Rheumatoid arthritis

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I. Introduction

Rheumatoid arthritis (RA) is a common type of arthritis that affects about 1% of the population in the US. Its cause is unknown although it is understood to be an *autoimmune* disease. What is an autoimmune disease?

II. Autoimmune disease.

The immune system is a very important part of the body. It is the defender of the body, i.e. it protects the body against invasion by germs. As an example, when someone acquires the "flu", he or she is infected, or invaded, by a virus. Viruses are living creatures that one needs a microscope in order to see. When the flu occurs, the virus has entered the body and the immune system, functioning as the body's "National Guard" sets out to destroy the virus. Muscle aches, fever, congestion, etc. are all symptoms of the battle that is going on inside a person as the immune system battles the virus. If the immune system wins, the virus is killed and all the symptoms disappear. If the virus wins, then the person dies.

For reasons that doctors don't understand, a person's immune system can become confused and attack the body itself. In other words, the protector attacks what it is supposed to protect, namely, the body itself. When this happens, an autoimmune disease is present and rheumatoid arthritis is an example of this type of disease.

III. Rheumatoid arthritis risk factors

Gender – Gender appears to play a major role in a person's susceptibility to RA. Women are about three times more likely than men to develop rheumatoid arthritis.
Genetics – Specific genes have been identified that increase the risk of acquiring RA. The story here, however, is complex. Indeed, when one identical twin has RA, the chance that the other will develop the disease is only about 1 in 3. Thus, it would appear that

the environment plays a bigger role than genetics in the cause of RA. Unfortunately, we don't have a good handle on what those environmental factors are.
Cigarette smoking – Smoking appears to increase the risk of developing RA. There is also some evidence that cigarette smoking increases the likelihood that RA will be severe when it occurs.
Stress – Stressful "life events" (divorce, accidents, grief, etc) are more common in people with RA in the six months before their diagnosis compared to the general population.

IV. Symptoms

Early symptoms may be present for weeks or months and include: fatigue, muscle pain, low-grade fever, weight loss and numbness and tingling of the hands (not all need to be present in a given person). As time goes by, joint symptoms become more prominent and include stiffness, warmth to the touch, swelling and, infrequently redness of the joints. The fingers, wrist, elbow, shoulder, hip, knee, ankle and foot can all be involved. In addition, the neck may be involved and cause an inability to bend the neck and turn the head. A joint near the windpipe (the cricoarytenoid joint) can become involved and cause hoarseness and difficulty breathing. The joint in the jaw (the temperomandibular joint or TMJ) can become involved and cause pain with opening and closing the jaw such as with chewing.

Recall that RA is an autoimmune condition and that the immune system's normal functioning requires it to defend the body. Therefore, the immune system can be called to act anywhere in the body and patients with RA can have involvement of other areas of the body besides the joints. Examples:

Rheumatoid nodules – painless lumps that appear beneath the skin. They most often occur on the underside of the forearm and on the elbow, but they can also occur on other pressure points, including the back of the head, the base of the spine, the Achilles tendon, and the tendons of the hand.

Inflammation of the tissue lining the chest cavity(pleurisy) and surrounding heart(pericarditis) may lead to chest pain and difficulty breathing.

Inflammation of the lung may cause shortness of breath and a dry cough.

Abnormal nerve function may cause numbness, tingling or weakness.

Inflammation of parts of the eye can cause redness of the eye, pain on exposure to bright light or even difficulty seeing.

Dryness of the eyes and mouth (Sjögren's syndrome) which can lead to a gritty feeling or sensation of irritating material in the eyes. Mouth dryness may make it difficult to chew or swallow without drinking something at the same time. Women may develop vaginal dryness leading to pain with sexual intercourse.

V. Rheumatoid arthritis diagnosis

Many physicians who are not rheumatologists believe that the diagnosis of RA can be made by ordering blood tests. This is incorrect. There is no single test used to diagnose RA. Instead, the diagnosis is based upon many factors, including characteristic signs and symptoms, the result of several laboratory tests, and, occasionally the result of X-rays. In other words, diagnosing RA involves placing several pieces of a puzzle together and the person best equipped to do this is the rheumatologist. The data is clear: earlier diagnosis leads to earlier treatment and better outcome. Therefore, if the question of the presence of RA in a given person is raised, it would be very prudent for that person to be evaluated by a rheumatologist.

Laboratory tests

Rheumatoid factor (RF) – This is an antibody found in the blood of about 80 % of patients with RA. Therefore, this test need not be positive in order for the disease to be present. Conversely, the presence of RF does not necessarily mean that the person has RA as there can be other reasons for its presence.

Anti-cyclic citrullinated peptide antibody (CCP) – This test is more specific for diagnosing RA and is positive in most (but not all) patients with the disease.

