What I tell my patients about glomerulonephritis

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Glomeruli are the filters of our kidneys. They clear the blood of unwanted waste products, allowing these to be excreted in the urine. We should have approximately one million glomeruli in each kidney. They are incredibly tiny – you could fit ten side by side on the head of a pin (see Figure 1). A tube (tubule) leading out of each glomerulus is actually a processing device from which 99% of the filtered fluid is reprocessed back into the blood, leaving waste products, excess salt and so on, to flow out into the urine (see Figure 2).

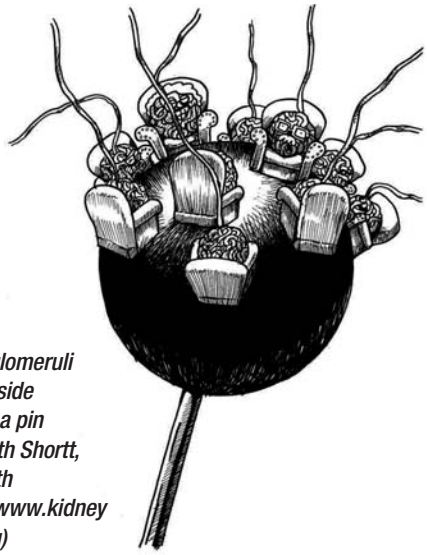

Figure 1. Ten glomeruli can fit side by side on the head of a pin (Cartoon by Beth Shortt, reproduced with permission of www.kidneyresearchuk.org)

Glomeruli filter over 150 litres of blood each day into the tubules. Glomerulonephritis is inflammation of the glomeruli. It can be divided into two types.

- Primary – only the kidneys are involved.
- Secondary – the kidneys are involved as part of a disease affecting other parts of the body.

What happens when our glomeruli do not work properly?

The first sign is leakage from the damaged glomeruli. They can leak either protein or blood.

Proteinuria

This is when the glomerular barrier leaks protein into the urine. The main protein involved, and the most important cause of proteinuria, is albumin. When the leak is very severe it can lead to nephrotic syndrome. This is when the leak is so large it can cause the levels of protein in the blood to fall (also known as hypoalbuminaemia). Nephrotic syndrome can cause other problems, including:

- Swelling of the ankles and legs (also known as oedema)
- A susceptibility to some infections
- Increased levels of cholesterol, particularly in patients who have had nephrotic syndrome for

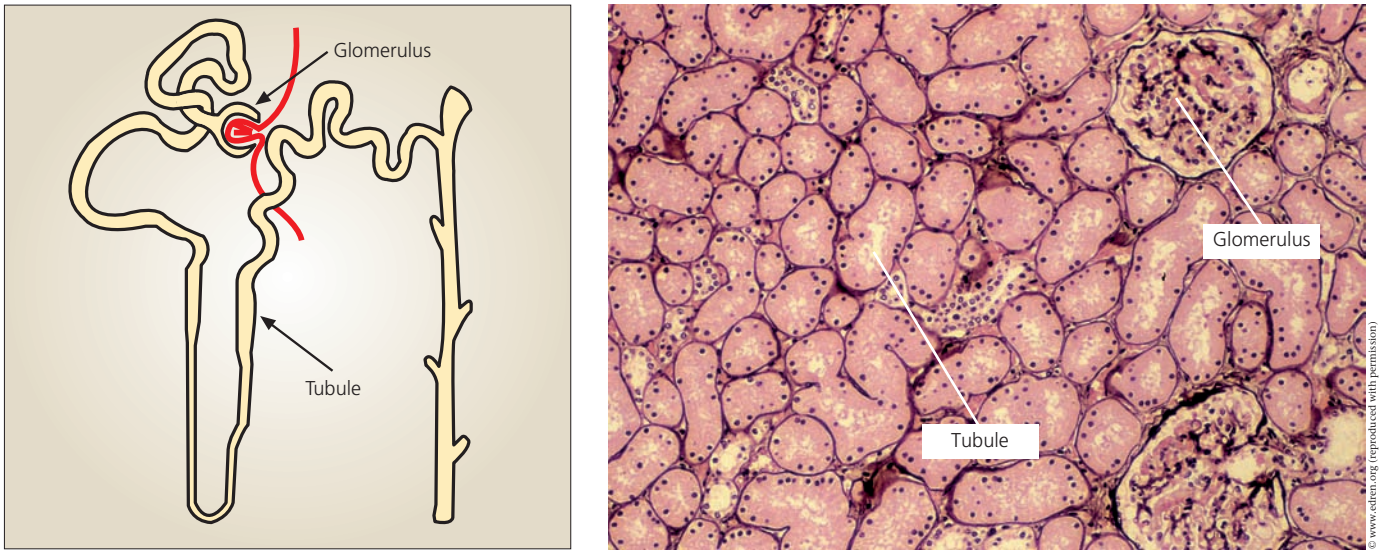

Figure 2. Left – Diagram of a glomerulus and its tubule. Right – A glomerulus as it appears through the microscope

a long time. This may increase the risk of narrowing of the arteries
- An increased likelihood of blood clotting in the veins, which can cause thrombosis in the leg veins or elsewhere in the body.

