What I tell my patients about anti-GBM disease (or Goodpasture's disease)

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As a young naval doctor during the flu pandemic of 1918–1920, Ernest Goodpasture described a young man with lung haemorrhage and kidney failure. He thought this was probably related to influenza. In the 1950s, it became possible to see antibodies in kidney biopsies, and anti-glomerular basement membrane (anti-GBM) disease was described. Goodpasture's name was given to the disease, although his main life's work was on the chickenpox virus.

What is Goodpasture's disease?

Goodpasture's disease is a rare condition in which there can be rapid destruction of the kidneys and bleeding into the lungs. Kidney function may be lost within days – it is one of the most rapidly destructive kidney diseases. Lung disease can also worsen very quickly. Fortunately, however, the disease is not always as rapid as this.

Who gets it?

Goodpasture's is a 'one in a million' disease, almost literally. There are maybe 50–200 cases per year in the UK. It mostly occurs in white Europeans, and seems even less common in other races, although many cases have been reported from China in recent years.

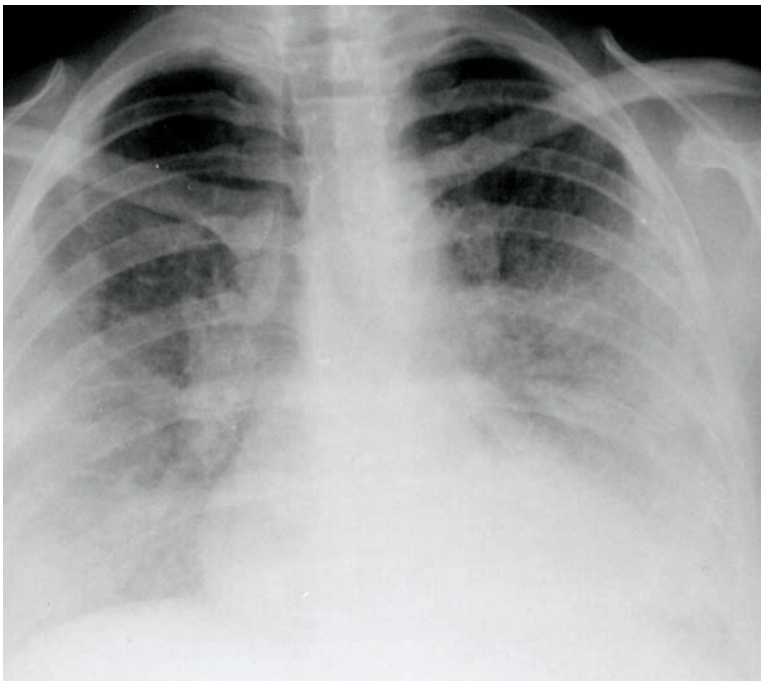
Although the disease can occur at any age, it is most common at the ages of 18–30 and 50–65. Men and women are equally likely to get it.

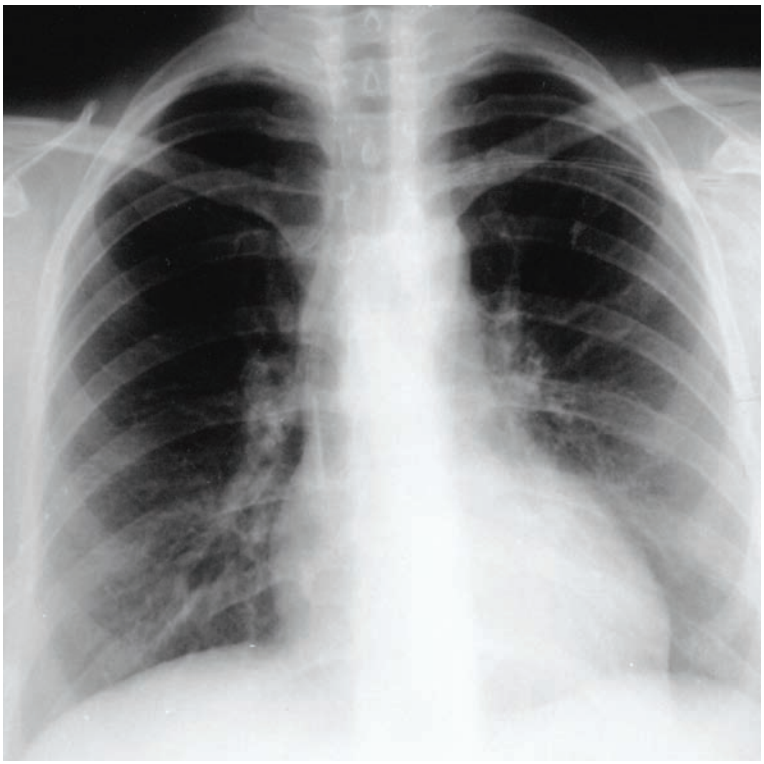
What happens?

Goodpasture's disease can result in kidney disease on its own, kidney and lung disease together, or (rarely) lung disease alone.

