

## Rheumatoid Arthritis

Rheumatoid arthritis causes inflammation, pain, and swelling of joints. Persistent inflammation over time can damage affected joints. The severity can vary from mild to severe. Treatments include disease-modifying drugs to suppress inflammation which can prevent or delay the progression of the disease, and medication to ease pain. The earlier treatment is started, the less joint damage is likely to occur. Surgery is needed in some cases if a joint becomes badly damaged.

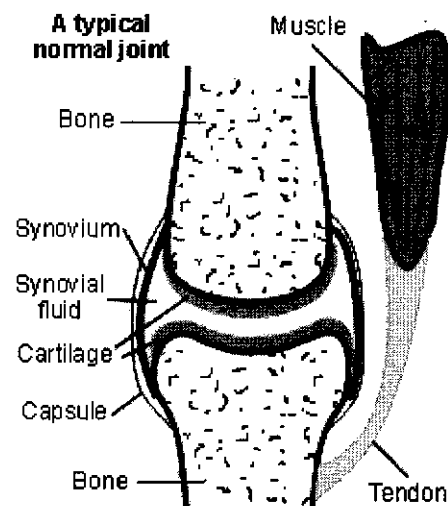
### What is rheumatoid arthritis?

Arthritis means inflammation of joints. Rheumatoid arthritis (RA) is a common form of arthritis. (There are various other causes of arthritis and RA is just one cause.) About 1 in 100 people develops RA at some stage in their life. It can happen to anyone. It is not an hereditary disease. It can develop at any age, but most commonly starts between the ages of 40 and 60. It is about three times more common in women than in men.

### Understanding joints

A joint is where two bones meet. Joints allow movement and flexibility of various parts of the body. The movement of the bones is caused by muscles which pull on tendons that are attached to bone. Cartilage covers the end of bones. Between the cartilage of two bones that form a joint there is a small amount of thick fluid called synovial fluid. This 'lubricates' the joint which allows smooth movement between the bones.

The synovium is the tissue that surrounds a joint. Synovial fluid is made by cells of the synovium. The outer part of the synovium is called the capsule. This is tough, gives the joint stability, and stops the bones from moving 'out of joint'. Surrounding ligaments and muscles also help to give support and stability to joints.



### What causes rheumatoid arthritis?

RA is thought to be an autoimmune disease. The immune system normally makes antibodies (small proteins) to attack bacteria, viruses, and other germs. In people with autoimmune diseases, the immune system makes antibodies against tissues of the body. It is not clear why this happens. Some people have a tendency to develop autoimmune diseases. In such people, something might trigger the immune system to attack the body's own tissues. The trigger is not known.

In people with RA, antibodies are formed against the synovium (the tissue that surrounds each joint). This causes inflammation in and around affected joints. Over time, the inflammation can damage the joint, the cartilage, and parts of the bone near to the joint.

### Which joints are affected in rheumatoid arthritis?

The most commonly affected joints are the small joints of the fingers, thumbs, wrists, feet, and ankles. However, any joint may be affected. The knees are quite commonly affected. Less commonly the hips, shoulders, elbows, and neck are involved. It is often symmetrical. So, for example, if a joint is affected in a right arm, the same joint in the left arm is also often affected. In some people, just a few joints are affected. In others, many joints are involved.

### What are the symptoms of rheumatoid arthritis?

#### Joint symptoms

The common main symptoms are pain and stiffness of affected joints. The stiffness is usually worse first thing in the morning, or after you have been resting. The inflammation causes swelling around the affected joints.

### Other symptoms

These are known as extra-articular symptoms of RA (meaning 'outside of the joints'). A variety of symptoms may occur. The cause of some of these is not fully understood.

- Small painless lumps or 'nodules' develop in about 1 in 4 cases. These commonly occur on the skin over the elbows and forearms, but usually do no harm.
- Inflammation around tendons may occur. This is because the tissue which covers tendons is similar to the synovium around the joints.
- Anaemia and tiredness are common.
- A fever, feeling unwell, weight loss, and muscle aches and pains sometimes occur.
- In a few cases, inflammation develops in other parts of the body, such as the lungs, heart, blood vessels, or eyes. This is uncommon but if it occurs can cause various symptoms and problems which are sometimes serious.

### How does rheumatoid arthritis develop and progress?

In most cases the symptoms develop gradually - over several weeks or so. Typically, you may first develop some stiffness in the hands, wrists, or soles of the feet in the morning, which eases by mid-day. This may come and go for a while, but then becomes a regular occurrence. You may then notice some pain and swelling in the same joints. More joints such as the knees may then become affected.

