

NATIONAL OFFICE
709 Tulbagh Centre
Hans Strijdom Avenue
Cape Town 8001
Box 6775

Roggebaai 8012
Tel: (021) 425 2344
Fax: (021) 421 7330
Website: <http://www.arthritis.org.za>
E-mail: info@arthritis.org.za

Western Cape Branch
705 Tulbagh Centre
Hans Strydom Avenue
Cape Town 8001
Tel/Fax: (021) 425 4759
E-mail: julie@arthritis.org.za

Johannesburg Branch
Box 87360
Houghton 2041
Tel: (011) 726 7498/726 7499
Fax: (011) 726 749
E-mail: Nadine@arthritis.org.za

Pretoria Branch
Box 145
Menlyn 0063
Tel: (012) 998 7203/421 6704
E-mail: patvdv@arthritis.org.za

Durban Branch
POSTNET # 309
P/B X04 Dalbridge 4014
Tel/Fax: (031) 539 5094
E-mail: roy@gmail.com

Bloemfontein Branch
Box 20269 Willows
Bloemfontein 9320
Tel/Fax: (051) 447 0451
E-mail: corrie@arthritis.org.za

Eastern Cape Branch
PO Box 7440
Newton Park 6055
Te: (041) 365 1419
Fax: 086 695 7117
E-mail: jeanette@arthritis.org.za



ARTHRITIS FOUNDATION

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RHEUMATOID ARTHRITIS

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Early diagnosis is critical for beating rheumatoid arthritis

Advances in the treatment of rheumatoid arthritis (RA) have raised hopes that further breakthroughs will one day prevent or cure this disease

As a result, early diagnosis and aggressive treatment, particularly in the case of children with arthritis, is critical. Fortunately an increased range of diagnostic tests are now available to help to identify RA at the early stage and pinpoint those children and adults who have a greater risk for persistent disease.

The critical very early diagnosis of RA is regarded as being at less than three months into the condition. After five months of having RA without treatment, 40% of patients already have irreversible joint erosions and at two years without treatment, 90% of patients have joint erosion.

Doctors usually classify RA in adults on the presence of at least four of the following criteria:

- Morning stiffness that lasts at least one hour and occurs for at least six weeks;
- Swelling of three or more joints, including hands and feet, for at least six weeks;
- Swelling of the same joints on both sides of the body;
- Changes in hand imaging that are characteristic of RA;
- Rheumatoid nodules under the skin;
- Rheumatoid factor found in the blood.

An estimated 1% of the world's population has RA, with the age of 40 to 50 years being when it most usually starts. Three times as many women as men are affected.

Taking control

People who find themselves with established rheumatoid arthritis beyond that two year mark without having had treatment, or treatment that wasn't aggressive enough, should not despair; they should start treatment right away.

Contact your doctor immediately if you experience any symptoms. For further information call the Arthritis Foundation Helpline 0861 30 30 30

About this booklet

This booklet aims to help people who have rheumatoid arthritis, and their families and friends. Rheumatoid arthritis is a complicated disease which varies a great deal from person to person, so a short booklet like this cannot tell you everything about it, but it will help you to understand rheumatoid arthritis – how it develops, and how to deal with it. We deal with the most common questions which people ask about the disease, and provide a brief glossary of medical words, such as cartilage, at the end of the booklet.

Please use this booklet as a guide to help you in your discussions with your doctor and with other health professionals. Do not be afraid to ask questions about your disease or your treatment. And do not be afraid to tell your doctor about all your problems. The more s/he knows about how the arthritis is affecting you, the better s/he can tailor your treatment to your needs. Managing rheumatoid arthritis involves a team of people, but you are the most important member of that team. The more you know, the more you will be able to contribute effectively to the management of your disease.

What is rheumatoid arthritis?

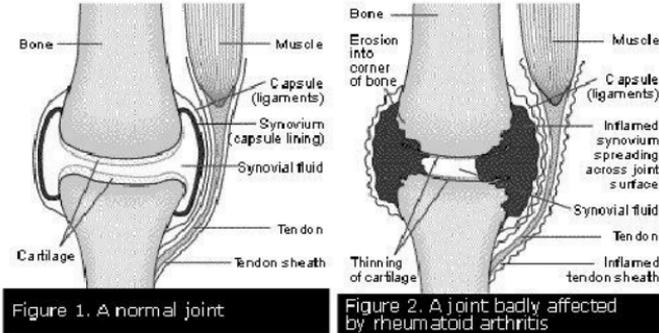
Rheumatoid arthritis is a disease in which the joints in the body become inflamed. There is a more detailed description of how this inflammation works later in this booklet (see 'What is inflammation?' in the section 'Questions and answers').

To understand how rheumatoid arthritis develops you need to understand how a normal joint works. A joint is where two bones meet. Most of our joints are designed to allow the bones to move in certain directions. For example, the knee is the largest joint in the body, and also one of the most complicated because it has many important jobs. It must be strong enough to take our weight and must lock into position so we can stand upright. But it also has to act as a hinge so we can walk. It must withstand extreme stresses, twists and turns, such as when we run or play sports.

Figure 1 shows a normal joint. The end of each bone is covered with cartilage which has a very smooth slippery surface. The cartilage allows the ends of the bones to move against each other almost without friction. It also acts as a

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shock absorber. The joint is surrounded by a membrane (the synovium) which produces a small amount of thick fluid (synovial fluid). This fluid acts as a lubricant to keep the cartilage slippery and help the joint to move smoothly. The synovium has a tough outer layer of ligaments called the capsule which holds the joint in place and stops the bones moving too much.