Haematuria

This means the appearance of blood in the urine. Red blood cells should normally be kept in the bloodstream by the filtering unit (the glomeruli). When the glomeruli become inflamed they can leak blood. If the blood is visible to the naked eye it is called macroscopic haematuria. Usually it is much less than you can see and is only detected by a urine dipstick test – this is called microscopic haematuria.

Blood pressure

High blood pressure (also known as hypertension) occurs in most kinds of glomerulonephritis and can lead to further kidney damage.

Loss of filtering power

If you lose a few glomeruli, the others can compensate, but if you lose too many you lose filtering capacity, so your kidneys do not work properly and waste products build up in the blood. The filtering capacity of glomeruli is called the glomerular filtration rate. You can lose 75% of your filtering capacity before you begin to feel unwell.

Kidney disease causes high blood pressure and high blood pressure damages kidneys further (Cartoon by Beth Shortt: reproduced with permission of www.kidneyresearchuk.org)

What can damage glomeruli?

Damage can result from:
- A congenital or inherited problem with some part of the glomeruli. The most common example is Alport's syndrome but other, usually rare, diseases can damage glomeruli
- Inflammation of either the kidneys alone or as part of a disease also affecting other organs
- Other problems, which can disturb some of the very special cells in the glomerulus, causing them to leak protein
- Diabetes, when extra material can be deposited in glomeruli, causing them to not work properly
- Different types of damage that cause different types of glomerulonephritis.

Table 1 (on page 17) lists the causes of glomerulonephritis and details the most common.

How do you make the diagnosis?

Sometimes the diagnosis is obvious from blood and urine tests. However, at other times a kidney biopsy is necessary in order to take a closer look at the kidney. A scanner is first used to find the kidney, and then, under local anaesthetic, a needle is placed into the kidney through the back. A very small sample of the kidney is taken and examined under a microscope.

Can glomerulonephritis be treated?

Although glomerulonephritis of all types cannot be cured, most can be slowed down by paying attention to blood pressure and other problems.

Minimal change disease (a kidney disease that causes nephrotic syndrome) does not cause permanent kidney failure but needs treatment to stop the protein leak. Most types of post-infectious glomerulonephritis get better if the infection does. Membranous nephropathy can either get better or progress. Crescentic glomerulonephritis can result in permanent kidney failure very quickly, but this can often be prevented by treatment. The other causes of glomerulonephritis, listed in Table 1, can progress over different periods of time, sometimes reaching end-stage renal failure up to 30 years after diagnosis. Dialysis or kidney transplantation may, therefore, be required at that stage.

Treating kidney disease

Two different methods can be used in the treatment of kidney disease.

Table 1. Causes of glomerulonephritis

	Proteinuria	Haematuria
Minimal change disease causes most cases of nephrotic syndrome in children but can cause it in adults too. However, it is unlikely to cause renal failure	++++	-
Focal and segmental glomerulosclerosis (FSGS) can cause nephrotic syndrome in adults. Those with other types of FSGS can progress to renal failure	++++	-
Membranous nephropathy causes proteinuria or nephrotic syndrome. Its cause is usually unknown, but it can sometimes be brought on by some medicines. Other diseases or cancer can also cause it. In some cases, patients with membranous nephropathy get better; others deteriorate	+++	-
Diabetes, after many years, can cause the kidneys to begin to leak protein. This is more likely to happen if the blood sugar level or blood pressure is poorly controlled	+++	-
Amyloid is a special protein that is deposited in the kidney. It can cause nephrotic syndrome and renal failure	++++	-
Lupus is a common cause of glomerulonephritis in young women. It can cause different types of glomerulonephritis. The worst cases need powerful treatment to prevent irreversible kidney damage	+++	+ to +++
Mesangio capillary glomerulonephritis can be caused by persistent infections (for example, endocarditis, and hepatitis B or C), other diseases, or it can occur alone	++	++
IgA nephropathy is the most common cause of glomerulonephritis worldwide (this is discussed in more detail later in the text)	+/-	++
Post-infectious glomerulonephritis is uncommon in the developed world. It occurs after an infection, often a streptococcal throat or skin infection. It causes haematuria, proteinuria, high blood pressure, fluid retention and reduced glomerular filtration rate. It usually gets better if the infection clears up	+	+++
Vasculitis is inflammation of small blood vessels in the glomerulus. It is often caused by diseases that also affect other organs (for example, microscopic polyangiitis and Wegener's disease). If severe, vasculitis can cause crescentic nephritis	+	++++
Crescentic nephritis is also known as rapidly progressive glomerulonephritis. It is a severe and usually very acute type of kidney inflammation that can cause loss of kidney function within days to weeks. It is important to make the diagnosis quickly so that kidney function can be saved	+	++++

Key: ++++ = heavy proteinuria/haematuria; + = slight proteinuria/haematuria; - = usually no proteinuria/haematuria; +/- = slight or no proteinuria/haematuria

General treatments – for all types of glomerulonephritis

As blood pressure is often high in patients with kidney disease, and can worsen kidney damage, it must be treated effectively. A type of blood pressure drug, known as an angiotensin-converting enzyme (ACE) inhibitor, has been proven to be particularly good at protecting kidney function and reducing the amount of protein in the urine. Blood pressure should be 120/75 mmHg or less. Blood pressure may need to be controlled using more than one type of medicine.