In a small number of cases, less common patterns are seen. For example:

- In some cases pain and swelling develop quickly in many joints - over a few days.
- Some people have bouts of symptoms which affect several joints. Each bout lasts a few days, and then goes away. Several bouts may occur before persistent symptoms develop.
- In some people, usually young women, the disease affects just one or two joints at first, often the knees.
- The non-joint symptoms such as muscle pains, anaemia, weight loss, and fever are sometimes more obvious at first before joint symptoms develop.

The severity of RA can vary greatly from person to person. It is usually a chronic relapsing condition. Chronic means that it is persistent. Relapsing means that at times the disease flares up (relapses), and at other times it settles down. There is usually no apparent reason why the inflammation may flare up for a while, and then settle down.

If untreated, most people with RA have this pattern of flare-ups followed by better spells. In some people, months or even years may go by between flare-ups. Some damage may be done to affected joints during each flare-up. The amount of disability which develops usually depends on how much damage is done over time to the affected joints. In a minority of cases the disease is constantly progressive, and severe joint damage and disability can develop quite quickly.

### Joint damage

Inflammation can damage the cartilage which may become eroded or worn. The bone underneath may become thinned. The joint capsule and nearby ligaments and tissues around the joint may also become damaged. Joint damage develops gradually, but the speed at which damage develops varies from person to person. Over time, joint damage can lead to deformities. It may become difficult to use the affected joints. For example, the fingers and wrists are commonly affected, so a good grip and other tasks using the hands may become difficult.

Most people with RA develop some damage to affected joints. The amount of damage can range from mild to severe. At the outset of the disease it is difficult to predict for an individual how badly the disease will progress. However, modern treatments can often limit or even stop the progression of the disease and limit the joint damage (see below).

### How is rheumatoid arthritis diagnosed?

When you first develop joint pains, it may at first be difficult for a doctor to say that you definitely have RA. This is because there are many other causes of joint pains. There is no single test which diagnoses early RA with 100% certainty. However, RA can usually be confidently diagnosed by a doctor based on the following combination of factors:

- Typical symptoms - as described above.
- A blood test. The common test is to check for a protein in the blood called 'rheumatoid factor'. This is present in about 2 in 3 people with RA. However, about 1 in 20 of the normal population has rheumatoid factor. Also, some people with RA do not have rheumatoid factor. So, a positive rheumatoid factor is suggestive of RA, but not conclusive. A more recently developed test detects the presence of an antibody to a substance called cyclic citrullinated peptide (CCP) in a blood sample. This has been found to be more specific than rheumatoid factor in the diagnosis of RA. This blood test may become more commonly done to help diagnose RA.
- X-rays of the hands or feet may be done. These may show the characteristic early damage to joints which is typical of RA.

You may also be advised to have a range of other blood tests to rule out other causes of joint pains.

## Some other associated diseases and possible complications

### Associated conditions

The risk of developing certain other conditions is higher than average in people with RA. These include: cardiovascular disease (such as angina, heart attack and stroke), anaemia, infections (joint infections and non-joint infections), and osteoporosis (thinning of the bones).

It is not clear why people with RA have a higher than average chance of developing these conditions. One possible reason is that, on average, people with RA tend to have more 'risk factors' for developing some of these conditions. For example:

- Lack of exercise and having high blood pressure are 'risk factors' for developing cardiovascular diseases. People with RA may not be able to exercise very easily, and some of the drugs used to treat RA may increase blood pressure.
- Some of the drugs used to treat RA suppress the immune system. This may be a factor for the increased risk of developing infections.
- Poor mobility and steroid drugs increase the risk of developing osteoporosis.

### Other complications

Other complications which may develop include:

- Carpal tunnel syndrome. This is relatively common. It causes pressure on the main nerve going into the hand. This can cause pain, tingling and numbness in parts of the hand. (See separate leaflet called *Carpal Tunnel Syndrome* for details.)
- Tendon rupture sometimes occurs (particularly the tendons on the back of the fingers).
- Cervical myelopathy. This is an uncommon but serious complication of severe, longstanding RA. It is caused by a 'dislocation' of joints at the top of the spine. This can cause pressure on the spinal cord.

