# Living with the Rare Kidney Diseases C3G and IC-MPGN

A Guide for Those Affected, by Patients, Caregivers, Nephrologists, and Other Experts


compcure

This guide was written by patients and caregivers, in conjunction with nephrologists and other experts in complement-mediated kidney diseases. We recognize that there are different approaches to treating C3G and IC-MPGN, depending on the country, the treating nephrologist, and the individual patient.

**While we believe the information offers useful advice from personal experiences and research, which can guide you on your journey, it does not replace the care from your treating physician.**

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# Preface

**Suddenly we found ourselves embarking on an unwanted journey, moving forward, but with uncertainty about the destination. There was no turning back. We had to come to terms with the unpredictable and progressive nature of the disease.**

This reality struck me when my daughter was diagnosed with IC-MPGN. Despite advanced medical care and highly skilled physicians, the diagnostic journey appeared long, while her disease progressed rapidly. It was a close call.

Following several failed treatment attempts, we were lucky to find a therapy that works for her. It felt like a miracle. She is still thriving today, but anxiety remains.

It helps to connect with experts and others with similar experiences. Our feelings, concerns, and questions often resonate. Yet we struggle to find meaningful support and fact-based answers. Inconsistent information may lead to suboptimal decisions, preventable disease progression, and serious complications.

It is our sincere hope that everybody affected by C3G or IC-MPGN will get the opportunity to live as full and healthy lives as possible. As science advances and new therapies become available, this dream becomes more attainable. Still, we recognize that various challenges persist.

With this book, we hope that the collective knowledge of patients, caregivers, nephrologists and other experts will support the readers navigating through the challenges associated with C3G and IC-MPGN, in collaboration with their treating physicians.

Although all journeys with C3G and IC-MPGN are unique, nobody needs to travel alone or without a compass.

Best wishes,
Marianne Silkjaer Nielsen

# About the Kidneys

*Mark Frankiw and*
*Dr. Giulia Bassanese*

The kidneys are two bean-shaped organs, each about the size of a closed fist. They are located in the lower back, with one on each side of the spine. Their main function is to filter out waste, toxins, and extra fluid from the blood to produce urine. They also help control blood pressure and maintain the balance of important minerals and electrolytes, as well as producing hormones that support healthy blood and bones. Since the kidneys perform so many vital functions, maintaining their health is crucial for survival and overall wellbeing.

# About the Complement System

*Alex Gibbs and*
*Dr. Jutta Schroeder-Braunstein*

The complement system is an essential component of the innate immune system. It consists of more than 30 proteins that circulate in the blood. It protects the body against pathogens by directly killing them and by triggering a rapid inflammatory response that includes activation of immune cells. Furthermore, by supporting the removal of immune complexes as well as damaged or altered body cells, it helps maintain tissue integrity.

Deficiencies in complement proteins can lead to increased risks of infections and chronic inflammatory and autoimmune diseases.

Complement molecules are organized in three activation cascades which all meet at C3, which is the central component of the complement system:

- Alternative Pathway
- Classical Pathway
- Lectin Pathway

These pathways are activated following detection of pathogens or cell damage by different sensor molecules. Complement activation means that complement molecules are split into smaller fragments (e.g., C3a, C3b, C5a) or form pore complexes (C5b-9). Some of these activation products then mediate the complement effector functions that is killing pathogens (e.g., C5b-9), removing irregular cells (e.g., C3b), and recruiting and activating immune cells (e.g., C3a, C5a).

Complement activation is tightly controlled by regulator proteins, such as factor H and factor I, to prevent damage to healthy cells. Overactivation of the complement system due to complement dysregulation or other causes can lead to chronic inflammation. Sometimes this requires a triggering event, such as an infection.

Eventually, chronic inflammation can destroy healthy tissues, affecting the kidneys and other organs.

