

How are the kidneys affected by Behçet's?

Kidney disease is not usually a significant problem for patients with Behçet's *syndrome* (or Behçet's *disease*). In the medical literature, of many thousands of patients, only around 250 have been reported to have Behçet's-related kidney problems. The *prevalence* of kidney involvement in clinics with large numbers of Behçet's patients has been reported to vary from 0% to 55%. However, in most cases the involvement is not significant; patients experiencing kidney-related symptoms are in a tiny minority. Because Behçet's-related kidney disease is uncommon, our knowledge comes from case reports of single patients, and a few reviews of the experience of larger clinics, so it is difficult to be absolutely certain whether the Behçet's has caused the kidney disease, whether it is a side effect of treatment, or whether the kidney disease is an incidental finding unrelated to Behçet's. However, it is likely that the following kidney disorders are associated with Behçet's:

- Amyloidosis (AA amyloid – deposits of proteinaceous material that interfere with kidney function).
- Glomerulonephritis (inflammation of the blood-filtering apparatus of the kidney).
- Vascular (blood vessel) disease (inflammation or thrombosis/clotting).
- Side effects of drugs used for treatment.

Serious kidney problems are more common in men, in people who have had other severe Behçet's-related problems for some time, and in people who have vascular (blood vessel) involvement such as thrombosis (blockage) or aneurism (bulging) of arteries or veins affecting other parts of the body.

Complications

Amyloidosis

Amyloidosis is the laying down of inert proteinaceous material that can affect the function of an organ. It can occur in almost any area of the body, but certain organs such as the kidney are more susceptible. Amyloidosis in Behçet's is almost always of the AA type and occurs following many years of poorly controlled *inflammation*. Some people of Mediterranean origin may be more *genetically susceptible* to this complication.

Glomerulonephritis

Glomerulonephritis refers to inflammation of the glomeruli, the areas in the kidney where the blood is filtered to remove waste products, which are then excreted via the bladder as urine. Significant glomerulonephritis is rare.

In one Turkish survey, only 0.16% of 4121 patients attending a Behçet's clinic over a 23-year period had glomerulonephritis (proven on *renal biopsy*).

Vascular (blood vessel) involvement

Behçet's can affect both arteries and veins. The consequences depend on the size and extent of the blood vessels involved. Blockage (thrombosis) or aneurism (bulging) of the renal artery (the main artery to the kidney) may occur. Occasionally, Behçet's can affect the aorta (the main artery leading from the heart) in the region of the renal (kidney) arteries, indirectly causing kidney problems. The kidneys help to control the blood pressure. Narrowing of the renal artery causes high blood pressure, which can be difficult to control and can cause more damage to the function of the kidneys, in extreme cases causing kidney failure. If only one side is affected, the normal kidney on the other side may nevertheless be damaged by the high blood

pressure. Aneurysms (bulging of the arteries) affect blood flow, cause pressure on surrounding structures, may develop blood clots (thrombosis or embolism) and may rupture. Any of these events may result in poor kidney function or high blood pressure, as described above. Small blood vessels internal to the kidney may become inflamed (vasculitis), or develop aneurysms or blockages.

Drug-related renal problems

Aspirin and other non-steroidal anti-inflammatory drugs (e.g. ibuprofen/Nurofen, diclofenac, indomethacin) can affect the kidney if used regularly in high doses. Intermittent or low-dose treatment is unlikely to be a problem. People with pre-existing kidney damage should avoid this type of medication unless advised otherwise by their doctor. Cyclosporine levels should be monitored regularly to avoid toxic doses. In people with pre-existing kidney damage, the risks and benefits of cyclosporine should be carefully considered before use. Cyclophosphamide in high doses can cause severe bladder inflammation, which can indirectly affect the kidney function. People on high-dose treatment (usually [intravenous](#)) can be given Mesna, an additional treatment that protects the bladder against the effects of cyclophosphamide. Tacrolimus may rarely cause impaired kidney function. Blood creatinine should be monitored.

Please note: this is not a comprehensive list of drugs that may affect the kidneys. Sometimes drugs with a risk of kidney side effects may nevertheless be the best choice to treat Behçet's-related kidney disease.

Investigations and diagnosis

Amyloidosis

Amyloid produces no symptoms in the early stages, although protein may be present on urine testing (proteinuria). If significant amyloid is present, nephrotic syndrome may occur, resulting in generalised swelling, large amounts of protein in the urine and low albumin (protein) in the blood. A biopsy (small sample of tissue for examination under the microscope) is necessary to diagnose amyloid. Fortunately, amyloid can usually be detected on rectal biopsy, a minor clinic based procedure, avoiding the necessity for a kidney biopsy, which is usually a day-case procedure, under local anaesthetic.