## The importance of early diagnosis and treatment

If your doctor suspects that you have RA you will usually be referred to a joint specialist (a rheumatologist). This is to confirm the diagnosis and to advise on treatment. It is very important to start treatment as early as possible after symptoms begin. This is because any joint damage done by the disease is permanent. Therefore, it is vital to start treatment as early as possible to minimise or even prevent any permanent joint damage.

## What are the treatments for rheumatoid arthritis?

There is no cure for RA. However, treatments can make a big difference to reduce symptoms and improve the outlook. The main aims of treatment are:

1. To decrease the disease activity as much as possible so as to prevent joint damage as much as possible.
2. To reduce pain and stiffness in affected joints as much as possible.
3. To minimise any disability caused by pain, joint damage, or deformity.
4. To treat other symptoms of the disease if they develop.
5. To reduce the risk of developing associated conditions such as cardiovascular disease or osteoporosis.

## Treatment aim 1 - to decrease disease activity and prevent joint damage

### Disease-modifying antirheumatic drugs

There are a number of drugs called disease-modifying antirheumatic drugs (DMARDs). These are drugs that ease symptoms but also reduce the damaging effect of the disease on the joints. They work by blocking the way inflammation develops in the joints. They do this by blocking certain chemicals involved in the inflammation process. DMARDs include: methotrexate, sulfasalazine, gold injections, gold tablets, penicillamine, leflunomide, hydroxychloroquine, azathioprine, ciclosporin, and mycophenolate mofetil (MMF). It is these drugs that have improved the outlook (prognosis) in recent years for many people with RA.

It is usual to start a combination of at least two DMARDs as soon as possible after RA has been diagnosed. This is commonly methotrexate plus at least one other DMARD. In general, the earlier you start DMARDs, the more effective they are likely to be. Sometimes just one DMARD is used in certain circumstances.

DMARDs have no immediate effect on pains or inflammation. It can take several weeks, and sometimes several months, before you notice any effect. Therefore, it is important to keep taking DMARDs as prescribed, even if they do not seem to be working at first. Whilst on treatment, you are likely to have a blood test called a CRP test every now and then. This test detects inflammation in the body. As the disease activity reduces, so should the blood level of CRP. The CRP test, in conjunction with assessing your symptoms, is a good way of monitoring disease activity and the effect of treatment in controlling the disease. If DMARDs work well, it is usual to take one or more DMARDs indefinitely. However, when a satisfactory level of disease control has been achieved, your doctor may advise a cautious reduction in drug doses. But, not to less than a dose that still maintain disease control.

Each DMARD has different possible side-effects. If one does not suit, a different one may be fine. Some people try several DMARDs before one or more are found to suit. Some side-effects can be serious. These are rare and include damage to the liver and blood-producing cells. Therefore, it is usual to have regular tests - usually blood tests - whilst you take DMARDs. The tests look for some possible side-effects before they become serious.

#### **Anti-TNF-alpha drugs**

These drugs have been introduced more recently. The chemical TNF-alpha plays an important role in causing inflammation in joints in RA. Blocking the effect of TNF-alpha has been shown to reduce damage to joints, and reduce symptoms. Drugs which modify or block the effect of TNF-alpha include: etanercept, infliximab, adalimumab and certolizumab. These drugs are sometimes called 'cytokine modulators' or 'monoclonal antibodies' or 'biological drugs'.

One problem with these drugs is that they need to be given by injection. They are also expensive. Recent guidelines state that one may be tried if there has been little success when using standard DMARDs. However, anti-TNF-alpha drugs may also be used in combination with methotrexate (a DMARD). Also, because these drugs suppress TNF-alpha, a chemical that is part of the immune system, there is an increased risk of developing serious infections whilst taking one of these drugs.

#### **Other drugs that suppress disease activity**

A drug called rituximab may also be an option. This is another type of monoclonal antibody that suppresses a part of the immune system that is involved in RA. It is given by an infusion into a vein. National guidelines published in 2007 stated that rituximab should be reserved for people with severe RA that has not been helped much by DMARDs or anti-TNF-alpha drugs.

There are other ongoing trials looking at other drugs. Also, there are ongoing trials trying to find which drug, or combination of drugs, is best to take if you have RA. For example, currently anti-TNF-alpha drugs and rituximab are used only when DMARDs are not effective. However, some trials are looking into whether there is a place for these drugs in people newly diagnosed with RA. One example is a trial which looked at using rituximab plus methotrexate in people with newly diagnosed RA. The initial report of this trial (cited at the end) is encouraging. The drug treatment of RA is a developing area of medicine and may change. Your specialist will be able to advise which is the best drug treatment for you.