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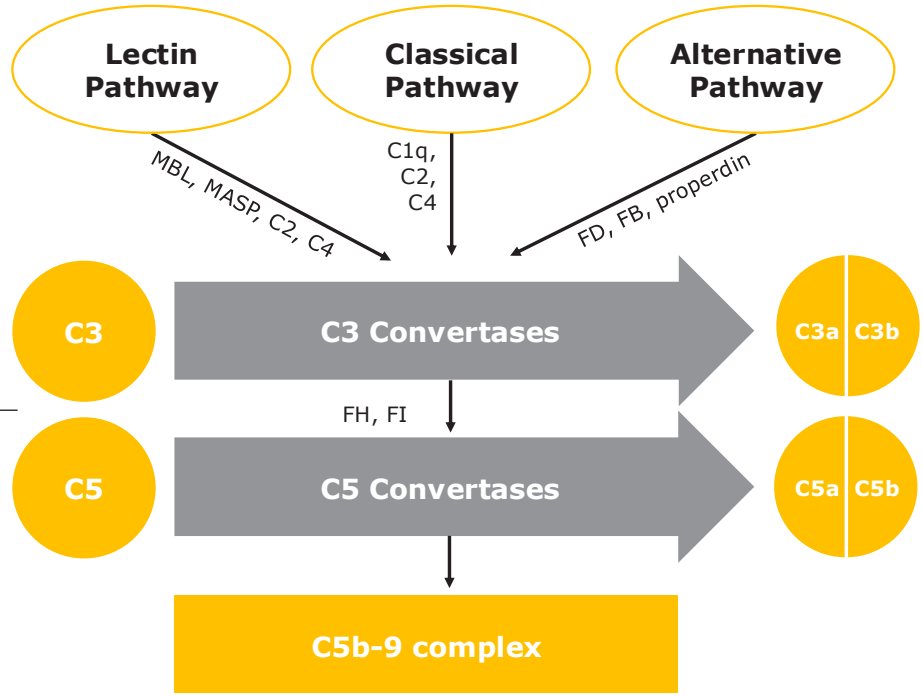
***C3 convertases cleave the central complement protein C3 into active C3a and C3b. This process is essential for amplifying the immune response and killing pathogens.***

***C5 convertases cleave the complement protein C5 into active C5a and C5b. They play a critical role in inflammation and killing pathogens.***

In C3G, dysregulation of the alternative pathway is frequently observed. In IC-MPGN, both the alternative and the classical pathways can be overactivated.

To optimally diagnose and treat complement-mediated diseases, such as C3G and IC-MPGN, it is important to understand complement dysregulations in individual patients. This requires advanced testing by a specialized laboratory.




**Top-line overview of the complement system**

# About C3G and IC-MPGN

*Ane Merino Guevara and Prof. Dr. Gema Ariceta*

Both C3G and IC-MPGN are rare, progressive kidney diseases caused by abnormal immune system activity. Both diseases can occur in children and in adults.

The diseases lead to inflammation and the accumulation of C3 deposits in the kidneys in C3G and immunoglobulins and/or other complement proteins in IC-MPGN. Over time, this process damages the kidneys and impairs their ability to filter waste and fluids from the blood in most patients. Fortunately, in some patients - more frequently children - the diseases may stay in remission with standard antiproteinuric treatment (ACEi/ARBs), and/or immunosuppression, and eventually even after pausing treatment. As the diseases can progress in silence, meaning that the patient does not feel any symptoms, it is important to be seen regularly by a nephrologist, or for children a pediatric nephrologist.

### C3G

In most cases, C3G is idiopathic, meaning the cause is unclear. In other cases, it is caused by genetic variants. Although infections are a common trigger of C3G flare-ups, the exact cause of the disease is often unknown.

There are two types of C3G: dense deposit disease (DDD) and C3 glomerulonephritis (C3GN). The difference between the two types is determined by examining kidney tissue following a biopsy (see the biopsy section).

### IC-MPGN

There are two types of IC-MPGN. Secondary IC-MPGN occurs when kidney disease is caused by other health conditions, such as infections (like hepatitis), autoimmune diseases (like lupus), or cancer. These conditions trigger the immune system to attack the kidneys, leading to inflammation and damage. This book focuses on primary IC-MPGN.

