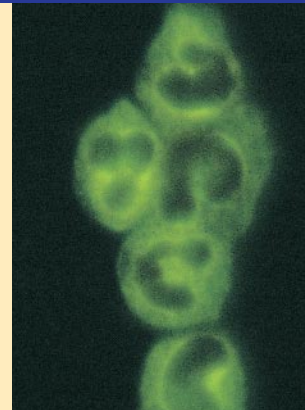


What *you* should know about

# Wegener's Granulomatosis

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***Guidelines for patients***

• *Symptoms* • *Diagnosis* • *Treatment*

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# *Wegener's Granulomatosis*

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## Wegener's Granulomatosis

The purpose of this booklet is to help you understand the medical condition Wegener's granulomatosis. It is set out as a series of questions, which you might want to ask about the condition. If you have difficulty in understanding some of the terms used in the booklet, or have other questions, the doctor caring for you will be able to provide this information.

*Before you read on any further* you may want to have a general overview of the disorder. Wegener's granulomatosis (or Wegener's for short) is a disease in which inflammation can affect different parts of the body. It is a rare condition and it is calculated that some 5 to 10 new cases per million of the population occur each year: in Ireland, this means that each year, some 30 to 60 new cases may be diagnosed.

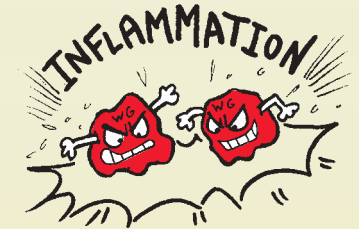
Nowadays, treatment of Wegener's is generally very successful but it is important to make an early diagnosis so that drug therapy can be commenced as soon as possible. If the disease is left untreated, severe damage to the body organs may result. In some patients, despite a good initial response to treatment, the disease may relapse. However, a repeat course of therapy usually controls the disease.

*If you wish, now read on...*

## Learning about Wegener's - how it affects the body

### What is Wegener's granulomatosis?

Wegener's granulomatosis is an inflammatory disease, in which the inflammation is located in small blood vessels. Inflammation is the normal response of the body to any type of injury or infection, with the body tissues becoming red, swollen and often painful.



The medical term for blood vessel inflammation is vasculitis. Other medical conditions can cause vasculitis besides Wegener's and it is important that these different disease types are distinguished from one another.

### Why is it called Wegener's granulomatosis?

Frederick Wegener, a German doctor, was one of the first to describe this condition in the 1930s. One of the features he noted, through microscopic examination of tissue from patients was the presence of collections of cells: these collections are given the medical term "granuloma". Hence the condition became known as Wegener's granulomatosis (or simply Wegener's).



## What causes Wegener's?

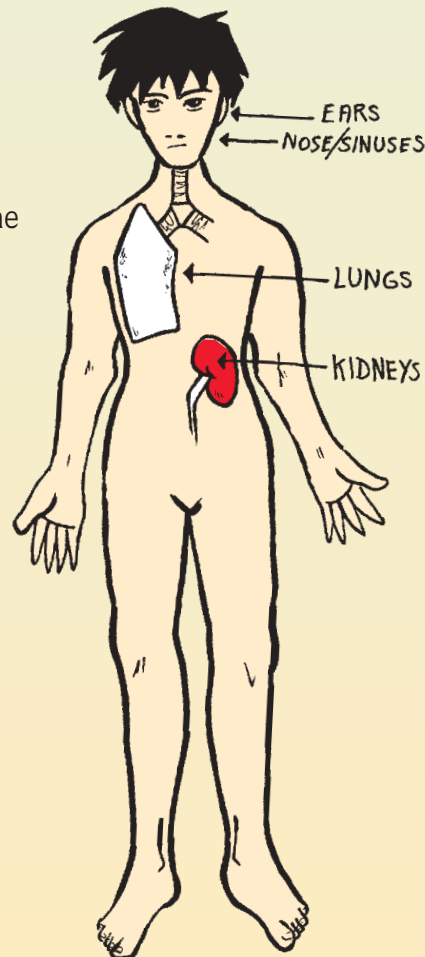
No-one knows the cause. This is very often the situation with prolonged inflammatory diseases. There is some evidence that an infection, for example caused by a bacteria, might start the process. Thus, a bacterial infection might cause inflammation which is focused around blood vessels and this then persists for unknown reasons.

## What parts of the body are affected by Wegener's?

Almost any part of the body can be affected. However, three sites are most typically involved: these are the upper airways - such as the ears, nose and sinuses; the lungs; and the kidneys.