The changes that take place in rheumatoid arthritis are shown in Figure 2. Inflammation takes place within the synovium. The result is very similar to inflammation which you may have seen taking place within your eye – it goes red, it swells, it 'cries', and it hurts. The redness is caused by the flow of blood increasing. As a result, the inflamed joint may feel warmer than usual. The swelling is caused by a build-up of fluid and cells in the synovium. When a joint 'cries' it produces excess fluid – not tears but synovial fluid – which remains inside the joint, resulting in swelling. The joint hurts for two reasons:

- Nerve endings are irritated by the chemicals produced by the inflammation.
- The capsule is stretched by the swelling in the joint.

Is it the same as osteoarthritis?

No, osteoarthritis is a different disease. Rheumatoid arthritis is caused by inflammation in the lining of the joint. Osteoarthritis is more like a wear process, in which the cartilage in the joint can no longer withstand the loads placed on it. Some inflammation does occur in osteoarthritis, but it is not the same as that in rheumatoid arthritis. And some wear may take place in joints which have previously been damaged

by rheumatoid arthritis, but this is a complication which only occurs later in rheumatoid arthritis. The two diseases are quite different in their treatment and it is important not to confuse the two. If you have any doubt about which type of arthritis you have, ask your doctor.

How does rheumatoid arthritis affect different people?

Our bodies normally produce inflammation to destroy things, such as bacteria, which cause illness. We do not know what sets off the inflammation in rheumatoid arthritis, but the result is the same – unfortunately, in this case it is not bacteria or other harmful substances which are attacked but the tissues in the joints. The inflammation in rheumatoid arthritis causes damage to the cartilage and sometimes to the bone itself. It may also damage any ligaments within the joints.

The extent to which this happens varies a great deal from person to person. Some people have little or no damage to the joints, or suffer only very minor damage to a few joints. Most people with rheumatoid arthritis have some damage in a number of joints, and a few – about 1 in 20 (5%) of those with rheumatoid arthritis – have quite severe damage in a lot of joints. The joints which are most likely to be affected by rheumatoid arthritis are shown in Figure 3.

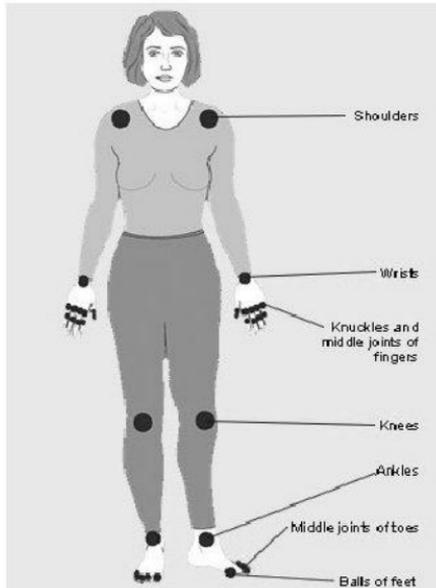


Figure 3. Joint frequently affected by rheumatoid arthritis. Less commonly affected are elbows, hips and the neck.

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Once joints have been damaged by inflammation they do not heal very well. Because of this, modern treatment tries to suppress the inflammation as much as possible in order to limit the damage which occurs. Suppressing inflammation early is one of the important ways in which treatment of rheumatoid arthritis has advanced and is one reason why treatment is more effective than it used to be.

Rheumatoid arthritis does not just affect the joints. Tendons are like ropes which run inside lubricated tubes. The lubricating system is very similar to that in the joints themselves, so it is not surprising that tendons can also be affected by rheumatoid arthritis. In a few people, other parts of the body such as the lungs and the blood vessels may become inflamed (see 'Are other parts of the body involved?' in the section 'How does rheumatoid arthritis develop?').

Inflammation in the joints can make some people feel generally ill. Sometimes this leads to overwhelming tiredness or fatigue, which may be as difficult, or even more difficult, to cope with than the painful joints. 'Feeling tired' is a symptom which may get little sympathy from those around you, who must be told that this is an important symptom of rheumatoid arthritis.

One problem with rheumatoid arthritis is that the symptoms tend to come and go with no particular pattern. You may have 'flare-ups' – periods when the joints become more inflamed and painful. Sometimes this has an obvious cause – either physical, such as unaccustomed physical exertion or another illness, or emotional, such as bereavement. Usually, though, there is no obvious cause, however hard you think about possible triggers. This unpredictability is frustrating and makes it difficult to plan ahead.

Rheumatoid arthritis can be a serious disease with a lot of symptoms. But most people, especially if they receive appropriate treatment, will have relatively few symptoms, and will be able to lead full, normal lives.

Who gets rheumatoid arthritis?

Many people believe that rheumatoid arthritis exists only in places with cool, damp climates such as Britain. This is not true. It exists all over the world. An estimated 1 % of the population has Rheumatoid Arthritis.

It can happen in people of any age, from children to those in their 90s, but the most common age for the disease to start is between 40 and 50. About three times as many women as men are affected.

There is some evidence that lifestyle factors are associated with rheumatoid arthritis. These are not direct causes of the disease, but rheumatoid arthritis may be more common, for example, in people who smoke, or eat a lot of red meat, or who are overweight. Those with high vitamin C intake seem to have a lower risk of developing rheumatoid arthritis. Those who drink alcohol in moderation are at less risk than either heavy or non-drinkers.

