What I tell my patients about IgA nephropathy

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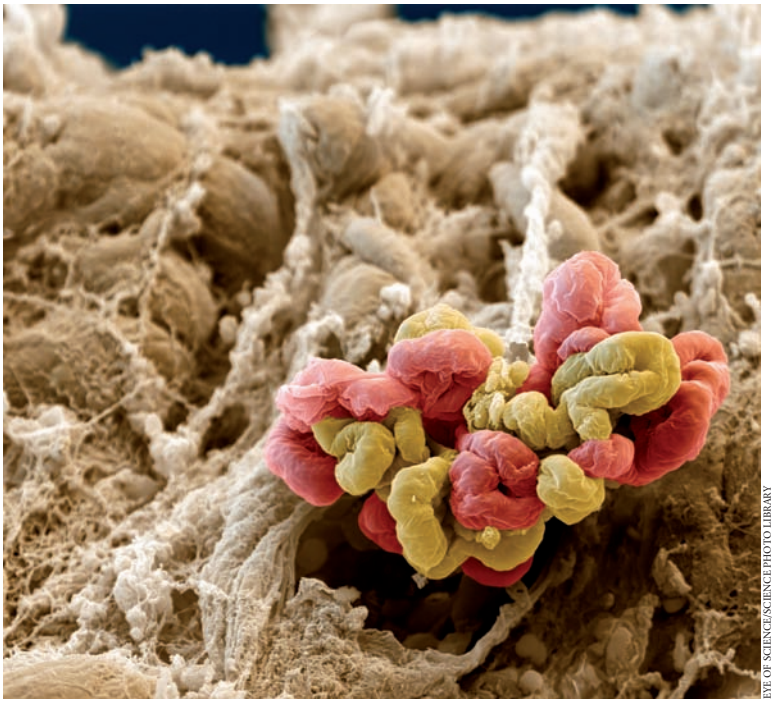
IgA nephropathy is a type of kidney disease that affects the very fine filters (glomeruli) of the kidneys (see Figure 1). In IgA nephropathy, a protein normally found in the blood, IgA (immunoglobulin A), deposits in these filters (see Figure 2, on next page) and causes inflammation and damage to the glomeruli (glomerulonephritis). IgA is a type of antibody – also known as immunoglobulin – whose normal function is to protect the body from infections; however, for some reason, in IgA nephropathy, IgA proteins have a tendency to deposit in the kidneys and cause damage.

IgA nephropathy is the most common cause of glomerulonephritis in the UK and an important cause of kidney disease worldwide. Both kidneys are affected equally and the disease involves all glomeruli. Inflammation in the glomerulus invariably causes a breakdown of the glomerular filtering membrane, with the appearance of red blood cells and/or protein in the urine. This is usually the earliest sign of IgA nephropathy.

In the UK, IgA nephropathy is more common in men and most commonly diagnosed when patients are in their teens and twenties. There is, however, a wide variation between countries in how often IgA nephropathy is diagnosed, the age at which it is diagnosed and the proportion of men and women affected. IgA nephropathy is seen most often in Mediterranean and Pacific Rim countries (such as Japan).



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A healthy kidney with a glomerulus highlighted in red and yellow

The extent of glomerular inflammation and scarring that occurs as a consequence of IgA deposition in the kidneys varies widely between patients. Some patients will simply have lifelong urine abnormalities on dipstick testing, while others will slowly develop progressive kidney failure. About one in three patients with IgA

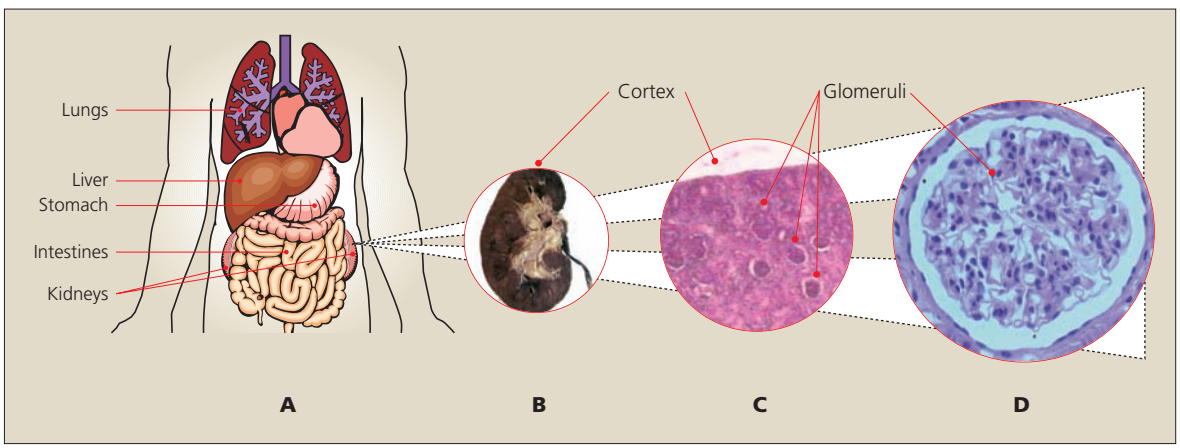

Figure 1. The kidneys are located in the flank areas in the region of the small of the back (A). Each kidney has an outer cortex (B) which contains all the filters (glomeruli) of the kidney (C). Each glomerulus is made up of a network of blood vessels across which the blood is filtered and the early urine is produced (D)