Glomerulonephritis

In the early stages, glomerulonephritis has either no symptoms or non-specific symptoms, such as fatigue, commonly experienced by people with Behçet's without kidney involvement. Blood pressure may be high.

However, high blood pressure is common and not usually caused by Behçet's-related kidney problems. Persistent presence of blood and protein on urine dipstick testing occurs.

Casts (clumps of red or white blood cells, accumulating as a result of inflammation) may be seen on microscopic analysis of urine. Presence of small amounts of blood and/or protein on urine dipstick testing is very common (2.5– 4% in healthy volunteers, 10.8% in the large Turkish survey of Behçet's patients) and usually does not indicate a serious problem. However, persistent abnormalities should be investigated further. Kidney biopsy is required to make the diagnosis in most cases in which glomerulonephritis is suspected. Kidney biopsy is the taking of a small sample of tissue from the kidney with a needle inserted through the skin. The sample is examined under the microscope for signs of inflammation.

Vascular involvement

Ultrasound studies show the structure of the large blood vessels and can diagnose aneurysms and large thromboses. Ultrasound also measures the size of the kidneys, bladder and tubes (ureters). Doppler studies use ultrasound techniques to measure blood flow and give useful extra information. Arteriography involves injecting a dye (contrast) into the artery and taking X-rays or CT scans to look for blockages or other abnormalities. Arteriography is riskier in people with Behçet's, as thrombosis is more likely to occur. Newer techniques using injections into veins are safer and, together with CT or MRI scanning, can often give the information required and may avoid the need for traditional arteriography. In the case of small vessel involvement, it may be difficult to decide if the kidney problem is Behçet's or polyarteritis nodosa, another

type of vasculitis. Presence of Behçet's-type symptoms affecting other parts of the body and the time course of events will help to determine the diagnosis.

Prevention and treatment

Amyloidosis

Amyloid can be prevented by good control of Behçet's, with anti-inflammatory or immunosuppressive drugs (for example, prednisolone, azathioprine, cyclosporine). The intensity of treatment required should be determined by the overall activity of Behçet's and blood tests to check levels of inflammatory markers such as **ESR** and **CRP**. In rare cases, monitoring of blood serum amyloid A protein (SAA) may be required. Colchicine may have additional anti-amyloid properties and in theory could be prevent the formation of amyloid. Once established, amyloid is difficult to treat. However, further deposition of amyloid, and in some cases regression of established amyloid, may be achieved by the above measures.

Glomerulonephritis

Immune suppression with corticosteroids (prednisolone) or immunosuppressive medication, as used for treatment of Behçet's elsewhere, is often required. Control of blood pressure is important to avoid further damage to the kidneys. Control of conditions unrelated to Behçet's, such as high cholesterol or diabetes, is important. Inflammation of other areas of the kidney (interstitial nephritis) has not been shown to be caused by Behçet's. However, some of the drugs used to treat Behçet's can cause interstitial nephritis.

Vascular involvement

Depending on the problem, corticosteroids or immunosuppressive agents may be given to reduce Behçet's activity. Anticoagulants, such as warfarin, may be required to reduce the chance of further blood clotting. Surgery may be required to relieve a narrowing or a blockage, or to remove an aneurism. Minimally invasive surgery, such as stenting (insertion of a tube to bypass the blockage or aneurism) via an artery in the leg, under local anaesthetic, may be possible. Treatment of Behçet's-related renal (kidney) vasculitis (and of polyarteritis nodosa) is with corticosteroids (prednisolone) and other immunosuppressive agents.

Dialysis and kidney transplantation

End-stage kidney failure is extremely rare in Behçet's, so only a handful of affected people are known to have required these treatments. Haemodialysis (use of a kidney machine) has been used successfully, although people with Behçet's are likely to have more complications initially. It is necessary to create a connection between an artery and a vein ('fistula') where the kidney machine can be connected. This connection is more likely to thrombose (block) in people with Behçet's. Peritoneal dialysis is feasible, although infection may be a problem. Kidney transplantation has been successful, although extra measures may need to be taken during surgery to avoid clotting of the transplanted renal blood vessels. On dialysis or after transplantation, Behçet's activity at any site is usually much reduced or absent.

Explanations of highlighted words, listed in the order they appear

Prevalence	how many people are affected by something
Genetically susceptible	this means that the genes you inherit from your parent's may make you more likely to have a particular condition
Inflammation	the way the body responds to irritation, infection or injury. Blood collects in infected areas causing pain and swelling or Redness
Biopsy	small sample of tissue taken for examination under a microscope, renal biopsy is tissue taken from the kidney
Intravenous	drugs or fluids that are given directly into a vein
ESR	Erythrocyte Sedimentation Rate, a blood test used to look at levels of inflammation in the body
CRP	C Reactive Protein' a protein in the blood which is often measured by a blood test, to check for signs of inflammation

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