Does it run in families?

Rheumatoid arthritis does seem to run in some families – but most relatives of people with rheumatoid arthritis do not develop it themselves. In particular, your children are more likely **not** to get it than to get it. There are lots of causes of arthritis and joint pain, many of which are more common than rheumatoid arthritis. If someone in your family develops joint pain, it may well be due to one of these other causes and it does not necessarily mean that they have rheumatoid arthritis. There are genes that increase the likelihood of developing the disease, but even the identical twin of somebody with rheumatoid arthritis, who shares all the same genetic material, only has a 1 in 5 (20%) chance of developing the disease. This shows that genes are only a part of the reason why rheumatoid arthritis develops. The severity of the disease is also often very different between affected family members.

How does rheumatoid arthritis develop?

The start of the disease

In most people rheumatoid arthritis starts quite slowly. A few joints – often the fingers, wrists or the balls of the feet – become uncomfortable and may swell, often intermittently. You may feel stiff when you wake up in the morning. Many people only seek help from the doctor when the symptoms become more severe or more frequent.

For about 1 in 5 (20%) of those with rheumatoid arthritis the disease develops very rapidly. There may be a sudden onset of pain and swelling in a lot of joints, with severe morning stiffness and great difficulty doing everyday tasks.

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Along with pain and swelling in the joints you may feel tired, depressed or irritable, even with mild arthritis. You may also feel frightened about the future, and angry – 'Why has this happened to me?' At the moment there is no answer to that question, but this booklet should help you understand what is happening.

When should I go to the doctor?

It is very important that treatment for rheumatoid arthritis is started as early as possible in the disease. This means it is essential that you see your doctor as soon as you can if you have any symptoms, such as pain and swelling in the joints and stiffness in the mornings, which might be caused by rheumatoid arthritis. Your symptoms may not be due to rheumatoid arthritis as there are many other causes of joint pain, but it is important to diagnose arthritis as soon as possible. The more we learn about the disease, the more we realize that early diagnosis and early treatment are very important if rheumatoid arthritis is to be managed effectively.

How will it progress?

This is the single question that most people want answered. For each individual patient the answer is 'We cannot tell for sure.' However, from the study of a large number of people with rheumatoid arthritis we can give some general guidelines (see Figure 4). Blood tests and x-rays will help your doctor to assess how fast the arthritis is developing and how quickly it is likely to progress in future. This in turn will help him or her to decide which form of treatment to

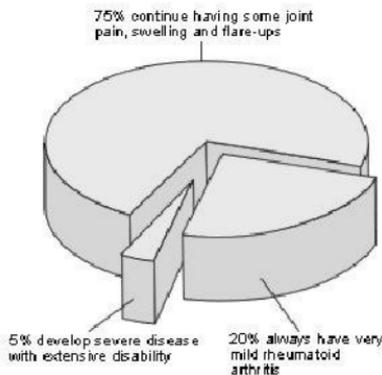


Figure 4. How people with rheumatoid arthritis are likely to be affected

recommend.

Some people, maybe as many as 1 in 5 (20%), always have very mild rheumatoid arthritis which causes few problems.

Most people follow a pattern of flare-ups with periods of months or even years in between when there is little inflammation. This does not mean there are no problems at all between flare-ups, as some damage is done to the joints every time they are inflamed. People whose disease follows this pattern will have some problems with their joints and may have to modify their activities a little, but overall they will lead normal lives.

A few people, no more than 1 in 20 (5%), will have rheumatoid arthritis which becomes progressively worse, often quite quickly. These are also the people who tend to have inflammation in other parts of the body besides their joints.

Are other parts of the body involved?

Although 'arthritis' means inflammation of the joints, it is not just the joints that are affected. Most people have some general problems such as fatigue and stiffness. A lack of red blood cells (anaemia) is very common – occasionally this can be a side-effect of the drugs used to treat rheumatoid arthritis, but it is more often caused by the disease itself. Some people with uncontrolled rheumatoid arthritis lose weight, and many complain of hotness and sweating brought on by the inflammation.

Sometimes other organs are involved. There may be inflammation in the eyes, and they quite often become dry and irritable. Inflammation may also affect the lungs and, rarely, the membrane around the heart. Rheumatoid nodules may appear. These are fleshy lumps which usually occur just below the elbows, but may appear on hands and feet as well. They may occur in other places but this is rare. If there is any doubt about the cause of the lumps, the doctor can if necessary remove a piece from them which allows them to be easily checked and identified under a microscope. (This is known as a 'biopsy'.)

It has also become apparent recently that people with rheumatoid arthritis are more at risk of heart attack and strokes. It seems to be an effect of the inflammation and the risk is probably reduced by controlling the disease, for

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example, with drugs. The risk is not very great, but it needs to be taken into account along with other risk factors such as high cholesterol and smoking. It is a very good idea to stop smoking if you develop rheumatoid arthritis.

How do doctors diagnose rheumatoid arthritis?

There is no single test which can make a certain diagnosis of early rheumatoid arthritis. Doctors have to make what is known as a 'clinical diagnosis', where they put together all the information from listening to you and examining you, and come to a diagnosis based on this information. This is one of the reasons why you should tell your doctor all the symptoms you have had, not just the ones you think are important.

There are two kinds of test which may help in confirming the diagnosis:

- blood tests
- x-rays and other imaging techniques.