## How do we recognise inflammation in these sites?

In the case of the ears and sinuses, the patient may complain of pain in these areas. Deafness may also develop. Bleeding from the nose is also a very common event. Indeed bleeding, the result of blood vessel inflammation, may occur at many sites. For example, lung inflammation may be noticed by the coughing up of blood and kidney inflammation by the passing of blood in the urine.



## What other areas of the body are commonly affected?

There are several other commonly affected sites. These include the skin - in which typical inflammatory spots or even ulcers may be present. Ulcers may also develop in the mouth. Redness and pain may occur in the eyes. Nerves are sometimes affected giving rise to numbness or weakness in a limb. Joints can become swollen and tender.



Joint inflammation



Fingertip inflammation



Skin rash



Tongue ulcer

## *Are patients with Wegener's always very ill at the start of the illness?*

No, in many patients the illness may be initially mistaken for a common mild disorder, such as sinus disease. Thus, it may be thought that a patient has a common problem with their sinuses, caused by allergy or infection. Likewise, joint swelling and pain may be the start of the illness. This initial, mild phase of the illness may persist for some time, occasionally even years.

## *Are there other general features of Wegener's ?*

Yes, some patients become very ill, at the time they develop Wegener's . Fever may be one of the initial symptoms and may cause severe sweating at night-time and patients sometimes need to change their bed clothes several times each night. Other symptoms include marked weight loss, lack of energy, aches and pains in joints and muscles and generally feeling unwell. These symptoms are sometimes very pronounced and may develop in the absence of other more typical features of Wegener's. Similar features may be present in other illnesses, such as a severe infection, for example pneumonia. As a result, there may be initial difficulties or delays in making the diagnosis.



## *Do all patients get inflammation at all sites?*

No, this would be very uncommon. However, many patients can develop symptoms at several sites at the same time: for example the airways, kidneys and skin may all be affected in some patients.

## *Wegener's - making the diagnosis*

### *What tests are used to diagnose Wegener's ?*

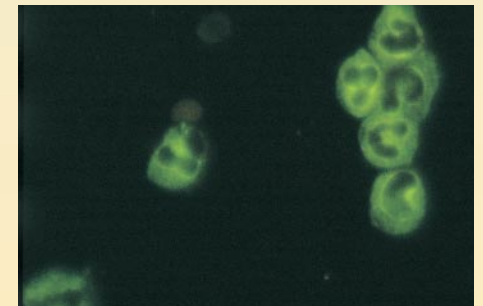
The commonest type of tests are blood tests, urine tests, tissue samples (biopsies) and X-rays.

### *Which blood tests are useful?*

Certain widely used blood tests are helpful. Many patients have low red cell counts (anaemia) and a high white cell count. Two other commonly used tests reveal the presence of inflammation - these tests are called the ESR\* and CRP\*. However, these two tests do not identify the type of inflammation or prove it is caused by Wegener's.

### *Are there better blood tests?*

Yes, a big breakthrough in diagnosing Wegener's was described in the 1980s, when it was found that a particular blood test was very useful in identifying patients with Wegener's. This is called the ANCA test. Use of the ANCA test has helped diagnose many patients with Wegener's, who in the past were left without a diagnosis or misdiagnosed. The test is also very accurate and can tell us very precisely what the diagnosis is.



An example of a positive ANCA test is shown - bright green staining of cells.

\* See abbreviations page 19.



### *Is the ANCA test always positive in patients with Wegener's?*

No, in some patients with disease confined to a single organ - such as the kidney or the sinuses - the ANCA test can be negative. If other findings are in keeping with the diagnosis, the doctor should not be misled by a negative ANCA result.

### *How important is examination of urine?*

Very! It is a very simple procedure to carry out a preliminary examination of the urine, using what is called a 'dipstick'. This is a special type of filter paper which can detect blood or protein in the urine. The finding of a positive test raises the possibility of kidney inflammation.



