



C3 Glomerulopathy

What is it?

C3 glomerulopathy (C3G) is one of a larger group of kidney diseases known as glomerulonephritis (GN). C3G causes inflammation in the glomeruli – the tiny filters in the kidneys responsible for filtering waste and excess fluid from the blood.

Here's what happens in C3G:

- The body's complement system¹ – a part of the immune system that normally helps defend the body against infections – becomes overactive or uncontrolled, leading to the excessive activation of a protein called C3.
- This abnormal activation causes fragments of complement proteins to build up in the kidneys' filters (glomeruli).
- The buildup triggers inflammation and damage in the glomeruli.
- As a result, the kidneys can become leaky, allowing blood and protein to spill into the urine.
- Over time, this persistent inflammation may lead to scarring (fibrosis) and a progressive loss of kidney function.
- There are several reasons, which might explain this:
 - Genetic reasons: Some people may be born with changes (mutations) in the genes that control the complement system. These changes can make it harder for the body to "switch off" the system when it's no longer needed.
 - Autoantibodies: Sometimes, the body makes antibodies² that attack the complement system itself (autoantibodies). These keep the system constantly "on", even when it shouldn't be.
 - Paraproteins (monoclonal proteins): In some people — usually older adults — abnormal proteins (called paraproteins) made by a small group of cells in immune system or bone

¹ The complement system is part of your immune system that defends your body against injury and foreign invaders like bacteria and viruses that can make you sick. Your complement system activates proteins that work with your immune system to keep you healthy. Source: <https://my.clevelandclinic.org/health/body/23370-complement-system>.

² Antibodies are protective proteins produced by your immune system. They attach to antigens (foreign substances) — such as bacteria, fungi, viruses and toxins — and remove them from your body. Source: <https://my.clevelandclinic.org/health/body/22971-antibodies>.

Autoantibodies are malfunctioning parts of your body's natural defenses. Instead of targeting germs and other invaders, they attack your body. This can lead to lots of different issues and health conditions. Source: <https://my.clevelandclinic.org/health/symptoms/autoantibodies>.



marrow can interfere with the complement system. These proteins aren't supposed to be there and can interfere with the complement system's regulation, leading to C3G.

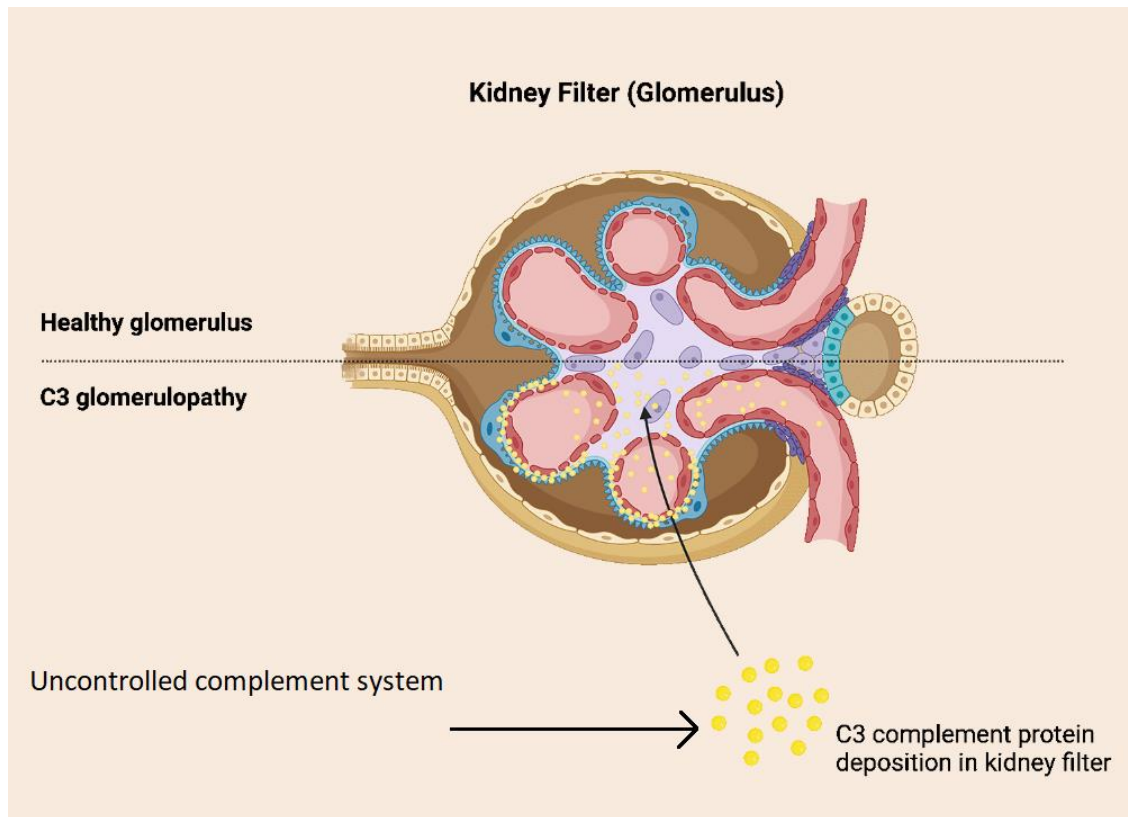


Figure source (modified): <https://tangoxstudy.com/patient-information-2/>

The symptoms of C3G may include:

- Fatigue (feeling tired).
- Swelling (edema) – puffiness in the legs, ankles, feet, and/or around the eyes.
- Foamy or bubbly urine – due to excess protein leaking into it from the kidneys.
- Blood in the urine – may look pink, red, or brown. This can sometimes get worse after recent viral or other infections.

