex hormones play a role.

Diagnosing rheumatoid arthritis
Diagnosis is difficult in the early stages because symptoms vary so much from person to person. It may be hard to differentiate RA from other arthritic conditions and even from common viral infections. A patient’s description of her symptoms and a thorough physical exam provide the most important clues.

The diagnostic process may involve a variety of blood tests, including erythrocyte sedimentation rate (a general measure of inflammation), a complete blood count, and a test for rheumatoid factor — an antibody found in the blood of most people who have rheumatoid arthritis. Not everyone who tests positive for rheumatoid factor develops the disease, so the test isn’t definitive.

X-rays aren’t particularly useful early on; it takes months of inflammation to cause the type of joint damage that will show up on an x-ray. Once such damage has occurred, x-rays may be used to monitor the progression of the disease or the effects of therapy.

Anatomy of rheumatoid arthritis
Joints (the places where bones meet) are surrounded by a capsule lined with a membrane called synovium. Synovium produces a fluid that fills the capsule, lubricating the joint and nourishing the cartilage and bones inside the capsule. In rheumatoid arthritis, the immune system, which normally protects the body from infection and disease, attacks tissues within the joint capsule.

White blood cells migrate to the synovium and cause inflammation. Inflamed joints become warm, swollen, red, and painful. The synovium thickens, and enzymes released by inflammatory cells destroy cartilage and bone. The joints become enlarged and lose their normal range of motion. Over time, the ligaments and tendons that hold bones in place become weak, and the bones fall out of alignment.
Treating rheumatoid arthritis

A combination of medications and nondrug therapies (see "Nondrug approaches,” page 5) is used to relieve pain, control inflammation, slow or stop joint damage, and improve overall function. Drug treatment is important for just about everyone with rheumatoid arthritis, except possibly those in remission.

In the past, physicians prescribed medications conservatively, increasing doses and adding new drugs only gradually. But many experts are now taking a more aggressive approach, treating RA early with powerful drugs and using drug combinations rather than a single medication. There are several reasons for this. Studies have shown a link between ongoing RA inflammation and an increased rate of death and illness. Also, more effective therapeutic drugs have become available, and it has been shown that drug combinations can improve long-term outcomes. For women whose joint damage is severe and a source of constant pain, surgery may be the best option. Artificial joints and procedures to reconstruct tendons can restore function and dramatically improve quality of life.

Because the course and features of the disease are so variable, it's difficult to predict early on who will develop debilitating joint damage. But if it's going to happen, it happens fast, usually within the first two years after the diagnosis, so clinicians must carefully weigh the benefits and risks of aggressive drug treatment in each person.

Complementary therapies

Medications and a modified exercise program are the mainstays of rheumatoid arthritis treatment. Some complementary approaches have shown promise in expanding the options, although their safety and effectiveness are not proven. Before trying any of them, consult your clinician.

Fish and plant oils. Certain essential fatty acids —eicosapentaenoic acid, found in fish oil, and gamma linolenic acid, found in some plant oils — have been shown in a number of studies to have modest effects on symptoms in some people.

Supplements. Certain vitamins, minerals, and supplements may help improve symptoms. These include B vitamins, copper and zinc, and the amino acid L-histidine. But it's best to get an adequate intake of vitamins and minerals through food and a standard multivitamin. Some supplements can interact with rheumatoid arthritis medications.

S-adenosymethionin (SAMe). SAMe is marketed as a supplement for improving joint mobility and pain symptoms in osteoarthritis. Preliminary studies suggest it may help relieve rheumatoid arthritis pain. People who take methotrexate should not take SAMe.

What about bee venom? There's no scientific evidence that bee venom injected — by bee or needle — into an affected joint helps in treating rheumatoid arthritis. Likewise, copper bracelets have no proven benefit.

Selected resources


The Arthritis Foundation, www.arthritis.org

Treating pain and inflammation

Three classes of drugs help relieve RA symptoms, although they don't influence the overall course of the disease.

Analgesics. Acetaminophen (Tylenol, others) and prescription analgesics relieve pain but have little or no effect on inflammation. They may help during a flare.

Anti-inflammatory drugs. Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen (Motrin), naproxen (Aleve), and aspirin reduce inflammation and relieve pain, but they all can have side effects on the stomach, including dangerous bleeding, especially with long-term use. The newer NSAIDs known as COX-2 inhibitors appear to have fewer such side effects in some people. But Vioxx, one of the drugs in this class, was recently withdrawn from the market when studies showed that it increases the risk of stroke and heart attack. (Scientists are reviewing other COX-2 inhibitors.)

Steroids. Prednisone and related steroids reduce inflammation by suppressing the immune system. They provide rapid, dramatic relief, but don't change the course of the disease. Over time, they may produce many adverse effects (see chart, page 5), so they're usually prescribed at the lowest dose possible for the shortest period of time.

Heading off joint damage

Newer drugs that actually alter the course of rheumatoid arthritis show promise in reducing long-term disability.

Disease-modifying antirheumatic drugs (DMARDs). Most people with rheumatoid arthritis will take a DMARD, usually methotrexate, as early as possible to reduce or prevent joint damage. These drugs take weeks or months to begin working and must be carefully monitored to prevent serious side effects. A DMARD may be given along with a steroid, which quiets inflammation and improves symptoms while the patient is waiting for the DMARD to take effect. The steroid is then gradually withdrawn.