Urine dipstick kit

### *Can additional tests be carried out on urine?*

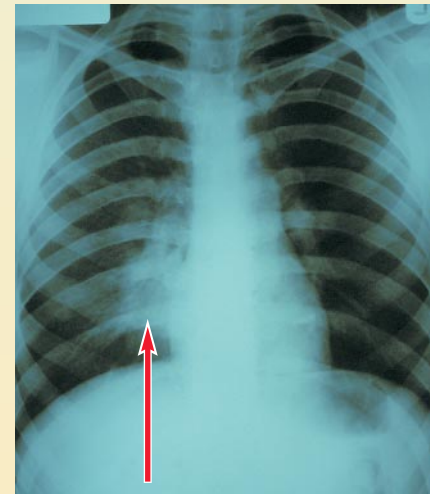
Yes, urine can also be examined using a microscope and useful information obtained. Red blood cells may be observed, again supporting a diagnosis of inflammation. Protein can sometimes be observed as string-like material, called 'casts'. If red cells are found bound to these casts, it is highly suggestive of significant kidney inflammation.

### *Why are urine tests so important?*

Testing the urine may give first evidence of kidney inflammation. A patient is often unaware that this is happening as no specific symptoms are likely to be present. 'Silent' kidney inflammation may lead to chronic kidney damage. Since kidney damage is one of the most serious outcomes in Wegener's, it is important to recognise this as early as possible, so that appropriate treatment can be given.

### *What about tissue samples?*

Sometimes a small sample of the patient's tissue is taken - this is called a 'biopsy'. Examining this tissue with a microscope can also help make the diagnosis of Wegener's. For example samples of kidney tissue, lung tissue or nose tissue may show features of inflammation which are very typically present in Wegener's. However, sometimes the tissue may just show inflammation and its cause or type is not clear.



Inflammation in chest x-ray

### *How helpful are X-rays?*

X-rays and scans are sometimes extremely useful. For example, Wegener's often causes inflammation of the lungs and the damage can result in the development of 'cavities' in the lung tissue. These may be observed readily by X-rays or scans. Likewise, if inflammation causes damage to the sinuses or ears, this may also be easily detected.

## *Is the diagnosis ever initially missed?*

Yes, when only one or two sites are affected, the correct diagnosis may not be made: for example, a patient with only sinus involvement may be thought to have common, allergic sinusitis. Since Wegener's is a rare condition, it is understandable that the doctor might initially diagnose a more common disorder such as allergy. In addition, many doctors will never have had direct experience of patients with Wegener's.

## *So, what actually is the best way to diagnose Wegener's?*

Since this is a rare disease, one of the most important points to emphasise is that the diagnosis must be kept in mind, when a patient presents with the symptoms which occur in Wegener's. Then using the tests listed above, an accurate assessment of whether Wegener's is present or not can be made. Generally, the combination of a patient's symptoms, the abnormalities found when the patient is examined and the laboratory test results will lead to the correct diagnosis. There is no doubt that the ANCA test has been extremely useful in helping in the diagnosis of patients in whom, previously, Wegener's would not have been recognised.

## *Can we alert doctors to the possible diagnosis of Wegener's?*

Yes, through medical education we can make doctors more aware of the condition. It should also be encouraged that doctors consult their colleagues when an unusual condition is encountered. With the combined experience and expertise of different specialists, a diagnosis such as Wegener's is more likely to be considered.

## *Wegener's - the treatment plan*

### *Tell me about the treatment of Wegener's*

The main purpose of treatment of Wegener's is to suppress the inflammation and thereby allow tissues to heal and recover from the damage that has happened. At present, two major types of drugs are used: steroids; and drugs which specifically suppress the immune system, referred to as immunosuppressive drugs. These drugs are used in different combinations and generally given for a minimum period of one year. It is important to stress that without these drugs, the disease is unlikely to go away and that serious organ damage may result.

### *What steroid drugs are used?*

The steroid drug, prednisolone is the one most commonly employed. It is also used to treat many different types of inflammation, for example asthma. A particular brand of prednisolone called Deltacortril is often used, because it has a special coating that reduces the possibility of stomach upset. In Wegener's, prednisolone is initially used in high amounts - such as 60mg per day. This dosage is reduced rapidly over the following weeks when the inflammation comes under control. However, patients usually remain on about 10mg per day for some time. The reason for the rapid reduction is to minimise steroid side effects.





### *What are the steroid side effects?*

These side effects are very numerous but most are reversible. Some such as obesity, increased appetite and restlessness are more likely to occur at high dosages. One side effect of concern is bone thinning or osteoporosis. In patients who are already prone to osteoporosis, it is important to keep steroids at the lowest dose possible and also to take other measures (such as calcium and vitamin D) to reduce this risk. In some patients, drugs termed bisphosphonates are also used: these recently developed drugs help protect bones from osteoporosis.