Disease-modifying treatments – for some types of glomerulonephritis

As many types of glomerulonephritis involve the immune system, treatments can involve drugs that try to 'dampen' down the immune system and reduce inflammation in the kidney (immunosuppressants). These include steroids (for example, prednisolone), cyclophosphamide, azathioprine, ciclosporin and mycophenolate mofetil. These are strong drugs that can have serious side-effects but that can rescue some severe types of glomerulonephritis (for example, crescentic glomerulonephritis, see Figure 3, overleaf). Consequently, they are often only used for those patients with severe disease or rapidly worsening kidney function. However, steroids alone are used frequently for the treatment of minimal change disease as it usually responds fully to treatment (although it may relapse and require re-treatment).

Immunoglobin A (IgA) nephropathy

This is a good example to discuss in more detail as it is the most common type of glomerulonephritis

worldwide. IgA is short for immunoglobulin A, an antibody that usually helps the body to fight infections. In IgA nephropathy, IgA is deposited in the glomerulus – though exactly why is not understood. About one in three cases of IgA nephropathy may progress to chronic renal failure, usually very slowly. It can, therefore, take ten to 30 years to reach end-stage disease requiring dialysis or transplantation.

IgA nephropathy may initially cause microscopic haematuria alone, or bouts of visible haematuria occurring with a sore throat or respiratory infection. It can also cause protein leak and sometimes nephrotic syndrome.

Most patients ... require only strict blood pressure treatment

Most patients with IgA nephropathy require only strict blood pressure treatment to slow down the progression of their disease. They may be given an ACE inhibitor that also reduces proteinuria. Immunosuppressants may be considered in those patients whose kidney function is deteriorating rapidly or if other symptoms are present. In a small number of patients with IgA nephropathy, the kidneys completely fail over time (which is known as end-stage renal failure) and dialysis or a kidney transplant is required.

This is one of the kinds of glomerulonephritis that can reappear in a transplant kidney, but usually not for a very long time.

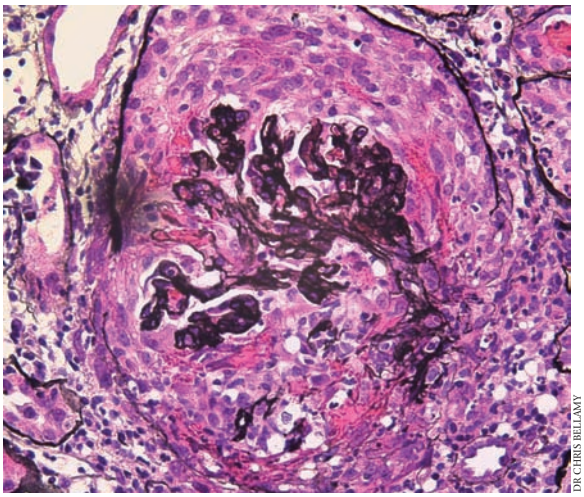

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Figure 3. A microscopic picture of a glomerulus affected by crescentic glomerulonephritis

Improving prospects

Glomerulonephritis is a common cause of end-stage kidney disease that requires dialysis or a kidney transplant, although in many people it never gets this bad. The very acute kinds of glomerulonephritis can quickly cause temporary or permanent kidney failure, but these are rare. More commonly there is a slow loss of kidney function over years. Modern treatments with ACE inhibitors and other blood pressure treatments seem to be greatly improving the prospects for people with this kind of kidney disease, and we hope to see fewer of them needing dialysis or kidney transplants in the future ■

Key points

- **Glomerulonephritis is inflammation of the glomeruli (the filters of our kidneys).**
- **The first sign of damaged glomeruli is leakage – both protein and blood can leak into the urine (known as proteinuria and haematuria respectively).**
- **When the glomerular barrier does not function properly and leaks a large amount of protein into the urine, it can cause nephrotic syndrome.**
- **Controlling blood pressure can protect the kidneys against further damage.**
- **As many types of glomerulonephritis involve the immune system, the treatments used can involve strong drugs that try to reduce kidney inflammation.**

Further information

For further information on glomerulonephritis, you may wish to visit the following websites

- **http://renux.dmed.ed.ac.uk/edren/EdRenINFOhome.html**
  This is the information site of the Renal Unit at the Royal Infirmary, Edinburgh
- **www.kidney.org.uk/Medical-Info/index.html**
  This is the website of the National Kidney Federation, providing medical information
- **http://kidney.niddk.nih.gov**
  This is the website of the National Institute of Diabetes and Digestive and Kidney Diseases