VI. Rheumatoid arthritis treatment

Unfortunately, no cure exists for this disease as yet although there is a lot of research that is ongoing and hopefully, one day, a cure will be forthcoming. In the meantime, it is of paramount importance to use medication early in the treatment of this disease. Untreated or improperly treated, RA will lead to permanent damage of the joints. Such damage will, in turn, lead to deformity and disability. Furthermore, recent research indicates that people with RA, particularly those whose disease is not well controlled, may have a higher risk for heart disease and stroke. It is of paramount importance to realize that not all patients with RA should be treated the same. In other words, it is critical that a rheumatologist who is experienced at the evaluation and management of RA assess the patient and individualize the therapy.

There are two broad types of medications used in the treatment of RA: those that control the symptoms, i.e. make people feel better, and those that help to slow down or arrest the disease, i.e. prevent or limit damage to the joints. The type of medication that can slow down or arrest RA is one of two types: the DMARD (disease modifying antirheumatic drug) and the biologic response modifier.

a. Medicines that reduce symptoms are of three basic types: NSAID's (nonsteroidal anti-inflammatory drugs), corticosteroids, and analgesics. There are many NSAID's on the market. Examples of these include: ibuprofen (Advil®, Motrin®), naproxen (Aleve), Celebrex, etc. These are very good medications but need to be used carefully as there are several risks including stomach irritation. Such irritation can lead to stomach pain, nausea and occasionally bleeding. They should probably be avoided in patients on blood thinners, e.g. warfarin, and in people with kidney disease.

   Examples of corticosteroids include prednisone and methylprednisolone (Medrol®). These medications work very quickly and usually do a very good job of reducing pain, stiffness and swelling in RA. Risk of side effects of these medications is significant, however, and can include weight gain, bruising of the skin, cataracts, softening of the bones (osteoporosis) and difficulty with wound healing. The good news is that at low doses, the risk of these medications decrease and may disappear completely at or below 5mg a day. Many healthcare workers do not realize this and frequently cause patients taking corticosteroids unnecessary anxiety about risks that may not exist.

   Analgesics, also called pain killers, are also frequently used. There is one over-the-counter analgesic available, acetaminophen (Tylenol®) and there are several prescription agents: tramadol, codeine, hyrdocodone, oxycodone, etc. With the exception of tramadol, the prescription analgesics are in the narcotic family. While it is true that some individuals have had trouble with substance abuse with narcotics, many times these agents are the most logical option in a patient who is at high risk of complications from NSAID's. The main side effects of the narcotics are constipation and drowsiness.

b. Disease-modifying antirheumatic drugs – substantially reduce the inflammation of RA, reduce or prevent joint damage, preserve joint structure and function, and enable a person to continue his or her daily activities. Depending on the DMARD, it can take between four and twelve weeks for the medication to become active and improve symptoms.

   Drugs in the class include hydroxychloroquine (Plaquenil®), methotrexate (Rheumatrex®), leflunomide (Arava®), sulfasalazine (Azulfidine®), gold salts (Ridaura®, Solganol®), d-penicillamine (Depen®, Cuprimine®), azathioprine (Imuran®), and cyclosporine (Sandimmune®, Neoral®). The risks of these medications vary but should all be monitored by a physician who is very familiar with them. Typically, the physician best trained to do this is the rheumatologist.

c. Biologic response modifiers. Biologics target molecules on cells of the immune system, joints, and the products that are secreted in the joints, all of which can

cause inflammation and joint destruction. The biologics are not oral medications; they all need to be injected. Some are self-injected, i.e. the patient or someone close to them injects the medication under the skin. Some are infusions, i.e. the patient goes to an infusion center and someone inserts a catheter into the patient's vein and the medicine infuses into their bloodstream. It is very important that infusion centers hire nurses as nurses are the most highly trained professionals to catheterize veins and monitor the patient during the infusion for adverse events.

i. Drugs administered intravenously, i.e. infusions:
    1. Infliximab (Remicade®) – targets tumor necrosis factor (TNF)
    2. Abatacept (Orencia®) – interferes with activation of T cells
    3. Rituximab (Rituxan®) – depletes B cells.
    4. Tocilizumab (Actemra®) – targets IL-6

ii. Drugs that are administered subcutaneously, i.e are "self-injectables":
    1. Adalimumab (Humira®) - targets TNF
    2. Etanercept (Enbrel®) - targets TNF
    3. Certolizumab pegol (Cimzia®) – targets TNF
    4. Golimumab (Simponi®) – targets TNF
    5. Anakinra (Kineret®) – targets IL-1

Unlike DMARD's, which can take between one and three months to begin working, biologics work rapidly, within two weeks for some medications. Because they are expensive (generally more than $15,000 per year in the US), biologics are often reserved for people who have not completely responded to DMARD's and for those who cannot tolerate DMARD's in large enough doses to control inflammation.

Biologic response modifiers interfere with the immune system's ability to fight infection and should not be used in people with serious infections or a history of hepatitis B exposure. Testing for tuberculosis is necessary before starting anti-TNF therapy. People with have evidence of prior TB infection should be treated because there is an increased risk of developing active TB while receiving anti-TNF therapy.

Anti-TNF agents are not recommended for people who have lymphoma or have been treated for lymphoma in the past. These agents are also not recommended for people who have multiple sclerosis.