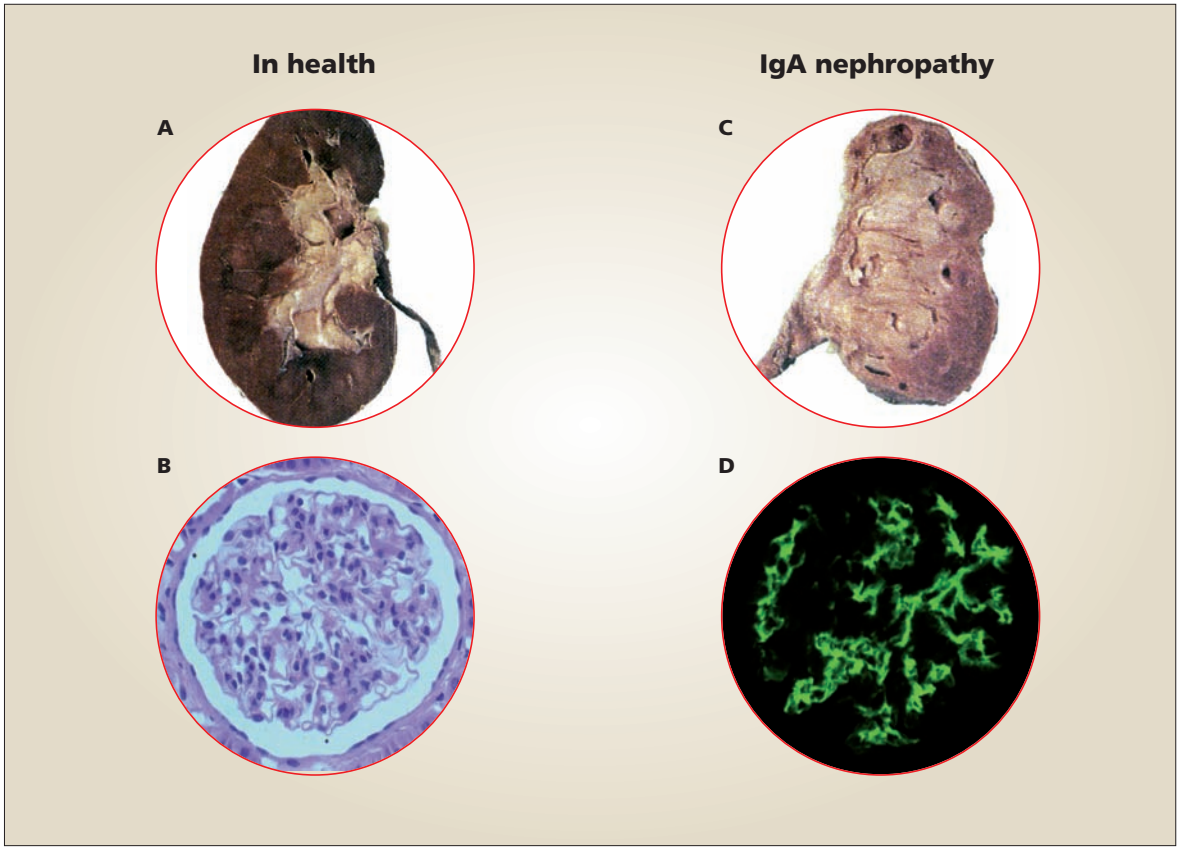

Figure 2. A healthy kidney measures 10–12 cm from top to bottom (A) and consists of an outer cortex which contains the glomeruli (B) that filter the blood to produce the early urine. In IgA nephropathy progressive inflammation and scarring of the glomeruli leads to scarring of the kidney (C). This inflammation is triggered by the deposition of the IgA protein in the glomeruli, shown in D as bright green staining in a single glomerulus. The high powered views of the glomeruli (B and D) are what kidney specialists look at when looking at a kidney biopsy

nephropathy will develop kidney failure requiring dialysis or a kidney transplant. The development of kidney failure usually occurs very slowly, often over a timescale of ten to 30 years.

How would I know if I had IgA nephropathy?