Biological response modifiers (BRMs). This new group of injected drugs works by interfering with substances that trigger inflammation as part of the body's normal immune response. Biological response modifiers include etanercept (Enbrel), infliximab (Remicade), adalimumab (Humira), and anakinra (Kineret). The main drawback of these drugs is that they interfere with the ability to fight infection. Their long-term effects are not fully known.
Protein-A immunoabsorption. This treatment filters the blood, trapping immune substances and removing them. The FDA has approved it for treating people with RA who don't respond to or can't tolerate other therapies.

Nondrug approaches
To live successfully with rheumatoid arthritis, you must learn how to manage your symptoms — especially when and how to exercise and rest. Resting an inflamed joint reduces the inflammation, but prolonged inactivity can result in muscle weakness and loss of joint motion. Knowing how to adjust your activities can help keep your joints strong and flexible without overusing them. A physical therapist can teach you exercises and recommend splints and other devices to support and immobilize joints when at rest. Exercise also helps to prevent osteoporosis — a condition that's more likely to occur in women who have rheumatoid arthritis.

Other nondrug approaches can help. An occupational therapist can show you how to protect your joints during daily activities and recommend devices that make it easier to eat, write, lift objects, and do other chores. A podiatrist can make foot orthoses — shoe inserts that help redistribute the weight of the body and improve foot function. Techniques such as cognitive behavioral therapy, biofeedback, and stress management have been shown to reduce disability and pain resulting from rheumatoid arthritis.

### FDA-approved medications to treat rheumatoid arthritis*

<table>
<thead>
<tr>
<th>Medications</th>
<th>Side effects</th>
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<tr>
<td><strong>Analgesics</strong>&lt;br&gt;Various over-the-counter and prescription drugs can help relieve pain. They include acetaminophen (Tylenol, others), tramadol (Ultram), and codeine.</td>
<td>Long-term high doses of acetaminophen (more than 4,000 mg a day) can lead to liver damage. Acetaminophen should not be taken with alcohol or with other acetaminophen-containing drugs. Prescription painkillers have various side effects and can interact with alcohol and other medications. Some are addictive.</td>
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<tr>
<td><strong>Nonsteroidal anti-inflammatory drugs (NSAIDs)</strong>&lt;br&gt;These over-the-counter and prescription drugs reduce pain, swelling, and inflammation. They include aspirin, ibuprofen (Advil, Motrin, others), naproxen (Aleve, Anaprox, Naprelan, Naprosyn), ketoprofen (Orudis, Oruvail), diclofenac (Voltaren), diflunisal (Dolobid), and indomethacin (Indocin).</td>
<td>Can cause stomach and abdominal upset or pain, increased bruising and bleeding, fluid retention, and ulcers. Aspirin in high doses can cause ringing in the ears. Overuse may cause liver or kidney problems. Can interact with blood thinners such as warfarin (Coumadin). May increase the rate of miscarriage. Most side effects go away when NSAID use is stopped.</td>
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<tr>
<td><strong>COX-2 inhibitors</strong>&lt;br&gt;This is a different class of NSAIDs that are available only by prescription.</td>
<td>Have a lower rate of ulcers, upset stomach, and bleeding than other NSAIDs. However, the safety of all COX-2 inhibitors is under review following reports of increased risks of stroke and heart attack.</td>
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<td><strong>Corticosteroids</strong>&lt;br&gt;Steroids given by mouth or injection can help reduce inflammation and pain and can slow joint damage. They include prednisone (Cortan, Deltasone, Melicorten, others) and methylprednisolone (Medrol).</td>
<td>Can dramatically relieve symptoms, but should not be used for months or years. Long-term use can result in osteoporosis, cataracts, weight gain, diabetes, increased susceptibility to infection, and hypertension. Other side effects include easy bruising, fragile skin, and muscle weakness.</td>
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<tr>
<td><strong>Disease-modifying antirheumatic drugs (DMARDs)</strong>&lt;br&gt;These powerful drugs are prescribed early on to relieve pain and swelling, limit joint damage, and alter the course of the disease. They include antimalarials, such as hydroxychloroquine (Plaquenil); the antibiotics sulfasalazine (Azulfidine) and minocycline (Minocin, Dynacin); injectable and oral gold; D-penicillamine (Depen, Cuprimine); methotrexate (Amethopterin); leflunomide (Arava); and immunosuppressant drugs, such as azathioprine (Imuran), cyclophosphamide (Cytoxan), and cyclosporine (Neoral, Sandimmune).</td>
<td>Can take weeks or months to have an effect. Side effects vary with each medication and include increased risk of infection, hair loss, stomach upset, skin rash, and kidney or liver damage. Any of these drugs may interact with other medications. Methotrexate can suppress the immune system and may cause birth defects. Azathioprine, cyclophosphamide, and leflunomide increase the risk for cancer and birth defects. All DMARDs require close supervision and monitoring by a physician.</td>
</tr>
<tr>
<td><strong>Biological response modifiers (BRMs)</strong>&lt;br&gt;This group of injected drugs targets specific immune chemicals and interferes with the inflammatory process. It includes tumor necrosis factor (TNF) inhibitors, such as etanercept (Enbrel), infliximab (Remicade), and adalimumab (Humira), and the interleukin-1 (IL-1) inhibitor anakinra (Kineret).</td>
<td>Side effects vary with the medication and include an increased risk of infection, especially tuberculosis. Side effects of TNF inhibitors include sore throat, abdominal or muscle pain, rash, headache, and nausea. Anakinra requires daily self-injection; it can cause headache, runny nose, and stomach pain. None of these drugs should be taken when an active infection is present. Their long-term safety is unknown.</td>
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* A clinician should monitor all drugs taken for rheumatoid arthritis.
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