

● Navigating C3G and primary IC-MPGN

Knowledge is a powerful tool in the management of your condition. The goal of this guide is to help you better understand complement 3 glomerulopathy (C3G) and primary immune-complex membranoproliferative glomerulonephritis (IC-MPGN), giving you the confidence to take an active role in your care.



The role of C3

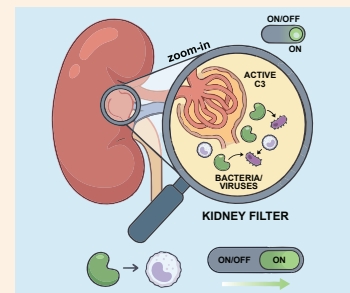
C3G and primary IC-MPGN are two different rare kidney diseases that share a common problem: An overactive C3 protein in the immune system (the complement system).

The complement system is a collection of proteins in the blood that usually helps, or *complements*, the immune system to fight against harmful bacteria or viruses.

How the complement system protects you

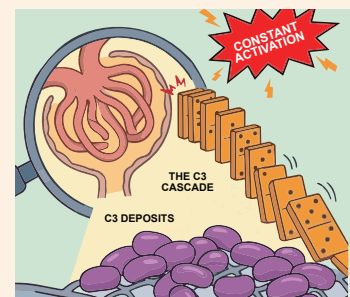
1 The complement system is part of the immune system

It is made up various proteins in the blood that usually helps – or complements – the immune system to help fight harmful bacteria and viruses. This helps to keep you healthy.



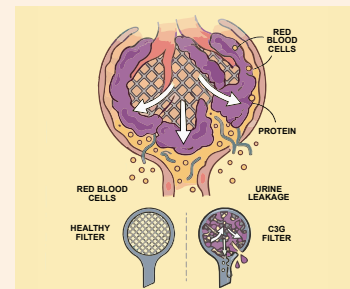
2 In C3G/primary IC-MPGN: An overactive complement system

In C3G and primary IC-MPGN, a mistake causes the complement system to become more active than usual.



3 The result: Clogged kidney filters (glomeruli)

The constant overactivity of the complement system causes more enzymes to be made that break down normal complement proteins such as C3. The breakdown products creates clutter in the kidneys where these pieces of C3 accumulate. C3 proteins clog up and set off reactions that damage the glomeruli (the kidney's filters), which prevents them from doing their job. This causes blood and protein to "leak" into your urine.



When C3 becomes overactive, it can mistakenly damage the kidneys.

This is because:

- The body needs to make more enzymes to break down normal complement proteins, such as C3
- These pieces of C3 are deposited and accumulate in the kidney
- This sets off reactions that injure the glomeruli, which are tiny filters in your kidney, and they can't filter the blood very well, resulting in less urine
- If this continues, more kidney tissue can become damaged, toxins can build up in the blood, and the kidney is unable to function properly

Characterizing C3G and primary IC-MPGN

Despite being different conditions, C3G and primary IC-MPGN have overlapping consequences, including:

- Proteinuria (high levels of protein in the urine)
- C3 deposits in the kidney
- Reduced kidney function

C3G

C3G stands for:

- **C3:** Complement 3, a blood protein involved in the immune system
- **G:** Glomerulopathy, meaning damage to the glomeruli
 - Glomeruli are tiny filtering units in the kidney that remove waste from the body

C3G occurs when an abnormal amount of the C3 protein is found in the kidneys **without significant antibody involvement**.

Primary IC-MPGN

IC-MPGN stands for **I**mmune-**c**omplex **m**embranoproliferative **g**lomerulonephritis. Primary IC-MPGN occurs when antibodies in your immune system mistakenly start to attack the healthy cells in your kidneys. Your immune system makes proteins called antibodies that attack substances in your body that they see as harmful (antigens). Antigens combine with antibodies to make immune complexes that get stuck in your kidneys and cause damage. When the cause for this unusual behaviour of the immune system is unknown, it is called primary IC-MPGN.

IC-MPGN may be caused or triggered by certain long-term infections (such as hepatitis C), autoimmune diseases (such as lupus), or some types of cancer – this is called secondary IC-MPGN.

Finding these differences in a biopsy helps your healthcare team provide an accurate diagnosis so that together you can choose the best care plan for you.

Recognizing the signs and symptoms of C3G and primary IC-MPGN

Both C3G and primary IC-MPGN disrupt the kidney's ability to filter blood effectively, leading to similar signs and symptoms, including:



Proteinuria

Excess protein in the urine (caused by damage to the glomeruli), often causing foamy or cloudy urine



Swelling (edema)

Fluid retention, particularly in the legs, ankles, hands and around the eyes



Hypertension (high blood pressure)

Reduced kidney function can lead to fluid buildup, causing the pressure of the blood in the body's arteries to be higher



Hematuria (blood in the urine)

When glomeruli become damaged, they leak red blood cells, causing urine to appear pink, red or brown, or microscopic blood may be detected during testing



Fatigue and reduced alertness

Caused by the buildup of waste products in the blood that can affect the brain and make you feel tired or unable to concentrate

Not everyone will experience the same symptoms

Symptoms can vary depending on the stage of the disease and underlying conditions that may be contributing to the kidney damage. Talk to your healthcare team if you experience any of these symptoms or notice a change in them.

Diagnosing C3G and primary IC-MPGN

People showing signs and symptoms of kidney dysfunction may be asked to go through a range of diagnostic procedures.

This may feel like a lot of tests, but they are essential for getting a clear and accurate diagnosis.

A kidney biopsy is required to definitively confirm a C3G or primary IC-MPGN diagnosis.

Having this clarity ensures you receive the right diagnosis so that you receive the right care that is tailored to your needs.



Medical history and **physical examination** are used to assess symptoms, family history and underlying conditions



Urine and blood tests can detect proteinuria and hematuria



Kidney biopsy is a procedure where a tiny piece of your kidney is surgically removed with a special needle and examined under special microscopes. The kidney biopsy may show the breakdown products of C3 (without antibodies) in the glomeruli, which usually confirms a diagnosis of C3G. The image from the microscope can also reveal the pattern of damage linked with IC-MPGN



Genetic and complement tests can identify abnormalities in the complement system that contribute to kidney damage



Additional tests can be conducted for primary IC-MPGN that help to rule out secondary causes and underlying conditions

Both C3G and primary IC-MPGN are chronic progressive diseases and, if left untreated, may result in irreversible damage.

An early diagnosis allows for a timely and individualized care plan to be put in place and optimize outcomes for you.

Help to keep your kidneys healthy

By maintaining a healthy lifestyle, you can help support your kidney health and protect your kidney function.

Here are some helpful lifestyle tips:

Gain control over other health conditions

- High blood pressure or high blood sugar levels may lead to a decrease in kidney function
 - If you have problems with your blood pressure or sugar levels, talk to your healthcare team about how you can get in control

Maintain a healthy weight

- Eat a well-balanced diet by incorporating whole foods as much as possible, including vegetables, fruits, whole grains, nuts and legumes and reduce your intake of sugary, canned and processed foods
- Engage in regular physical activity, such as walking, yoga, biking and swimming

If you smoke, try to quit

- Smoking can increase the risk of progression to end-stage kidney disease

Take note

Use this space to write down any information you receive from your healthcare team or questions you may have, such as:

- How can we decide, together, on the optimal care plan for me?
- What outcomes are you expecting from my care plan?
- What lab values are you monitoring to track my condition?

To learn more or to find support resources, scan to visit:



Living with C3G-ICMPGN
livingwithc3g-icmpgn.com



National Kidney Foundation of Canada
kidney.org