Blood tests

Blood tests may show you are anaemic, a problem which affects about 8 out of 10 people with rheumatoid arthritis (80%). They may also detect changes in your blood which are produced by inflammation. The original test of this type was called the erythrocyte sedimentation rate (ESR). The most recent test is for a protein called C-reactive protein (CRP). Each of these may show a high value when inflammation is present. Which test is used depends on the laboratory to which your doctor sends blood samples.

The 'rheumatoid factor' is another blood protein which is produced by a reaction in the immune system. About 8 out of 10 people with rheumatoid arthritis (80%) have positive tests for this protein. But its presence does not make the diagnosis certain – about 1 in 20 people without rheumatoid arthritis (5%) also have positive tests. Also, only about half of all people with rheumatoid arthritis have a positive rheumatoid factor when the disease starts. Other people with rheumatoid arthritis will never develop positive rheumatoid factor. So although the rheumatoid factor test is sometimes called 'the test for rheumatoid arthritis', it isn't really. It is just one of the tests that can help doctors make the diagnosis.

New tests are being developed which are more accurate in diagnosing rheumatoid arthritis. These will make early diagnosis easier in the future. One of these is anti-cyclic citrullinated peptide antibody (anti-CCP) which is a further screening test in seronegative rheumatoid arthritis.

X-rays and other imaging techniques

X-rays can reveal any damage caused to the joints by the inflammation in rheumatoid arthritis. One thing which may puzzle you is that you may have x-rays taken of your feet even if they are not causing you any problems. This is because the changes caused by rheumatoid arthritis often show up in x-rays of the feet before they appear in other joints.

Doctors now want to make the diagnosis of rheumatoid arthritis even before the changes show up on the x-rays. Magnetic resonance imaging (MRI) and ultrasound scanning are more sensitive in picking up changes and are being studied to see how useful they are for diagnosing early disease and for monitoring its progress. They may be widely



used in the future. An MRI scan of a normal knee joint is shown in Figure 5.

How can rheumatoid arthritis be treated?

We have not yet found a cure for rheumatoid arthritis, but treatment is improving all the time. A team of health professionals will work with you to try to get the best possible result. However, you are by far the most important person in the team, and one way you can help is by understanding as

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much as possible about your disease and its treatment.

Reading this booklet is part of that process.

There are three main ways of treating rheumatoid arthritis:

- **Taking care of your joints.** You can do this by following the practical tips in the next part of this booklet.
- **Treatment with drugs.** Many people are worried about taking drugs because of the risks of side-effects, so this is discussed in detail later in this booklet.
- **Surgery.** This is occasionally needed. You may receive advice about the need for surgery both from your rheumatologist and from a surgeon with a special interest in surgery for arthritis. Operations vary from quite minor ones such as the release of a nerve or a tendon to major surgery such as joint replacement.

How can I take care of my joints?

Balancing rest and exercise

One of the most important balancing acts you will need to achieve is the balance between rest and exercise. We have known for centuries that resting inflamed joints makes them more comfortable. However, the joints and muscles are parts of the locomotor system, the parts of the body which are involved in movement. Without movement your joints will stiffen and your muscles will waste away. So what should you do? The most important thing is to use your muscles and joints as much as possible without harming them. This helps retain movement and stops muscles wasting away. We also know that exercise is a good thing in general, and that exercise helps you feel better.

How do you know if you are doing harm? Some people have been told it is best to stop as soon as something hurts. This is not necessarily true. The signs to stop are if a particular activity causes one or more of your joints to become warm and swollen or if there is severe pain. If neither of these things happens, keep going.

There is no magic formula which can tell you how to balance rest and exercise – it is something you will need to discover for yourself. However, there are some things worth bearing in mind. If you are having a good day, avoid overdoing things. This particularly applies to tasks such as housework or gardening. Many people suffer the next day because of

overexertion on a good day. Do make it clear to family, friends and colleagues at work that not all days are the same. They must realize that activities you find easy on a good day may be impossible on a bad one. If a particular activity always causes problems, ask yourself if it is really essential and, if it is, could it be done in an easier way (or by somebody else)? But above all try to use both periods of activity and periods of rest to their best advantage.

What about sport?

If you have rheumatoid arthritis you should avoid contact sports such as rugby or football, and should probably avoid other violent types of exercise such as squash. Do continue with less violent activity such as badminton or walking. You should always take a lot of care over choosing your footwear if you are playing sport. Good shoes with shock-absorbing soles are essential, as is a good warm-up routine. Swimming is the best exercise of all. The muscles can be exercised with minimal strain on the joints because the water supports your weight, and the level of activity can be varied from very mild

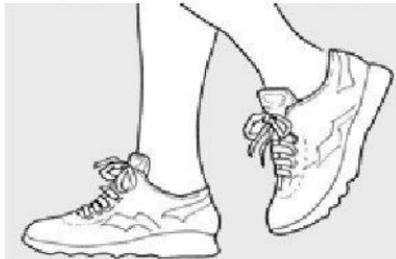


Figure 6. Trainers with thick soles help absorb shocks when exercising.

to very strenuous. If you cannot swim, learning could be one of the best investments you can make in your future.