Most patients with IgA nephropathy do not feel unwell and are found to have IgA nephropathy following a routine dipstick test of their urine as part of a health check, insurance medical or employment medical. If a patient has IgA nephropathy, this test will be positive for either blood (invisible haematuria) and/or protein (proteinuria). Some patients, typically teenage men, may develop obvious blood in their urine (macroscopic haematuria) after an infection (usually a chest infection). They usually pass cola-coloured urine within a couple of days of the infection, which is painless and gets better by itself over a few days. Rarely, patients may lose large amounts of protein in their urine and develop nephrotic syndrome, in which there is marked swelling of the ankles and legs (oedema). The presence of blood (visible or invisible) or protein in the urine always requires further investigation and your GP will in the first instance organise some urine and blood tests and then, depending upon the results of these, seek the advice of a kidney specialist (nephrologist).

Most patients with IgA nephropathy do not feel unwell

How is IgA nephropathy diagnosed?

At the present time there are no blood or urine tests that can reliably diagnose IgA nephropathy. The only way to make the diagnosis is with a biopsy of the kidney and for this reason IgA nephropathy can only be diagnosed by a kidney specialist.

For the kidney biopsy, you are asked to lie on your front and the kidney is identified by ultrasound. Local anaesthetic is injected between the skin and the kidney and then a biopsy needle is inserted into one of the kidneys to obtain a sample that can be examined under a microscope. This takes about 20 minutes and can often be done as a day case, with the result available within a week.

A diagnosis of IgA nephropathy is made when IgA protein is seen deposited in the glomeruli (Figure 2, previous page). Not only does the biopsy allow the kidney specialist to make the diagnosis but it also helps them to assess how much damage has already been done to the kidneys and how much inflammation has occurred. This can help the kidney specialist to decide which treatment to give and how likely you are to develop kidney failure in the future.

What causes IgA nephropathy?

IgA nephropathy is a relatively 'young' kidney disease – having only been recognised as a disease in 1968. Over the past 40 years, a number of abnormalities have been found in patients with IgA nephropathy; however, the cause of IgA nephropathy is currently unknown. In the vast majority of patients it is not a hereditary disease but occasionally families have been observed where IgA nephropathy runs in successive generations.

One of the most promising areas of research has been the study of the structure of the IgA protein and, in particular, the sugars that coat the surface of IgA (see Figure 3). A number of research teams have shown that these sugars are different in IgA nephropathy patients. It is thought that changes to the sugars of IgA render the IgA protein 'more sticky' and make it more likely to stick to both proteins in the kidney and proteins in the blood, including other antibodies. The overall result is that IgA in the bloodstream of patients with IgA nephropathy aggregates together and is prone to stick in the glomeruli of the kidney, where these deposits trigger inflammation and scarring of the kidney. At the moment we do not know where in the body the IgA with the abnormal sugar coating is produced and how, once it is deposited in the glomeruli, it triggers kidney damage.

How is IgA nephropathy treated?

It is perhaps not surprising that with so many gaps in our understanding of the causes of IgA nephropathy there are no drugs available at the present time to treat this common kidney disease. The approach to managing patients therefore focuses on both general measures and, when necessary, modulation of the immune system with immunosuppressive drugs.

General measures

Maintaining general health

The association of kidney disease with high blood pressure and protein in the urine increases the risk of future problems with blood vessels, particularly heart disease and strokes. It is therefore important to stop smoking, avoid being overweight, take plenty of exercise, eat a healthy diet and ensure you have regular blood pressure and cholesterol checks.

Blood pressure

High blood pressure is very common in patients with kidney disease. In itself, high blood pressure can further damage the kidneys and speed up the rate of decline in kidney function. It is mainly treated with tablets and often more than one drug is needed. Limiting salt and alcohol intake can also help. Your blood pressure should be ≤120/75 mmHg.

Proteinuria

In addition to high blood pressure, large amounts of protein in the urine can also lead to further kidney damage. Two types of blood pressure