Lung disease

If there is lung disease, this is usually the first thing the patient will notice. It can occur days to months before kidney trouble is discovered. Bleeding into the lungs (lung haemorrhage) may cause anything from just a dry cough to very severe breathlessness with coughing up bright red blood, and becoming dangerously short of





Figures 1 (top) and 2. X-rays of a woman with lung haemorrhage caused by anti-glomerular basement membrane antibodies, before (1) and after (2) treatment

oxygen, thus requiring intensive case and artificial ventilation (a 'breathing machine'). Coughing up blood, however, is not in itself a good guide to how severe the lung disease is. In Goodpasture's disease, bleeding into the lungs occurs mostly in smokers or in those with previous lung infection. Sometimes it occurs in people who are exposed to fumes, such as those arising from paint or petrol. Lung haemorrhage can be very severe, and can even be fatal, but when it responds to treatment the lungs usually recover completely. Figures 1 and 2 show X-rays of a patient with bleeding into the lungs in Goodpasture's disease.

Kidney disease

Kidney involvement in Goodpasture's disease is an inflammation of the millions of tiny filtering units (glomeruli) that you have in each kidney. Specifically, it is the basement membrane of each glomerulus that becomes inflamed, which is why Goodpasture's disease is also known as anti-GBM disease – see the *Quick reference glossary* for an explanation of some of the terms used.

In Goodpasture's disease, antibodies attack a molecule in the glomeruli

Goodpasture's disease is usually only diagnosed when it picks up speed to cause 'rapidly progressive' glomerulonephritis – this is inflammation of the glomeruli. Under the microscope, the glomeruli seem to develop a 'collar' or crescent of abnormal cells. This kind of severe glomerulonephritis is also called crescentic nephritis (because of the crescent of abnormal cells), and it can have some other causes beyond Goodpasture's disease. Figure 3 shows a glomerulus that has been damaged by the effects of Goodpasture's disease.

In Goodpasture's, the urine contains blood on testing and may become visibly red. Later, the amount of urine produced may reduce. However, kidney failure is slow to cause symptoms, and, when it does, the symptoms can easily be confused with other, less serious, illnesses.

The symptoms of kidney failure are that you will not feel well and will experience loss of appetite and energy. This will progress to feeling sick and, later, vomiting. Some patients will get hiccups. Later, fluid accumulation occurs.

What causes Goodpasture's disease?

Goodpasture's disease is caused by the immune system attacking one of the body's own molecules. Diseases like this are what are known as autoimmune conditions. More common autoimmune diseases include thyroid disease, systemic lupus erythematosus, and diabetes in young people. Antibodies are molecules that usually fight infection, but, in Goodpasture's disease, antibodies attack a molecule in the glomeruli and the lungs. This can happen out of the blue, but, thanks to decades of research, how it happens is much better understood in Goodpasture's disease than in most other autoimmune diseases.

How is Goodpasture's disease diagnosed?

Because of the vague early symptoms and speed of the disease progression, it is common for the diagnosis of Goodpasture's disease to be reached late. Kidney biopsy is almost always necessary and is often the quickest way to make the diagnosis.

Biopsy may also provide valuable information about the likely value of treatment. Tests for anti-GBM antibodies can be very useful. Tests for other conditions that can cause similar symptoms, and which can affect the lungs and kidneys, will be performed at the same time, especially looking for antibodies known as ANCAs (antibodies to neutrophil cytoplasm antigens – certain components of white blood cells).

What is the treatment for Goodpasture's disease?

In the 1970s, a 'cocktail' of treatments was developed that knocked back the immune system enough to be able to stop Goodpasture's disease. This includes the following drugs and treatments.

Prednisolone

Prednisolone is a steroid. It provides large doses of the hormone naturally produced by the adrenal glands, which suppresses the immune system and also acts as an anti-inflammatory.

Cyclophosphamide

Cylcophosphamide is a drug that works by slowing or stopping cell growth, including the growth of white blood cells (part of the immune system responsible for 'attacking' infections). This ability to slow cell growth is why cyclophosphamide is also used in the treatment of some cancers.

Plasma exchange (plasmaphaeresis)

Plasmaphaeresis is a procedure for clearing antibodies from the blood. Blood is withdrawn from the patient and is filtered or spun to remove the plasma, which is then replaced with plasma or

purified protein solutions from blood donors; the blood is then transfused back into the patient's circulation (see Figure 4).

What is the length of treatment for Goodpasture's disease?

Plasmaphaeresis may be continued for two weeks, or even longer, until the antibodies have been cleared and the lungs have recovered. Cyclophosphamide is usually needed for three months, and steroids for around the same length of time or a little longer. It is unusual for the disease to come back after this time, but early on the disease can be aggravated by infections or by resuming smoking.

Although lung disease usually recovers with this treatment, kidney damage is often too severe to recover completely. In many patients it does not recover at all, leaving them with permanent and complete renal failure, so that they require regular dialysis treatment to stay alive.