Many people now go to gyms or health clubs and people with rheumatoid arthritis often find them a valuable part of their lives. If you go, do tell the fitness instructor about your disease so that an appropriate exercise plan can be developed for you. Your physiotherapist can advise you about this too. In general it is best to avoid exercises involving hard impacts,



Figure 7. Learning to swim could be one of the best investments you can make in your future.

such as step exercises. Aquaerobics (aerobics in a swimming pool) is a very valuable form of exercise for most people.

Protecting your joints

Protect your joints from unnecessary strain. There are different ways of carrying out many everyday activities, so use the methods which put the least strain on your joints. Your occupational therapist can give you detailed advice about this, and also about ways of avoiding some tasks or using simple aids or adaptations to make them easier. Help of this sort can often allow you to continue many activities despite having rheumatoid arthritis. Do ask for, and listen to, advice which will help you increase the activities you can undertake.

How can drugs be used to treat rheumatoid arthritis?

Many people are worried about taking drugs because of the risks of side-effects. We have to accept that all drugs have side-effects, including common everyday drugs such as alcohol and caffeine – and especially nicotine. For most people with rheumatoid arthritis, the benefits of drug treatment far outweigh any possible side-effects. Treatment is more effective than ever, and drugs are checked for safety more carefully than ever before.

Before we look at the specific drugs used for rheumatoid arthritis, three things are worth thinking about:

- First, if there were a drug-free, side-effect-free wonder cure available for rheumatoid arthritis, we would know about it. Do not believe tales about treatments of this kind. They do not exist.

- Second, some of your friends or relatives may take a contemptuous view of drug-taking, with comments like 'You'd never catch me poisoning my body with that rubbish'. Remember, they do not have your disease and do not need your treatment, so that is an attitude they can afford to take. Discuss treatment with your friends and relatives, but remember it is your disease and your body, and you deserve the best possible advice, which will be given to you by your rheumatology team and your general practitioner's team.
- Third, remember that the earlier treatment is started the more effective it will be. Think carefully about your treatment, but do not delay until your joints are badly damaged. Treatment is less effective when it starts late.

Which drugs are used?

Several of the drugs mentioned here have more than one name. This is because each drug is given an 'approved' name, but each manufacturer gives their own brand name to the drug eg. Diclofenac is an approved name; Voltaren, Panamor, Cataflam are different brand names of the same drug. If you have any doubt ask your doctor, pharmacist or nurse for advice. We will use the approved names here.

Four kinds of drugs may be used to treat rheumatoid arthritis; analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying anti-rheumatic drugs (DMARDs) and corticosteroids.

1. Analgesics

These drugs are painkillers. They are not sufficient by themselves as a treatment for rheumatoid arthritis, but they are useful to 'top up' the pain-relieving effects of other, more specific, drugs. Paracetamol is most often used. It may be given by itself, or alongside codeine tablets, or as combination tablets in which it is combined with codeine or other drugs. The most common side-effect of stronger analgesics is constipation, which can occasionally be severe.

2. Non-steroidal anti-inflammatory drugs (NSAIDs)

The first drug in this group was aspirin, which used to be given in very large doses to treat arthritis (10–20 tablets a day). There are now about 20 drugs of this kind available.

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They reduce pain and swelling and start working within a few hours. The effect of some will only last a few hours but others are effective all day. Your doctor will help you to find the preparation and dose best for you.

Although NSAIDs are very useful drugs, they do have a tendency to cause indigestion and, rarely, bleeding from the stomach.

There have been two approaches to reducing the stomach problems caused by NSAIDs. Extra drugs can be given alongside the NSAIDs to prevent the side-effects in question. The most potent of these are called proton pump inhibitors (PPIs) which both reduce indigestion and protect the stomach. Many people feel uncomfortable about taking drugs just to avoid the side-effects of other drugs, but most people with rheumatoid arthritis do need the pain-relieving effects of their NSAIDs, so such a combination might be essential.

The other way of dealing with the stomach problems associated with NSAIDs relies on our growing understanding of the way in which they cause their good and bad effects. Both are due to their effect on an enzyme called cyclo-oxygenase (COX). We now know that COX exists in two forms, called COX-1 and COX-2. It is the effect on COX-1 which causes side-effects such as the stomach problems and the effect on COX-2 which reduces pain and inflammation. Some of the newer NSAIDs, known as COX-2 inhibitors (or 'coxibs'), are less likely to cause stomach problems. However, these have been linked with increased risks of heart attack and stroke, so they are not suitable for people who have had a heart attack or stroke in the past, or for people who have uncontrolled high blood pressure. You should consult your doctor or rheumatology nurse if you are concerned about whether these drugs are suitable for you.

3. Disease-modifying anti-rheumatic drugs (DMARDs)

As their name suggests, these drugs do not treat the symptoms of rheumatoid arthritis but reduce the effects of the disease itself. They do improve symptoms over time, but they are not painkillers – they only reduce pain and stiffness by reducing the underlying rheumatoid process in the joints. They also appear to slow down the effects of the disease on the joints, especially if they are taken early in the course of the disease.

These drugs are our most important weapons in combating rheumatoid arthritis. They do not act quickly, taking weeks or

even months to become effective. It is important to continue taking them, even if they do not seem to be working at first. They are taken for long periods, usually many years. Not everyone with rheumatoid arthritis will need one of these drugs, but most people with rheumatoid arthritis should expect to take drugs of this type, sometimes for the rest of their lives. They can all cause side-effects, which very rarely may be dangerous. Because of this they all require regular supervision by doctors and nurses who understand them. This often includes regular blood and urine tests. These are important, as they ensure your safety. With careful, knowledgeable supervision, these drugs are not only safe but also very effective in treating rheumatoid arthritis. There are a number of drugs in this group, and new ones are on the way. A few of the more commonly used ones are described below.

