13325 Hargrave Road, Suite 250 Houston, Texas 77070

RHEUMATOID ARTHRITIS

Introduction:

RA is not a generic term for just any type of arthritis. It also is not a term applied to any form of severe arthritis. It is a specific type of arthritis that begins in the soft tissue around the joint known as the synovium (sin-O-vee-um). RA affects 1% of the U.S. population, with women outnumbering men 2:1 to 4:1. While the peak age of onset is in the 30's to 50's, RA can begin at any age. It is a disease that progresses most rapidly within the first two years of onset, and those afflicted with RA have twice the mortality rate of individuals of the same age in the general population.

Features of RA:

The basic problem in RA is inflammation of the synovium, causing swelling, pain, and morning stiffness, and which can lead to irreversible joint damage and loss of function. The joints most often affected are the wrists and the small joints of the hands, usually the first and second row of knuckles past the wrists. Other commonly affected joints include those in the balls of the feet, the ankles, the knees, the elbows, and the shoulders. While neck involvement is common, the lower back is typically spared. The pattern of arthritis has a strong tendency to be symmetrical, affecting the same joints on both sides of the body.

When joints become affected in RA, they don't simply hurt; they become progressively damaged. The inflamed synovium, when not properly treated, can invade the bone and cartilage surrounding the joint and result in irreversible damage and loss of function. This may result in not only pain, but also limited mobility, deformity, and difficulty using the impaired joint. This process does not discriminate according to age, race or gender; all affected with RA are at risk for complications.

While the joint disease is the most striking manifestation of RA, the inflammation will often affect other organs. Up to 40% of RA patients will have abnormalities in lung function, which are often subtle and may go unnoticed. Many patients, however, can experience serious lung damage requiring more aggressive therapy. Roughly ¼ of patients will have dry eyes and dry mouth known as secondary Sjögren's syndrome (see section on Sjögren's), and about 20% will have inflammation that may cause irritation of the eyes, or less commonly, vision loss. A condition known as Felty's syndrome causes low blood counts and frequent enlargement of the spleen, and rheumatoid vasculitis (inflammation of the blood vessels) may result in rash, skin ulcers, or less commonly damage to the nerves or other organs. Both of these conditions are infrequently encountered in RA (about 1% of patients).

Diagnosis:

RA is predominantly diagnosed by a thorough review of a patient's symptoms and physical examination. While laboratory studies help in the evaluation, no laboratory test can either establish or rule out a diagnosis of RA. The rheumatoid factor (RF), markers of inflammation, and a new antibody know as anti-CCP are useful studies and are often used to predict the severity of RA in individual patients. X-rays are also useful diagnostic tools, particularly films of the hands and feet, and can be used to monitor disease progression by assessing the degree of joint damage.

Treatment (see Medications section):

Therapy in RA has two goals: reducing symptoms and preventing joint damage and disability. We have more tools available to treat RA today than ever before, and studies have documented that early treatment with specific medications has a long-term impact on the course of the disease. While all therapies have potential side effects, the consequences of not treating RA are generally much greater. Your doctor will work carefully with you to select the right medications for you as an individual. Non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen (Motrin) and simple analgesics such as acetaminophen (Tylenol) or even narcotic-strength pain relievers have a role in treating RA. These therapies, however, are limited to their effects on reducing day-to-day symptoms and have no effect on the long-term course of the disease. Many of these medications may be given in combination with other RA therapies to reduce pain in inflamed joints.

Corticosteroids such as prednisone may be very effective in rapidly reducing pain and swelling in inflamed joints, both when given orally and injected directly into a joint. Some evidence suggests that these medications may even slow down joint damage. Long-term side effects, however, limit the use of corticosteroids in RA. Generally speaking, steroids should be used for disease flares, for brief periods of time, or in low doses to avoid these complications (see Medications section).

Disease-modifying anti-rheumatic drugs (DMARDs) should be the mainstay of therapy for most patients with RA. Generally speaking, the sooner they are started after the onset of symptoms, the more effective they are at treating the disease. Ideally, DMARDs should be initiated within three months of disease onset to achieve an optimal response. Because patients are individuals, your doctor will work with you to determine which DMARD is appropriate for the severity and stage of your disease. All of the agents listed below fall under this category.

Anti-malarial drugs are generally among the safest of the DMARDs but are generally utilized to treat milder RA. Hydroxychloroquine (HCQ), marketed under the trade name Plaquenil, takes 3 to 6 months to begin working and can be used either by itself or in combination with other DMARDs. The only potential complication requiring monitoring is that of damage to the retina, the layer in the back of the eye, which can potentially impair color vision. While this is of concern, it occurs in only one of 1,000 people taking the drug and is detectable before serious damage occurs if monitored by your eye doctor every 6-12 months. HCQ doses of less than 6.5 mg/kg/day generally have a very low incidence of retinal damage.

Sulfasalazine (SSZ) was developed many decades ago to treat RA and is also commonly used to treat Crohn's disease, an inflammatory intestinal disorder. SSZ takes effect in 1 to 3 months and seems to have a modest effect on slowing down joint damage in RA. This drug also seems to be more effective in patients who are "seronegative" (with a negative RF). The most common side effect of SSZ is stomach upset, which may be eliminated by using a coated preparation of the drug. Allergic reactions are also no unusual. Serious problems, such as a drop in the white blood cells or acute damage to the liver, are unusual and typically occur early in the course of therapy, if at all. Blood tests to monitor for these complications will generally pick up any problems before they become severe.