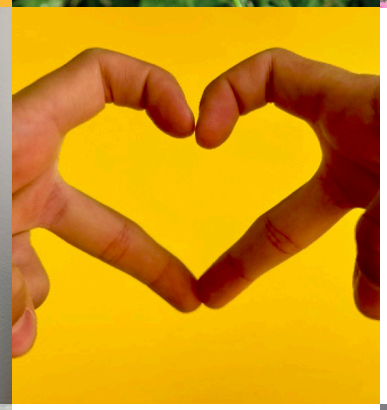
Idiopathic IC-MPGN means the cause is unknown. However, once secondary forms are excluded, highly specialized analyses often reveal the same complement system abnormalities that cause C3G, leading nephrologists to consider these two diseases to be part of one spectrum.

Both C3G and IC-MPGN are complex diseases that develop differently in each patient. In addition to the kidneys, there may be an impact on mental health and other organs. Historically around half of the affected patients progressed to end-stage kidney disease within a decade after they were diagnosed. Fortunately, the prognosis is improving. We are entering into a new era, where new targeted therapies are becoming available, and we are learning more about the diseases. Putting together the right team of healthcare professionals, nurses, nutritionists, psychologists, pediatricians (for children), etc. according to the individual needs of the patient will make a big difference.







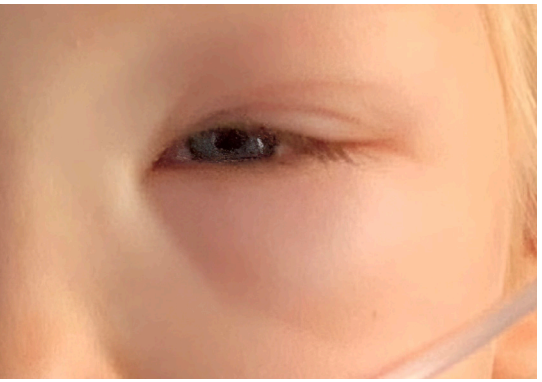



# Symptoms and Screening

*Oksana Paulsen and*
*Prof. Dr. Yoshitaka Isaka*

The symptoms of C3G and IC-MPGN tend to be unspecific and can vary widely. It may not be obvious that they are linked to kidney disease, which can delay diagnosis and the initiation of treatment.

In the initial phases, many patients do not feel any symptoms at all. When C3G and IC-MPGN are detected early, it is commonly in connection with screening or a health check where blood and/or proteins are detected in the urine. The insidious thing about this disease is that urine samples are sometimes normal during the initial phase. In this case, protein and/or blood are found in urine only when someone has an infection.



As the diseases progress, many patients feel more tired, they might feel nausea and their blood pressure may increase. It is also common to notice puffiness around the eyes, swollen legs, and sudden weight gain. Recurring infections and other signs that the immune system is not functioning properly are other common symptoms of C3G and IC-MPGN.

It is important to act on these symptoms, as they indicate the severity of the diseases. The inflammation in the small filters in the kidneys, the glomeruli, is called glomerulonephritis. If left untreated, glomerulonephritis can lead to kidney failure and other serious complications.

Regular screening programs offer a meaningful approach to helping patients with all kidney diseases, including C3G and IC-MPGN, to get diagnosed early. Such programs successfully exist in Japan, where most of the population is screened for proteinuria annually. This enables patients to receive an early diagnosis and treatment, which is crucial given that loss of kidney function tends to be irreversible.

In countries where urine tests are not part of routine medical examinations, it is advisable for patients to check their or parents to check their children's urine themselves for proteins and blood from time to time. This can be done at home at any time using an inexpensive urine test strip from a drugstore.

# Diagnosis and Testing

*Marianne Silkjaer Nielsen,*
*Prof. Dr. Carla Nester and*
*Dr. Jutta Schroeder-Braunstein*

A kidney biopsy is required for diagnosing C3G and IC-MPGN, and a specialist experienced in these diseases must interpret the analysis. Before undergoing a biopsy, patients usually get several urine and blood tests. These are the same tests often used to monitor the disease after diagnosis. This section will cover the most common tests used for diagnosing and monitoring C3G and IC-MPGN.

### Urine Tests

**Hematuria** is the presence of blood in the urine. There are two types: macrohematuria, which is visible and makes the urine appear red or brown, and microhematuria, which can only be seen under a microscope. Since hematuria can be harmless or a sign of serious kidney disease, such as C3G or IC-MPGN, determining the cause is important.