Methotrexate This drug is immunosuppressive, that is it has the effect of suppressing the immune system. It is usually taken by mouth in weekly doses, but can also be given by weekly injections. It is probably the most effective of the conventional disease-modifying drugs. Methotrexate should not be taken by pregnant women, or by men or women wishing to start a family, so it is *essential* to take effective contraceptive precautions while taking methotrexate. Most people also take a small dose of the vitamin folic acid with their methotrexate, as this reduces side-effects. The main side-effects are nausea and indigestion. Methotrexate can affect the blood (one of the effects can be that fewer blood cells are made), but regular blood tests will be undertaken so that any problems can be identified at an early stage. There is also a slightly increased risk of infections while you are on methotrexate. Note that if you drink alcohol you should only drink it in small amounts because methotrexate and alcohol can interact and damage your liver. Discuss this with your doctor or nurse.

Leflunomide This is a more recently introduced drug which is about as effective as methotrexate. It is given as a daily dose by mouth. The main side-effects are abdominal (tummy) pain, sickness and diarrhoea, all of which are quite common. Women must not become pregnant while taking leflunomide, nor for 2 years after treatment has stopped unless the drug is 'washed out' of the system. Men who have taken leflunomide should not try to father children until 3 months after stopping the drug. Regular blood tests are needed while taking leflunomide.

Sulfasalazine This drug was specifically designed to treat

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rheumatoid arthritis and was first made more than 50 years ago, but has come into more common use in the past 20 years. It is taken by mouth in a dose which is slowly increased. Side-effects such as a feeling of sickness are usually short-lasting.

Azathioprine This is also an immunosuppressive drug, although a little less effective than methotrexate for most people. Similar blood tests need to be taken while it is being used.

Gold Gold injections have been used to treat rheumatoid arthritis since the 1930s. The injections are given each week at first, although the frequency may be decreased as the gold becomes effective. Gold injections can be continued for life if they are helpful. Side-effects can occur, affecting the blood and the kidneys, and regular blood and urine tests are used to check for any abnormalities. Skin irritation may sometimes occur. Gold tablets were introduced at one point but are very rarely used because they are not as effective as the injections.

Penicillamine This drug is a distant relative of penicillin, but can be used safely by people who are allergic to penicillin. It is taken by mouth in a slowly increasing dose. Its effects, side-effects and precautions are very similar to those of gold injections. Occasionally penicillamine can diminish your sense of taste, but this effect is short-lasting and disappears after a time.

- The use of gold and penicillamine has declined in the past 15 years.
- Gold injections are not marketed in South Africa anymore.

BIOLOGICAL THERAPIES The most recently introduced disease-modifying treatments for rheumatoid arthritis are known as biological therapies. This name is used because they have been developed through our increased understanding of the processes in the body which lead to inflammation and damage in joints. This knowledge has enabled scientists to develop drugs which target individual molecules which are involved in these processes. This has led to some new and very effective treatments for rheumatoid arthritis.

(a) Anti-TNF

The first three of these drugs to be approved for use, all target a substance called tumour necrosis factor (TNF). This has a

key role in the complicated process of inflammation. The drugs are sometimes referred to as 'anti-TNF' therapies.

- **Infliximab** is given by an intravenous 'drip' every 8 weeks, either in a hospital day unit or in a dedicated area within the rheumatology department. It is usually given in combination with methotrexate, as this prevents the body developing antibodies which would make the infliximab less effective. It is not, therefore, suitable for anyone who has had to stop methotrexate because of side-effects, but it is useful in people who have found that methotrexate by itself does not work.
- **Etanercept** is given twice a week by injection just under the skin (subcutaneous injection). People who are prescribed this drug are taught to inject themselves, which most people manage very easily. Etanercept can be given alone or in combination with methotrexate.
- **Adalimumab** is also given by subcutaneous injection but the frequency of injections is once every other week. The side-effects are similar to those of infliximab and etanercept. Like etanercept, adalimumab can be given either alone or in combination with methotrexate.

These are all new drugs, so any long-term side-effects are not yet known. The monitoring of these drugs is aimed at assessing how well they work as well as at checking their safety. People taking methotrexate as well will also need the usual safety monitoring for that drug. In some people these drugs have proved very effective in improving their arthritis and in helping them feel better generally.

(b) Anti-IL-1

- **Anakinra** works in a different way from the anti-TNF drugs. It inhibits one of the messenger substances in the body called interleukin-1 (IL-1). It is given by daily injections under the skin which patients are taught to give themselves. It is used along with methotrexate when that drug is proving ineffective by itself. Side-effects include pain at the injection sites and some increase in infections. Regular blood monitoring is needed.

(c) B-cell depletion

The B-cells are the cells of the immune system that produce antibodies, including rheumatoid factors. B-cells can be attacked and killed by drugs that recognize molecules only

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found on the surface of the B-cells.

· **Rituximab** is a drug that recognizes and attacks the molecule CD20 on the surface of B-cells and this leads to those B-cells being destroyed. Research has shown that when people with rheumatoid arthritis are given two infusions of rituximab 1–2 weeks apart, the number of B-cells in the blood falls dramatically. Many of these patients also showed improvements in their arthritis which were sustained for many months. Although the patients did not need to have more doses of rituximab during this period, some of them continued to take other drugs such as methotrexate. Rituximab is not used routinely to treat rheumatoid arthritis at present but it may be used more often in future to treat patients who have not benefited from other therapies.