Methotrexate (MTX) is perhaps the most popular and most commonly prescribed DMARD among rheumatologists, and for good reason. MTX slows joint damage, improves symptoms and physical functioning in RA patients, and has an onset of action of 1 to 3 months after starting the medication. It is taken once weekly in the form of pills or injections, with injections being associated with better availability of the medication and often less side effects. Nausea, mouth sores, thinning of the hair, lowering of blood counts, susceptibility to infection, and liver damage are among the more common side effects and can be reduced by taking folic acid or folinic acid (Leucovorin) supplementation. Rarely, acute lung injury may occur that can resemble pneumonia. Despite these potential side effects, problems with MTX can generally be detected with regular lab monitoring every 1 to 2 months. Most importantly, patients with RA taking MTX have a mortality rate that is only 40% of the mortality rate of RA patients not taking the drug. This finding seems to indicate that for most patients, the trade-off between benefit and side effects is very good.

Leflunomide (LEF), marketed under the trade name Arava, is a relatively new drug used to treat RA. It is taken orally once daily and begins to take effect in 1 to 3 months. The efficacy of LEF is similar to that of MTX, and it does seem to slow down the development of joint damage. LEF can result in nausea, diarrhea, hair loss, and liver damage, but the incidence of lowered blood counts and infection are lower than with MTX.

TNF antagonists are perhaps the most exciting class of medications to be recently introduced for the treatment of RA. Currently, there are 3 available medications in this class: etanercept (Enbrel), infliximab (Remicade), and adalimumab (Humira). Enbrel is given as a once weekly injection, Remicade is given as an intravenous infusion every 4-8 weeks, and Humira is administered as an injection every 2 weeks. Each of these medications inhibits a substance known as tumor necrosis factor (TNF) in one way or another. TNF is known to play a key role in inflammation in inflammation and joint damage in RA, and for this reason these medications are highly effective in controlling both the symptoms of the disease and the joint damage. In fact, some studies suggest that these medications actually halt joint damage in RA patients.

Each of the TNF antagonists may begin working within a few weeks of starting therapy. While individual patients may respond more favorably to one agent over another, all of these drugs seem to have similar efficacy. Disadvantages of these therapies include cost, inconvenience of injections or infusions, injection site or infusion reactions, and suppression of the immune system. Respiratory infections occur in increased frequency in patients treated with TNF antagonists, and those exposed to tuberculosis may experience reactivation of their disease. For this reason, a TB skin test is recommended prior to starting therapy. Patients with multiple sclerosis or severe congestive heart failure may experience worsening of their disease and therefore should not take these medications. Thus far, cancer rates have not been clearly shown to be increased in RA patients taking TNF antagonists versus other RA patients, but the data is somewhat confusing. Recently, the press has publicized an increased rate of a cancer known as lymphoma in patients taking these medications, but this was compared to the normal population. Because RA patients as a whole have an increased risk of lymphoma, it is not clear if the medications themselves or the disease accounts for this increased rate.

On the whole, we have found these medications to be well worth the cost and the potential side effects and have seen them virtually eliminate signs of active disease in patients resistant to many of our standard therapies. Currently, we are using TNF antagonists mostly in patients who have inadequately responded to MTX or other therapies. Most often, these drugs are added to MTX and may be more effective when used in this manner but may also be used alone. Use of TNF antagonists earlier in the course of the disease is being investigated and may be recommended for certain patients in the future.

Miscellaneous drugs that are less commonly used to treat RA but which may be useful in certain individuals include minocycline, azathioprine (Imuran), injectable gold, D-penicillamine, and anakinra (Kineret).

Minocycline is an antibiotic that is also used to treat acne and other skin diseases. Like HCQ, minocycline is usually used to treat milder RA, but one study showed that if started within one year of disease onset and continued for one year, up to 40% of patients went into remission. Other than nausea, dizziness, and sun sensitivity in some individuals, minocycline is usually very well tolerated.

Imuran is a medication that suppresses the immune system and may be effective at reducing the inflammation in the joints of RA patients as well as in other organ systems, such as the lungs. Increased infection rates, lowered blood counts, and liver damage are potential side effects.

Injectable gold is given once weekly in the doctor's office and must be monitored closely, including blood and urine tests with each visit to screen for low blood counts and protein in the urine. Rashes, damage to the liver, and lung damage are also potential side effects. While effective in treating RA, the inconvenience, toxicity, and delayed onset of action (4 to 6 months) have made gold a less popular choice among rheumatologists and patients.

D-penicillamine, a drug also used to bind toxic levels of heavy metals in the body, has a therapeutic effect in RA. The toxicity of this agent, however (blood cells, kidneys, liver, secondary autoimmune diseases), has led to less frequent use in treating RA patients.

Kineret is a newly introduced injectable drug given once daily and inhibits a substance know as interleukin-1 (IL-1). While effective in a subset of RA patients, responses to therapy are generally less dramatic that those seen with TNF antagonists. A somewhat increased infection rate and injection site reactions are the most commonly observed side effects.