Diseases And Conditions

Question: What causes glomerular disease?

Answer: A number of different diseases can result in glomerular disease. It may be the direct result of an infection or a drug toxic to the kidneys, or it may result from a disease that affects the entire body, like diabetes or lupus. Many different kinds of diseases can cause swelling or scarring of the nephron or glomerulus. Sometimes glomerular disease is idiopathic, meaning that it occurs without an apparent associated disease. The categories presented below can overlap: that is, a disease might belong to two or more of the categories. For example, diabetic nephropathy is a form of glomerular disease that can be placed in two categories: systemic diseases, since diabetes itself is a systemic disease, and sclerotic diseases, because the specific damage done to the kidneys is associated with scarring. **Autoimmune Diseases** When the body's immune system functions properly, it creates protein-like substances called antibodies and immunoglobulins to protect the body against invading organisms. In an autoimmune disease, the immune system creates autoantibodies, which are antibodies or immunoglobulins that attack the body itself. Autoimmune diseases may be systemic and affect many parts of the body, or they may affect only specific organs or regions. **Systemic lupus erythematosus (SLE)** affects many parts of the body: primarily the skin and joints, but also the kidneys. Because women are more likely to develop SLE than men, some researchers believe that a sex-linked genetic factor may play a part in making a person susceptible, although viral infection has also been implicated as a triggering factor. **Lupus nephritis** is the name given to the

kidney disease caused by SLE, and it occurs when autoantibodies form or are deposited in the glomeruli, causing inflammation. Ultimately, the inflammation may create scars that keep the kidneys from functioning properly. Conventional treatment for lupus nephritis includes a combination of two drugs, cyclophosphamide, a cytotoxic agent that suppresses the immune system, and prednisolone, a corticosteroid used to reduce inflammation. A newer immunosuppressant, mychophenolate mofetil (MMF), has been used instead of cyclophosphamide. Preliminary studies indicate that MMF may be as effective as cyclophosphamide and has milder side effects. **Goodpasture's syndrome** involves an autoantibody that specifically targets the kidneys and the lungs. Often, the first indication that patients have the autoantibody is when they cough up blood. But lung damage in Goodpasture's syndrome is usually superficial compared with progressive and permanent damage to the kidneys. Goodpasture's syndrome is a rare condition that affects mostly young men but also occurs in women, children, and older adults. Treatments include immunosuppressive drugs and a blood- cleaning therapy called plasmapheresis that removes the autoantibodies. **IgA nephropathy** is a form of glomerular disease that results when immunoglobulin A (IgA) forms deposits in the glomeruli, where it creates inflammation. IgA nephropathy was not recognized as a cause of glomerular disease until the late 1960s, when sophisticated biopsy techniques were developed that could identify IgA deposits in kidney tissue. The most common symptom of IgA nephropathy is blood in the urine, but it is often a silent disease that may go undetected for many years. The silent nature of the disease makes it difficult to determine how many people are in the early stages of IgA nephropathy, when specific medical tests are the only way to detect it. This disease is estimated to be the most common cause of primary glomerulonephritis—that is, glomerular disease not caused by a systemic disease like lupus or diabetes mellitus. It appears to affect men more than women. Although IgA nephropathy is found in all age groups, young people rarely display signs of kidney failure because the disease usually takes several years to progress to the stage where it causes detectable complications. No treatment is recommended for early or mild cases of IgA nephropathy when the patient has normal blood pressure and less than 1 gram of protein in a 24-hour urine output. When proteinuria exceeds 1 gram/day, treatment is aimed at protecting kidney function by reducing proteinuria and controlling blood pressure. Blood pressure medicines—angiotensin- converting enzyme inhibitors (ACE inhibitors) or angiotensin receptor blockers (ARBs)—that block a hormone called angiotensin are most effective at achieving those two goals simultaneously. **Hereditary Nephritis— Alport Syndrome** The primary indicator of Alport syndrome is a family history of chronic glomerular disease, although it may also involve hearing or vision impairment. This syndrome affects both men and women, but men are more likely to experience chronic kidney disease and sensory loss. Men with Alport syndrome usually first show evidence of renal insufficiency while in their

twenties and reach total kidney failure by age 40. Women rarely have significant renal impairment, and hearing loss may be so slight that it can be detected only through testing with special equipment. Usually men can pass the disease only to their daughters. Women can transmit the disease to either their sons or their daughters. Treatment focuses on controlling blood pressure to maintain kidney function. **Infection-related Glomerular Disease** Glomerular disease sometimes develops rapidly after an infection in other parts of the body**. Acute post-streptococcal glomerulonephritis (PSGN)** can occur after an episode of strep throat or, in rare cases, impetigo (a skin infection). The *Streptococcus* bacteria do not attack the kidney directly, but an infection may stimulate the immune system to overproduce antibodies, which are circulated in the blood and finally deposited in the glomeruli, causing damage. PSGN can bring on sudden symptoms of swelling (edema), reduced urine output (oliguria), and blood in the urine (hematuria). Tests will show large amounts of protein in the urine and elevated levels of creatinine and urea nitrogen in the blood, thus indicating reduced kidney function. High blood pressure frequently accompanies reduced kidney function in this disease. PSGN is most common in children between the ages of 3 and 7, although it can strike at any age, and it most often affects boys. It lasts only a brief time and usually allows the kidneys to recover. In a few cases, however, kidney damage may be permanent, requiring dialysis or transplantation to replace renal function. **Bacterial endocarditis**, infection of the tissues inside the heart, is also associated with subsequent glomerular disease. Researchers are not sure whether the renal lesions that form after a heart infection are caused entirely by the immune response or whether some other disease mechanism contributes to kidney damage. Treating the heart infection is the most effective way of minimizing kidney damage. Endocarditis sometimes produces chronic kidney disease (CKD). **HIV**, the virus that leads to AIDS, can also cause glomerular disease. Between 5 and 10 percent of people with HIV experience kidney failure, even before developing full-blown AIDS. HIV- associated nephropathy usually begins with heavy proteinuria and progresses rapidly (within a year of detection) to total kidney failure. Researchers are looking for therapies that can slow down or reverse this rapid deterioration of renal function, but some possible solutions involving immunosuppression are risky because of the patient's already compromised immune system. **Sclerotic Diseases Glomerulosclerosis** is scarring (sclerosis) of the glomeruli. In several sclerotic conditions, a systemic disease like lupus or diabetes is responsible. Glomerulosclerosis is caused by the activation of glomerular cells to produce scar material. This may be stimulated by molecules called growth factors, which may be made by glomerular cells themselves or may be brought to the glomerulus by the circulating blood that enters the glomerular filter. Diabetic nephropathy is the leading cause of glomerular disease and of total kidney failure in the United States. Kidney disease is one of several problems caused by elevated levels of blood glucose, the central feature of diabetes. In addition to scarring the kidney, elevated glucose levels