Because biological therapies are very expensive and there is little experience of their long-term use, rheumatologists are encouraged to enter their patients on a register (through their Professional Society SAARA). This allows the progress of all people taking these medications to be followed using a set of standard methods. This information will be invaluable in finding out how best to use these new drugs so that they give the most benefit.

4. Corticosteroids

Corticosteroids are often called 'steroids' for short. They are not the same as the 'steroids' used by athletes to build up their bodies – these are compounds properly called 'anabolic steroids'. Cortisone, a natural hormone produced by the body, was first used in the 1950s to treat rheumatoid arthritis. From this early work two things were observed. First, corticosteroids (steroids) have a very powerful effect on inflammation, reducing it more than any other drug used. Secondly, there are quite a lot of side-effects if high-dose steroids are given for long periods of time; these include problems such as thinning of the bones (osteoporosis) (see AF booklet 'Osteoporosis'). Since then, a lot of research has been carried out to try and find the best way of gaining the benefits of steroids while minimizing the side-effects. Steroids are now used in three ways:

· by injection into an inflamed joint. This is an effective way of reducing inflammation in that joint. Provided the

injection is given carefully and skilfully, it is very safe.

- by intramuscular or intravenous injection to damp down a severe inflammatory flare-up of arthritis. This form of treatment must also be used skilfully to maximize benefits and minimize side-effects.
- by mouth. If the steroids are used in low doses most of the side-effects are not a great problem, but even with low doses it is now recommended that anti-osteoporosis medication be taken if the steroids are used for more than 3 months. In general, rheumatologists like to give only small doses of steroids (up to 7.5 mg of prednisolone a day) to treat rheumatoid arthritis, but there are some rare complications of the disease such as inflammation of blood vessels (vasculitis) where higher doses are needed.

Used properly, steroids can be a very valuable treatment for rheumatoid arthritis and can help to control the symptoms of the disease.

Questions and answers

What is inflammation?

Inflammation is a normal body defence mechanism. Your body recognizes that something abnormal is present. It responds by increasing the blood flow to the affected area in order to bring in the body's defences and to raise the temperature, which also helps in dealing with the unwanted germs or substances. The blood vessels become more leaky so that cells can move out of them to join in the attack.

The cells themselves produce chemical messengers which call other cells to join them in the immune response. These chemical messengers are the targets of the biological therapies mentioned earlier. The cells also produce chemicals designed to destroy the invader, and antibodies to help in the fight. The messengers, chemicals and antibodies are all the focus of research which may lead to new treatments for rheumatoid arthritis.

So why does inflammation occur in rheumatoid arthritis?

The normal process of inflammation described above starts off with some sort of foreign substance, such as a bug,

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invading the body. The process ends when the invader is overcome. Inflammation in rheumatoid arthritis is unusual for two reasons. First, nobody knows what starts it off. It seems that in rheumatoid arthritis the body thinks that a part of itself is an invader and therefore attacks it. Why this happens is unknown. Finding out why is a key to discovering a cure for rheumatoid arthritis. Because the body attacks itself in rheumatoid arthritis, it is known as an 'autoimmune' disease. Secondly, the inflammation in rheumatoid arthritis is unusual because it does not stop of its own accord – it becomes a long-lasting (chronic) process.

The main site of inflammation in rheumatoid arthritis is the lining (synovium) of the joints. This becomes swollen and full of cells. The destructive process may then attack the cartilage and bone in the joint. The swelling causes the tough capsule to stretch. When the swelling goes down the capsule remains stretched and fails to hold the joint in its proper position. As a result the joint becomes less stable and can move into unusual or deformed positions.

Can complementary therapies help?

Many people with rheumatoid arthritis take 'complementary', 'alternative', or 'natural' therapies. It is quite understandable that people with rheumatoid arthritis want to do as much as possible to help themselves. Unfortunately, the promises made by most of these remedies are not borne out in reality. Certainly none of them offers either a cure or a reduction in the joint damage caused by rheumatoid arthritis. Many are also very expensive, and add a financial burden to that of the disease.

Cod liver oil and other fish oils, evening primrose oil and some vitamins may have a mild effect on the symptoms of rheumatoid arthritis (see AF booklets 'Diet and Arthritis' and 'Complementary Therapies and Arthritis'). Herbal remedies are usually safe to use, but some may interfere with your anti-rheumatic medication. A good herbal practitioner will be able to advise you about this. Do remember also that some herbal remedies can have unpleasant side-effects.

Treatments such as acupuncture, which some people find helpful, are now generally available. Homoeopathy is also available, but sadly has proved ineffective in treating rheumatoid arthritis. Massage is often very soothing and relaxing, although there is little evidence that specific oils add

any particular benefit.

Most complementary therapies are harmless, and, as mentioned above, some may be of some help. But be careful what you buy, as unfortunately some 'traditional' medications, especially Chinese remedies, sold in this country have been found to contain large quantities of steroids and other drugs. Be critical about whether you are getting a benefit from what you are doing. Do discuss any remedies you are thinking of taking with your doctor, nurse or pharmacist, and do remember the general rule: 'Things that seem too good to be true are too good to be true'.

Is there a diet which will help my rheumatoid arthritis?