What are the side-effects of treatment for Goodpasture's disease?

The most important risk of treatment is serious infection. Steroids can cause gastritis and occasionally bleeding from the stomach, osteoporosis (brittle bones), weight gain and problems with high blood pressure, but some of these can be minimised by the use of additional tablets. Cyclophosphamide can also cause cystitis and there may be a small long-term increased risk of some cancers.

Because of the risks and side-effects of treatment, patients who do not have lung haemorrhage and who have little chance of recovering kidney function may best be left untreated. This decision is not taken lightly, and should only be made after ensuring that the diagnosis of Goodpasture's disease is definite.

What happens if my kidneys fail?

If you do experience kidney failure, you may require dialysis, either temporarily or permanently. This may take place in a hospital or, after training, at home. Kidney transplantation can be safely carried out in a patient who has had Goodpasture's disease after anti-GBM antibodies are no longer detectable.

An interval of at least three to six months after the first negative result for anti-GBM antibodies is usually advisable before kidney transplantation takes place. This may prove to be a problem if no treatment was given initially, as the time for safe transplantation may then be one to two years

Quick reference glossary

- Antibody – a protein produced by white blood cells in response to an antigen
- Antigen – a foreign substance (generally a protein or virus) that causes the body to produce antibodies with which to defend itself
- Autoimmune – a range of conditions in which the body produces antibodies to attack its own tissues
- Biopsy – removal of small piece of tissue from an organ to examine it and determine the nature of a disease
- Cystitis – inflammation of the bladder, which can result in painful urination
- Gastritis – inflammation of the lining of the stomach
- Glomerular basement membrane – the base of the glomerulus; this membrane performs the actual filtration
- Glomerulonephritis – inflammation of the glomeruli
- Glomerulus – a capillary (very fine blood vessel) that functions as a filtering unit in the kidney. The plural is glomeruli
- Haemorrhage – the loss of blood from a ruptured blood vessel
- Neutrophil cytoplasm antigen – a foreign substance in the cytoplasm (interior of a cell) of white blood cells (neutrophils). Antibodies that may result can confirm or rule out Goodpasture's disease
- Plasma – the liquid component of blood, in which the blood cells are suspended

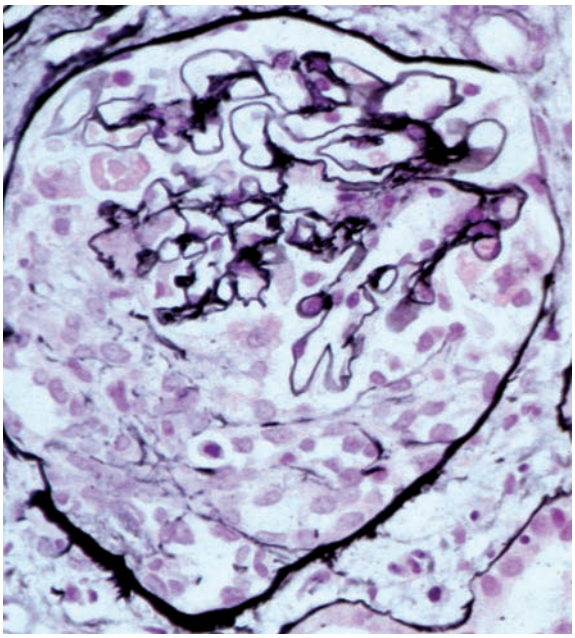


Figure 3. A kidney glomerulus damaged by Goodpasture's disease

Figure 4. A female patient undergoes plasmaphaeresis

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away. These precautions are necessary to prevent destruction of transplants caused by a return of Goodpasture's disease.

What else can cause this damage?

Any cause of kidney failure can result in accumulation of fluid in the lungs, and this is the first thing that has to be checked out. Severe pneumonia can also cause kidney failure.

However, there are a few other diseases that can cause lung haemorrhage and severe kidney inflammation similar to Goodpasture's disease. The most important is caused by inflammation of small blood vessels (vasculitis). Diagnosis of vasculitis usually requires a kidney biopsy, although tests for ANCAs are also very useful.

Although the treatment for both these conditions is broadly quite similar, it is worth distinguishing them, as the long-term outcomes, and possibly treatment methods, are different.

Further information

Further information on Goodpasture's disease and its treatment can be found online. For example, the website of the Edinburgh Renal Unit (at www.edren.org/pages/edreninfo/goodpastures-anti-gbm-disease/goodpastures-disease-more-info.php) is a useful source of information on the condition ■

Key points

- **Goodpasture's disease is another name for anti-glomerular basement membrane (anti-GBM) disease, in which antibodies are formed to your own glomeruli – the filters in the kidney.**
- **Goodpasture's disease causes one of the most aggressive types of kidney inflammation.**
- **In some cases of Goodpasture's disease, bleeding into the lungs can also occur.**
- **Treatment with drugs that suppress the immune system can control the disease, if it is caught in time.**
- **Unfortunately, permanent kidney damage is a common result of Goodpasture's disease.**