appear to increase the speed of blood flow into the kidney, putting a strain on the filtering glomeruli and raising blood pressure. Diabetic nephropathy usually takes many years to develop. People with diabetes can slow down damage to their kidneys by controlling their blood glucose through healthy eating with moderate protein intake, physical activity, and medications. People with diabetes should also be careful to keep their blood pressure at a level below 140/90 mm Hg, if possible. Blood pressure medications called ACE inhibitors and ARBs are particularly effective at minimizing kidney damage and are now frequently prescribed to control blood pressure in patients with diabetes and in patients with many forms of kidney disease. **Focal segmental glomerulosclerosis (FSGS)** describes scarring in scattered regions of the kidney, typically limited to one part of the glomerulus and to a minority of glomeruli in the affected region. FSGS may result from a systemic disorder or it may develop as an idiopathic kidney disease, without a known cause. Proteinuria is the most common symptom of FSGS, but, since proteinuria is associated with several other kidney conditions, the doctor cannot diagnose FSGS on the basis of proteinuria alone. Biopsy may confirm the presence of glomerular scarring if the tissue is taken from the affected section of the kidney. But finding the affected section is a matter of chance, especially early in the disease process, when lesions may be scattered. Confirming a diagnosis of FSGS may require repeat kidney biopsies. Arriving at a diagnosis of idiopathic FSGS requires the identification of focal scarring and the elimination of possible systemic causes such as diabetes or an immune response to infection. Since idiopathic FSGS is, by definition, of unknown cause, it is difficult to treat. No universal remedy has been found, and most patients with FSGS progress to total kidney failure over 5 to 20 years. Some patients with an aggressive form of FSGS reach total kidney failure in 2 to 3 years. Treatments involving steroids or other immunosuppressive drugs appear to help some patients by decreasing proteinuria and improving kidney function. But these treatments are beneficial to only a minority of those in whom they are tried, and some patients experience even poorer kidney function as a result. ACE inhibitors and ARBs may also be used in FSGS to decrease proteinuria. Treatment should focus on controlling blood pressure and blood cholesterol levels, factors that may contribute to kidney scarring. **Other Glomerular Diseases Membranous nephropathy**, also called membranous glomerulopathy, is the second most common cause of the nephrotic syndrome (proteinuria, edema, high cholesterol) in U.S. adults after diabetic nephropathy. Diagnosis of membranous nephropathy requires a kidney biopsy, which reveals unusual deposits of immunoglobulin G and complement C3, substances created by the body’s immune system. Fully 75 percent of cases are idiopathic, which means that the cause of the disease is unknown. The remaining 25 percent of cases are the result of other diseases like systemic lupus erythematosus, hepatitis B or C infection, or some forms of cancer. Drug therapies involving penicillamine, gold, or captopril have also been associated with membranous nephropathy. About 20 to 40 percent of patients with membranous

nephropathy progress, usually over decades, to total kidney failure, but most patients experience either complete remission or continued symptoms without progressive kidney failure. Doctors disagree about how aggressively to treat this condition, since about 20 percent of patients recover without treatment. ACE inhibitors and ARBs are generally used to reduce proteinuria. Additional medication to control high blood pressure and edema is frequently required. Some patients benefit from steroids, but this treatment does not work for everyone. Additional immunosuppressive medications are helpful for some patients with progressive disease. **Minimal change disease (MCD)** is the diagnosis given when a patient has the nephrotic syndrome and the kidney biopsy reveals little or no change to the structure of glomeruli or surrounding tissues when examined by a light microscope. Tiny drops of a fatty substance called a lipid may be present, but no scarring has taken place within the kidney. MCD may occur at any age, but it is most common in childhood. A small percentage of patients with idiopathic nephrotic syndrome do not respond to steroid therapy. For these patients, the doctor may recommend a low-sodium diet and prescribe a diuretic to control edema. The doctor may recommend the use of nonsteroidal anti-inflammatory drugs to reduce proteinuria. ACE inhibitors and ARBs have also been used to reduce proteinuria in patients with steroid-resistant MCD. These patients may respond to larger doses of steroids, more prolonged use of steroids, or steroids in combination with immunosuppressant drugs, such as chlorambucil, cyclophosphamide, or cyclosporine.