There is a lot of publicity for diets which claim to cure rheumatoid arthritis. None do, although there is some scientific evidence that diets may help the symptoms in some people. A few people notice that individual foods tend to make their arthritis flare up. The foods which do this vary from person to person. If you suspect that an individual food causes your joints to flare up, then try avoiding it, but do not give up anything because it makes someone else's joints flare up – remember, we are all different. (See AF booklet 'Diet and Arthritis'.)

Do any diets help everyone?

Probably not, but the ones most likely to help are low in saturated fats and high in unsaturated fats, especially fish oils. Supplements of fish oils are likely to help. There is some evidence that a very strict vegetarian diet can help, although the reasons for this are not clear, and that there may be a small increase in the risk of rheumatoid arthritis among people who eat a lot of red meat. However, you should consult your doctor or a dietitian before starting any strict diet as the disadvantages may outweigh the advantages. There is some evidence that increasing your intake of vitamin C may also help. It is a good idea to make sure you keep your weight down. You put the equivalent of four times your body weight through your joints when you are just walking, so keeping your weight down will help reduce that stress. More information is given in the AF booklet 'Diet and Arthritis'.



Figure 8. Keeping to the correct weight reduces stress on joints.

Should I move to a different climate?

The weather does affect the symptoms of some people with rheumatoid arthritis, but it does not affect the progression of the disease. Many people who are affected find warm weather better than cold, although damp heat often makes people uncomfortable. For some people, cold crisp winter days are the best of all.

If you do think of moving, try the new climate in all seasons before you make your final move. Also weigh up the consequences of leaving your friends and family, as well as the support of your familiar health care system. Above all, remember that a change of climate will not affect the disease itself and will not prevent it progressing.

Should I avoid becoming pregnant?

The answer is no, unless you already have a very large family which is consuming all your energy. Most mothers with rheumatoid arthritis feel better during pregnancy. The exact mechanism for this is unknown. The immune system, while 'tolerating' the growing baby, seems to 'tolerate' the joints more. Unfortunately the symptoms are likely to flare up again after the baby is born, but this can usually be dealt with quickly. What is important is to make sure you are not taking any drugs which could harm your baby. Methotrexate is especially harmful. Discuss your medication with your doctor

before you become pregnant.

What about having sex?

There is no reason at all why you should stop having sex. You may find that some positions for intercourse are more comfortable than others, so do experiment.

Is it all right for me to take the pill?

Yes, it will make no difference to your arthritis or its treatment, and it may be important if you are taking any drugs such as methotrexate or leflunomide which mean that pregnancy must be avoided.

What about work?

The aim of treatment is to keep you doing as many activities as you did before the arthritis started. This includes both work and hobbies. You should be able to keep on with your work, unless it involves a lot of manual effort.

Why me? What have I done to get rheumatoid arthritis?

You have done nothing to bring on your disease. It is just random bad luck that means you have got it. Do not waste your energy trying to think how you or someone else could have caused your disease. Use your energy instead to fight the disease and to learn how to do as much as possible to minimize the effects it has on you. Modern drugs and a helpful rheumatology team make an enormous difference, but the difference you make is just as great, so make sure you make the strongest possible contribution to your own care.

What are we learning from research?

We now understand far more about the process of inflammation, and this understanding has led to the promise of new and better forms of treatment for rheumatoid arthritis.

Glossary

Analgesics – painkillers. As well as dulling pain they lower raised body temperature, and most of them reduce inflammation.

Antibodies – blood proteins which are formed in response to germs, viruses or any other substances which the body sees as foreign or dangerous. The role of antibodies is to attack foreign substances and make them harmless.

Capsule – the tough, fibrous sleeve of ligaments around a joint. Its inner layer is the synovium.

Cartilage – strong material on bone ends that acts as a shock-absorber. Its slippery surface allows smooth movement between bones.

Corticosteroids – drugs which have a very powerful effect on inflammation. Often called 'steroids' for short.

C-reactive protein (CRP) – concentrations of this protein in the blood can be measured as a test of inflammation or disease activity.

Disease-modifying anti-rheumatic drugs (DMARDs) – drugs which reduce pain and stiffness in rheumatoid arthritis.

Erythrocyte sedimentation rate (ESR) – a test which shows the level of inflammation in the body and can help in the diagnosis of rheumatoid arthritis. Blood is separated in a machine with a rapidly rotating container (a centrifuge), then left to stand in a test tube. The ESR test measures the speed at which the red blood cells (erythrocytes) settle.

Locomotor system – the parts of the body which allow us to move. It includes bones, joints, muscles and other connective tissues.

Magnetic resonance imaging (MRI) – a type of scan which uses high-frequency radio waves in a strong magnetic field. The radio waves interact with water molecules in body tissues, and give out a characteristic signal in the magnetic field. The signals which come back are processed by computer to build up pictures of the inside of the body.

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Non-steroidal anti-inflammatory drugs (NSAIDs) – a large family of drugs, prescribed for different kinds of arthritis, which reduce inflammation and control pain, swelling and stiffness.

Proton-pump inhibitor (PPI) – a drug which acts on an enzyme in the cells of the stomach to reduce the secretion of gastric acid.

Synovial fluid – the fluid produced by the synovium to nourish and lubricate the joint.

Synovium – the inner membrane of the joint capsule which produces synovial fluid.

Ultrasound scan – a type of scan which uses high-frequency sound waves to examine and build up pictures of the inside of the body.