### *Tell me about the immunosuppressive drugs.*

The most commonly used drugs are cyclophosphamide and azathioprine. However, other drugs are now sometimes employed including methotrexate and mycophenolate. Because all of these drugs suppress the immune system, an increased risk of infection is present and a careful watch for this possibility is necessary.

### *Is cyclophosphamide always used in the treatment of Wegener's ?*

Yes, this drug is almost always used in the early stages of treatment and it has made a dramatic impact on the outcome of this disease. Before its use in Wegener's patients, the mortality of this disease in certain patients was high. This trend has been completely reversed through the use of this drug.

### *What are the side effects of cyclophosphamide?*

Cyclophosphamide may cause excessive suppression of the bone marrow, making a patient susceptible to infections. The bone marrow produces all types of blood cells, including cells of the immune system called white cells which are very important in fighting infection. Regular white cell counts are performed when a patient is taking this drug, to monitor for a damaging bone marrow effect.

### *What other side effects does cyclophosphamide cause?*

Some patients develop suppression of their gonads (ovaries or testes), making them infertile. Others experience hair loss. These side effects often reverse when the drug is stopped. Some complications happen a long time after therapy. For example, in some patients, chemical inflammation of the bladder (cystitis) may occur. In a few patients, a malignancy can develop.

All of these problems with cyclophosphamide are dose related - the higher and longer the amount of drug used, the more likely they are to happen.

## *What about the other immunosuppressive drugs?*

When Wegener's comes under control with steroid and cyclophosphamide treatment, cyclophosphamide is often replaced by a less toxic drug. Azathioprine (also called Imuran) is the most commonly employed substitute drug. long-term use of azathioprine can also be associated with serious side effects but these are much less common than with cyclophosphamide.

Two further drugs are also occasionally used: methotrexate and mycophenolate. A table listing the drugs commonly given to patients with Wegener's is shown on page 18.



Commonly used drugs

## *Wegener's - response to treatment*

### *Does Wegener's usually respond to these treatments?*

Yes, the majority of patients rapidly improve with therapy. The dosage of drugs is then gradually reduced and they are often stopped after about one year.

### *Does the disease ever return?*

Yes, it is estimated that recurrence of Wegener's may happen in up to 50% of patients. However, these recurrences may be milder and usually respond rapidly to further therapy. To help identify such relapses at an early stage, patients are monitored on a long-term basis so that further therapy can be started as soon as possible. In some patients, more severe disease develops in the relapse and it is very important to bring this under control.

### *Can Wegener's be cured?*

Not at the moment. Wegener's is a chronic condition which, in the strict sense, cannot be "cured". Most patients, even when they no longer require drug therapy, continue to have some low level of inflammation present. This usually causes mild symptoms only.

### *Is long-term, continuous drug therapy ever used?*

Yes, some doctors use continuous drug therapy for several years in the hope this will prevent relapses developing. For example, the long-term use of azathioprine may be advised. However, the evidence that this approach is definitely useful, is still being studied.

## *Are there better therapies on the horizon for Wegener's ?*

Yes, newer therapies are continuously being evaluated and the European Union have funded several studies, currently taking place in some 20 European states, including Ireland. However, at present the therapies described above are the mainstay drugs. Investigation of the safer use of these drugs is also being assessed.

### *What happens if Wegener's affects the kidneys?*

Normally, the type of treatment described above prevents or limits the damage that may be caused to the kidneys. However, since the kidney is such an important organ, every effort is made to minimise existing damage. For this reason, certain blood pressure tablets may be given to Wegener's patients, since reducing the blood pressure can help protect the kidneys. The common type of blood pressure tablet used for this purpose is called an ACE inhibitor.

### *What about patients in whom the ordinary drugs do not work?*

This is a rare event but does happen. Various novel therapies have been used in such patients and are often successful. One of these therapies is to carry out plasma exchange - the patient's blood plasma is removed and with it the harmful factors responsible for the inflammation. Other newer therapies include the use of drugs which specifically inhibit the action of cells which are directly involved in the disease process.

### *So, what is the long-term outlook for patients with Wegener's ?*

Nowadays, the outlook is good. Most patients respond successfully to therapy. It is always important to make the diagnosis and start treatment as soon as possible. This will reduce the amount of damage caused by the inflammation. However, some long-term damage to affected tissues may remain and this is quite common. Occasionally the inflammatory damage is severe and, for example, if this involves the kidney, dialysis treatment may be required. In a few patients kidney transplantation is performed.