#### **Maintaining good oral hygiene may help**

There seems to be an association between gum disease and the activity of RA. (Gum disease is very common.) One recent research trial looked at 40 people with RA who also had gum disease. The trial

compared 20 people who had treatment for their gum disease with 20 people who did not. It found that the disease activity of RA seemed to decrease when gum disease was treated. The treatment for the gum disease was scaling/root planing and oral hygiene instructions. That is, basically, good dental care and oral hygiene such as tooth brushing and flossing.

Gum disease causes an ongoing inflammation in the gums. The theory is that this inflammation may in some way 'add fuel' to immune mechanisms involved in the inflammation of RA. Further research is needed to confirm this association. But, in the meantime, it seems sensible to make sure your oral hygiene is good as it may have a beneficial effect. See leaflet called *'Dental Plaque and Gum Disease'* for details.

## **Treatment aim 2 - to reduce pain and stiffness**

DMARDs and other drugs mentioned in the section above control the activity of the disease and will ease symptoms when they take effect. However, whilst waiting for them to take effect, or if they do not work so well, you may need treatment to treat symptoms.

During a flare-up of inflammation, if you rest the affected joint(s) it helps to ease pain. Special wrist splints, footwear, gentle massage, or applying heat may also help. Medication is also helpful. Drugs which may be advised by your doctor to ease pain and stiffness include the following:

### **Non-steroidal anti-inflammatories**

These are sometimes just called anti-inflammatories and are good at easing pain and stiffness, and also help to reduce inflammation. There are many types and brands. Each is slightly different to the others, and side-effects may vary between brands. To decide on the right brand to use, a doctor has to balance how powerful the effect is against possible side-effects and other factors. Usually one can be found to suit. However, it is not unusual to try two or more brands before finding one that suits you best.

The leaflet which comes with the tablets gives a full list of possible side-effects. The most common side-effect is stomach pain (dyspepsia). An uncommon but serious side-effect is bleeding from the stomach. Therefore, your doctor will usually prescribe another drug to 'protect the stomach' from these possible problems. If you develop abdominal (stomach) pains, pass blood or black stools, or vomit blood whilst taking anti-inflammatory painkillers, stop taking the tablets and see a doctor urgently.

After starting a DMARD (discussed earlier), many people take an anti-inflammatory tablet for several weeks until the DMARD starts to work. Once a DMARD is found to help, the dose of the anti-inflammatory tablet can be reduced or even stopped.

### **Painkillers**

Paracetamol often helps. This does not have any anti-inflammatory action, but is useful for pain relief in addition to, or instead of, an anti-inflammatory tablet. Codeine is another painkiller that is sometimes used.

### **Steroids**

Steroids are good at reducing inflammation. It is common practice to advise a short course of steroids to 'damp down' a flare-up of symptoms which has not been helped much by a non-steroidal anti-inflammatory drug. Also, when RA is first diagnosed, a short course of steroids is commonly used to control symptoms whilst waiting for DMARDs to take effect.

An injection of steroid directly into a joint is sometimes used to treat a bad flare-up in one particular joint.

The main side-effects from steroids occur when they are used for more than a few weeks. Serious side-effects that may occur if you take steroids for more than a few weeks, or if you have injections frequently, include: thinning of the bones (osteoporosis), thinning of the skin, weight gain, muscle wasting and an increased risk of serious infection.

**Note:** non-steroidal anti-inflammatories, painkillers, and steroids ease the symptoms of RA. However, they do not alter the progression of the disease or prevent joint damage. You do not need to take them if

symptoms settle with the use of disease-modifying drugs.

### **Treatment aim 3 - to minimise disability as much as possible**

- As far as possible, try to keep active. The muscles around the joints will become weak if they are not used. Regular exercise may also help to reduce pain and improve joint function. Swimming is a good way to exercise many muscles without straining joints too much. A physiotherapist can advise on exercises to keep muscles around joints as mobile and strong as possible. They may also advise on splints to help rest a joint if needed.
- If such things as your grip or mobility become poor, an occupational therapist may advise on adaptations to the home to make daily tasks easier.
- If you develop a joint deformity then surgery to correct it may be an option. If severe damage occurs to a joint, operations such as knee or hip replacements are an option.

### **Treatment aim 4 - to treat other symptoms of the disease if they develop**

As mentioned earlier, sometimes people with RA develop inflammation in other parts of the body such as the lungs, heart, blood vessels, or eyes. Also, anaemia may develop. Various treatments may be needed to treat these problems if they occur.