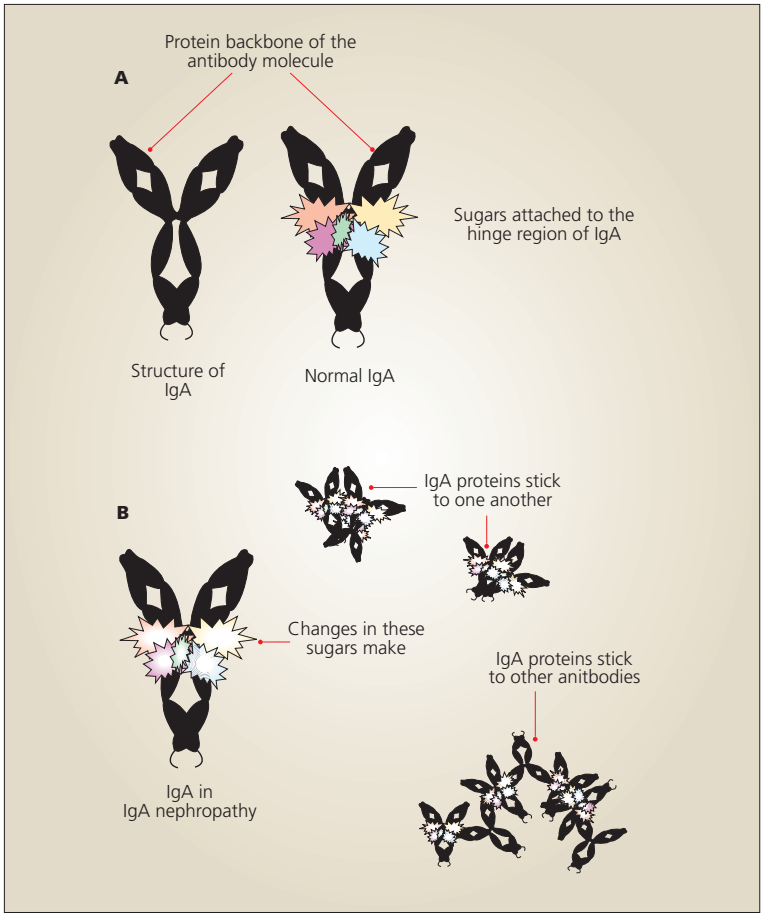

Figure 3. The IgA protein, like other antibodies such as IgG, has a protein backbone. Unlike other antibodies, IgA also has sugars attached at its hinge region (A). These sugars are relatively large and can greatly affect how the IgA protein interacts with other proteins. In IgA nephropathy, the hinge region sugars are abnormal and this makes the IgA protein 'sticky', resulting in IgA proteins sticking to one another and other antibodies such as IgG (B). These aggregates are prone to getting trapped in the filters (glomeruli) of the kidneys where they can cause inflammation and damage

drugs, known as angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, have been shown not only to reduce blood pressure but also to reduce the amount of protein in the urine. The dual function of these drugs means they are particularly good at protecting kidney function.

Fish oil

There have been some studies suggesting that supplementation of the diet with fish oil (omega-3 fatty acids) may slow down the rate of kidney damage in IgA nephropathy, although not all kidney specialists believe fish oil is beneficial. Fish oil treatment is safe, apart from a minor decrease in the ability of the blood to clot, although this is not usually a problem. Fish oil supplements can have an unpleasant taste and may be associated with flatulence.

Tonsillectomy

In certain parts of the world, notably Japan, tonsillectomy is favoured as a treatment for IgA nephropathy. While tonsillectomy may stop recurrent attacks of visible blood in the urine, there is little evidence that it protects the kidneys against future kidney failure and, because of this, tonsillectomy is not routinely carried out in the UK as a treatment for IgA nephropathy.

IgA nephropathy is one of the kinds of kidney disease that can reappear in a transplant kidney

Immunosuppressive drugs

There is a great deal of debate among kidney specialists as to whether immunosuppressive drugs are useful in IgA nephropathy. The drugs commonly considered for patients whose renal function is either deteriorating rapidly, or deteriorating despite all of the general measures discussed above, are steroids (prednisolone), cyclophosphamide, azathioprine and mycophenolate mofetil. As the evidence for use of these drugs is not clear-cut in IgA nephropathy, it is recommended that you discuss the role of immunosuppression with your kidney specialist.

Will I need dialysis or a kidney transplant?

If your kidneys fail, you will need dialysis or a kidney transplant. Dialysis is a technique for removing the waste products from your body that are normally removed by your kidneys. Some people with kidney failure are suitable for a kidney transplant.

The kidney may come from an anonymous donor or from a living friend or relative. IgA nephropathy is one of the kinds of kidney disease that can reappear in a transplant kidney, but as it does not reappear for a very long time this should not dissuade you from trying to find someone willing to give you a kidney ■

Key points

- **IgA nephropathy is a common cause of kidney disease.**
- **The disease usually comes to the attention of doctors because of an abnormal urine dipstick test.**
- **IgA nephropathy can only be diagnosed with a kidney biopsy.**
- **Changes to the sugars coating the IgA protein are likely to be important in the development of IgA nephropathy.**
- **There are no specific treatments for IgA nephropathy, but control of blood pressure, use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers and a healthy lifestyle can help protect the kidneys against ongoing damage.**

Further information

For further information on IgA nephropathy you may wish to visit the following websites.

- How your kidneys work **www.howstuffworks.com/kidney.htm**
- The British Kidney Patient Association **www.britishkidney-pa.co.uk/**
- The International IgA Nephropathy Network **www.igan-world.org**