### *How can the outlook for patients be improved?*

It is very important to control the inflammatory condition as early as possible and to continue on treatment as advised by your doctor. Long-term follow up is essential and so it is important that the patient remains in regular contact with their doctor. In this way, complications, such as raised blood pressure can be diagnosed and treated early.

Research into Wegener's is very important. In this way, we will develop a better understanding of the cause of the disease and in turn this should lead to more specific therapy in the future.

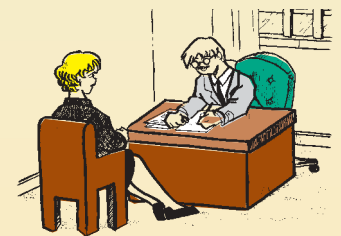
### *Are self-help measures ever useful?*

Patients often wonder if there are steps they can take to improve their medical condition. Simple, common sense measures are of benefit. In the early stages of the disease, plenty of rest is appropriate - to allow the body inflammation to settle. Later, ordinary good practices of sensible living apply - regular exercise, a balanced, nutritious diet and avoidance of tobacco. Alcohol is permissible, but in moderation of course!

### *How can I find out more about Wegener's ?*

Nowadays, the Internet is one of the best ways of getting information about medical conditions and support groups.

A list of useful Web sites is shown on page 17. However, getting expert advice from a doctor who is familiar with Wegener's is still one of the most important ways of learning about the condition. It is also important to note that some of the information on the Internet may be difficult to understand and may cause unnecessary anxiety in patients. A list of web addresses are given in the table.



## Web sites and addresses

<http://www.btinternet.com/~wegeners.uk/> - this is the web site of Wegener's granulomatosis, UK. It is specifically aimed at informing patients about Wegener's, including details about treatment.

<http://www.wgassociation.org> - this is the web page an USA patient organisation, the Wegener's Granulomatosis Association. They produce a newsletter on a regular basis.

<http://vasculitis.med.jhu.edu/> - this is the web page of the Johns Hopkins Vasculitis Centre in the USA. It provides background information on Wegener's, particularly written for patients, including details about treatment.

<http://www.vasculitis.org> - this is the web page of the European Vasculitis study group and gives details about the studies being performed and the centres involved. Information about different patient support groups is given.

## Drugs commonly used in the treatment of Wegener's

Drug type	Name (chemical)	Name (brand*)	Action
<b>Steroid</b>	<b>Prednisolone</b>	<b>Deltacortril</b>	<b>Anti-inflammatory</b>
<b>Cytotoxic</b>	<b>Cyclophosphamide Azathioprine Methotrexate Mycophenolate</b>	<b>Endoxana Imuran Methotrexate Cellcept</b>	<b>Suppress the immune system</b>
<b>Stomach protection</b>	<b>Omeprazole</b>	<b>Losec</b>	<b>Inhibits acid production</b>
<b>Bone protection</b>	<b>Vitamin D/calcium Bisphosphonate</b>	<b>Calcichew D3 Fosamax</b>	<b>Increases calcium absorbtion Strengthens bone structure</b>
<b>Kidney protection</b>	<b>ACE inhibitor</b>	<b>Coversyl</b>	<b>Lowers blood pressure in kidney</b>
<b>Antibiotics</b>	<b>Suphamethoxazole /trimethoprim Mupirocin</b>	<b>Septtrin Bactroban</b>	<b>Prevents bacterial infection Inhibits bacterial infection in nose</b>
<b>Statins</b>	<b>Pravastatin</b>	<b>Lipostat</b>	<b>Blood vessel protection, lowers cholesterol</b>

\* Note: these are examples of brand names of drugs commonly used; other brands may also be prescribed.

**Biopsy:** a small sample of patient's tissue, taken for examination under the microscope.

**Casts:** a string-like material, composed of protein, found in urine, when examined by microscope.

**Granuloma:** a collection of cells, often with a round or oval appearance, observed under the microscope.

**Immunosuppressive drugs:** drugs with the property of suppressing the immune system.

**Vasculitis:** blood vessel inflammation. Can be recognised when tissue is examined under the microscope.

**ESR:** abbreviation for erythrocyte sedimentation rate: this is a commonly used laboratory test for measuring the amount of inflammation.

**CRP:** abbreviation for C-reactive protein: this is a further commonly used laboratory test for measuring the amount of inflammation.

**ANCA:** abbreviation for anti-neutrophil cytoplasmic antibody: this is a laboratory test which is very useful in the diagnosis of Wegener's granulomatosis.



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