The complications of C3G may include:

- Declining kidney function, which may lead to kidney failure over time requiring dialysis or transplant.
- High blood pressure – the kidneys help regulate blood pressure, so damage to the kidneys can cause it to rise.



- Weight gain – caused by fluid retention, not actual fat gain.
- Sometimes there are no symptoms at all, and the condition is only found through routine urine or blood tests.

What happens after you have been diagnosed with kidney disease due to C3G?

- After your kidney biopsy is reported and a final diagnosis of C3G is made, your kidney doctor (nephrologist) and/or kidney care team may order further tests or scans and will discuss appropriate treatment with you.
- You may be referred to other specialists for assessment of damage in other organs. For example, you may be referred to a rheumatologist or a respirologist.

How is C3G treated?

The aim of treatment is to lower the inflammation in the kidneys to prevent further damage. Not all patients require treatment. This depends on the findings of the kidney biopsy and the amount of protein in the urine.

- Treatment options may include:
 - Corticosteroids
 - Mycophenolate mofetil (MMF)
 - Medications that inhibit the complement system, such as eculizumab or others
- When taking these medications, you are at a higher risk of bacterial and viral infection. Depending on which drug is needed, you may need specific vaccines to prevent infections including meningococcus, pneumococcus and hemophilus. If you develop a fever, please seek medical attention immediately.
- The length of treatment is individualized based on disease severity, response to treatment and previous relapses.
- New medications may become available for controlling C3G over the coming years as more research is being done in this area.



General therapies:

- **Lab tests:** Your kidney doctor and/or kidney care team will follow you closely with frequent urine and blood tests to monitor your response to treatment and help you manage any symptoms.
- **Antibiotics during immunosuppressive therapy:** If you are receiving immunosuppressive therapy, depending on its type, you may be started on a combination of trimethoprim and sulfamethoxazole. These antibiotics are used to reduce the risk of very serious infection that can occur in patients on medications that reduce the immune response.
- **Other medications while undergoing treatment for C3G:**
 - While on high doses of corticosteroids, your kidney care team may recommend calcium, vitamin D, and medication to maintain bone health.
 - Also, while on immunosuppression, your kidney care team may offer you medication to prevent stomach upsets.
 - Medications to control swelling (diuretics) and/or blood pressure may be initiated depending on your symptoms.
- **Medication options:** Your kidney doctor and/or kidney care team will support you in learning about the medication options that would be best for you.
- **Medication cost:** BC Renal covers the cost of a wide range of medications used for C3G treatment.

- **Important:** Patients need to check with their kidney doctor and/or kidney care team before taking any over-the-counter (OTC) medications and natural health products.
- **Important:** Patients with chronic kidney disease like C3G need to keep their vaccinations updated. Some treatments may reduce the effectiveness of vaccination. You are encouraged to discuss with your kidney doctor and/or kidney care team what vaccinations may be appropriate for you.
- **Important:** Pregnancy may impact kidney function. If you are planning a pregnancy, please consult with your kidney doctor.
- **Important:** Smoking cessation is important – it can help slow down the worsening of kidney disease. Your family doctor can provide resources to help quit smoking.

Living with C3G



- Support of kidney care team: BC kidney patients registered with BC Renal have access to a comprehensive kidney care clinic (KCC) team that includes nurses, dietitians, and social workers. In most cases, patients will also have access to a pharmacist.
- Support for your wellbeing: It will be important for you to stay active and healthy. The Kidney Foundation's online Kidney Wellness Hub (<https://kidneywellnesshub.ca/>) has a lot of useful information. It covers staying active, eating well, mental wellbeing, and socially connecting, including peer support groups. It also provides online classes, webinar recordings, and activity suggestions for patients of all ability levels.
- Ongoing follow-up: The disease course of people living with C3G is unpredictable. Relapses are common, even many years after C3G is diagnosed. You will need ongoing follow-up with your kidney doctor and/or kidney care team.
- Risk of kidney failure: There is a portion of C3G patients who will end up with kidney failure, despite treatment. If your kidneys fail, your treatment options may include transplant, dialysis, and conservative care³. However, a portion of C3G patients may experience recurrences of the disease even after transplantation. Your kidney doctor and/or kidney care team will be there to educate and support you throughout your journey.
- Participation in clinical trials: Sometimes, people living with C3G may be invited to participate in a clinical trial for new therapies and medications. If you choose to volunteer in a trial, your kidney doctor and/or kidney care team will help you navigate the process.

Further information

- There may be a lot of confusing information about C3G and other kidney diseases on the Internet. The following websites are good sources of information for people living with this disease:
 - The Kidney Foundation of Canada - <https://kidney.ca/>
 - Kidney Wellness Hub - <https://kidneywellnesshub.ca/>

³ Conservative care, sometimes called conservative kidney management (CKM) or supportive kidney care, focuses on treating the symptoms of kidney failure to make you feel as well as possible. It does not treat the causes or attempt to cure kidney failure. Although conservative care does not include dialysis or transplant, it does include all of the other parts of kidney care and support from your team. For more information see this BC Renal's handout: http://www.bcrenal.ca/resource-gallery/Documents/Patient_Guide-Transitioning_to_Conservative_Care-Kidney_Care_Clinics.pdf.



- BC Renal GN web page - <http://www.bcrenal.ca/health-info/kidney-care/glomerulonephritis>
- C3 glomerulopathy web page - by University of Iowa - <https://morl.lab.uiowa.edu/what-c3-glomerulopathy-c3g>
- C3 glomerulopathy web page – by NephCure Kidney International - <https://nephcure.org/intro-to-rkd/types-of-rkd/complement-3-glomerulopathy-c3g/>
- If you continue to have questions about your condition or treatment, please keep track of these questions and ask your kidney doctor and/or kidney care team.