### **Treatment aim 5 - to reduce the risk of developing other diseases**

As mentioned earlier, if you have RA you have an increased risk of developing cardiovascular diseases (for example, angina, heart attack, and stroke), osteoporosis, and infections. Therefore, you should consider doing what you can to reduce the risk of these conditions by other means.

For example, if possible:

- Eat a good healthy diet and exercise regularly.
- Lose weight if you are overweight.
- Do not smoke. (In addition to increasing the risk of cancer, heart disease and stroke, smoking may also make symptoms of RA worse.)
- If you have high blood pressure, diabetes, or a high cholesterol level, they should be well-controlled on treatment.

See leaflets called '*Preventing Cardiovascular Diseases*' and '*Osteoporosis*' for details.

### **Immunisations**

To prevent certain infections, you should have:

- An annual flu jab if you are over the age of 65 years, or are taking immunosuppressive drugs, or are taking steroids equivalent to 20 mg or more of prednisolone each day for more than a month.
- A 'one-off' pneumococcal immunisation if you are over the age of 65 years, or are taking immunosuppressive drugs, or are taking steroids equivalent to 20 mg or more of prednisolone each day for more than a month.

### **Other treatments**

Some people try complementary therapies such as special diets, bracelets, acupuncture, etc. There is little research evidence to say how effective such treatments are for RA. In particular, beware of paying a lot of money to people who make extravagant claims of success. For advice on the value of any treatment it is best to consult a doctor, or contact one of the groups below.

### **What is the outlook (prognosis)?**

The outlook regarding joint damage is perhaps better than many people imagine.

- About 2 in 10 people with RA have a relatively mild form of the disease, and can continue to do most normal activities for many years after the condition first starts.
- About 1 in 10 people with RA become severely disabled.
- About 7 in 10 fall somewhere in between with varying degrees of difficulties and disability. Most will have to modify their lifestyle to some extent, but can expect to lead a full life.

However, these figures are probably becoming out-of-date as treatment has improved in recent years.

Symptoms can often be well-controlled with medication. Also, the outlook for a person who is diagnosed with rheumatoid arthritis these days is likely to be much better than it was a few years ago. This is because of the newer and better drugs, in particular the newer disease-modifying drugs. Follow-up studies of people being treated with the newer drugs should give a clearer idea of prognosis over the next few years.

Another factor to bear in mind is the increased risk of developing 'associated diseases' such as cardiovascular disease (see above). Because of this, the average life expectancy of people with RA is a little reduced compared with the general population. This is why it is important to tackle any factors that you can modify such as smoking, diet, weight, etc.

### In summary

- Rheumatoid arthritis can range from relatively mild to severe.
- The outlook cannot be predicted for an individual when the disease starts.
- Treatment usually includes a combination of disease-modifying antirheumatic drugs (DMARDs) which aim to reduce disease activity and joint damage. The earlier this treatment is started, the less damage is likely to occur in the joints.
- Other disease-modifying drugs such as anti-TNF-alpha drugs may be used.
- If you have gum disease, good oral hygiene may help to reduce disease activity.
- A steroid drug may be advised for a while to control inflammation whilst disease-modifying drugs take effect.
- An anti-inflammatory drug and/or other painkillers may be used to ease pain and reduce inflammation. These help to ease symptoms but do not affect the progress of the disease. You do not need to take them if symptoms settle.
- Other treatments such as physiotherapy, occupational therapy, and surgery may also be advised, depending on the severity of the disease and other factors.
- If possible, leading a healthy lifestyle such as not smoking, eating healthily, taking regular exercise, etc, can help to reduce the chance of developing associated cardiovascular diseases and osteoporosis.

### Further help and advice

#### Arthritis Research UK

Copeman House, St Mary's Court, St Mary's Gate, Chesterfield, Derbyshire, S41 7TD  
Tel: 01246 558033 Web: [www.arthritisresearchuk.org](http://www.arthritisresearchuk.org)

#### Arthritis Care

18 Stephenson Way, London, NW1 2HD  
Helpline: 0808 800 4050 Web: [www.arthritiscare.org.uk](http://www.arthritiscare.org.uk)

#### National Rheumatoid Arthritis Society (NRAS)

Unit B4 Westacott Business Centre, Westacott Way, Littlewick Green, Maidenhead, Berks, SL6 3RT Helpline: 0800 298 7650 Web: [www.rheumatoid.org.uk](http://www.rheumatoid.org.uk)

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