**Proteinuria** means protein in the urine. Normally, there is very little protein in the urine. Low levels of proteinuria usually do not result in symptoms. However, when there is a lot of protein in the urine, it may appear foamy. If patients have high levels of proteinuria for a long time, the level of an important protein called albumin in the blood will decrease because it is being lost in the urine. This causes fluid to leak from blood vessels into tissues, leading to swelling and weight gain. This condition is known as **edema**. Instead of testing for total proteinuria, some doctors will test only for the level of albumin in the urine **(albuminuria)**, which is acceptable.

The concentration of protein and other constituents in urine can vary throughout the day, which can affect lab results. Therefore, testing urine collected over an entire 24-hour period can be meaningful. Another common method for assessing the severity of proteinuria or albuminuria is considering the ratio of protein or albumin in the urine compared to the amount of creatinine in the urine, known as the **protein-to-creatinine ratio (UPC).** This method is particularly useful in children, as collecting a 24-hour urine sample can be difficult. The best time to test the UPC is in the first morning urine, collected immediately after the patient wakes up.

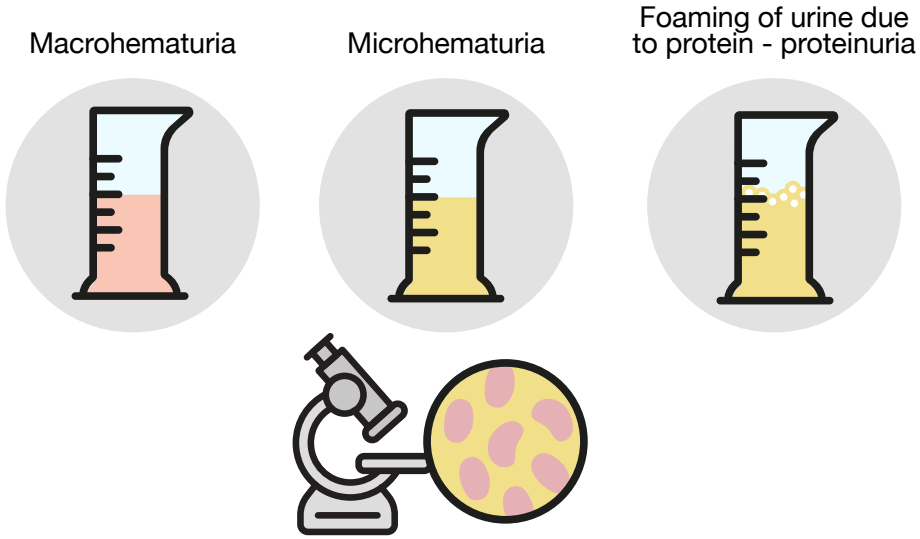



**Illustration of urine with presence of macrohematuria, microhematuria, and proteinuria**

### Blood Tests

C3G and IC-MPGN are heterogeneous glomerular diseases, meaning they manifest differently from patient to patient. This makes them difficult to treat. This heterogeneity stems from the various causes of the diseases. Sometimes genetic abnormalities cause the disease. Other times, autoimmune reactions may underlie the disease. In many cases, the cause is unknown.

To better understand potential causes, it can be helpful to periodically have a full blood panel done at a specialized lab, in addition to routine tests performed during doctor's visits. These tests can help define the underlying features of the disease and are often useful in diagnosis, disease management, and important treatment decisions.

| Common Blood Tests | What Is Measured |
|---|---|
| **eGFR** | The Estimated Glomerular Filtration Rate is a measure of how well the kidneys are filtering waste out of the blood. Higher numbers indicate better function. |
| **Creatinine** | Creatinine is a waste product from muscle metabolism that healthy kidneys filter from the blood. Because creatinine is filtered from the blood by the kidneys, it can be used to estimate how well the kidneys are doing their filtering job. |
| **Blood Urea Nitrogen (BUN)** | Blood urea nitrogen is produced when your body breaks down the urea component of the proteins in your body. Rising values can suggest that the kidneys are not working as well. |
| **Albumin** | Albumin is the most abundant protein in human blood plasma and has many functions. It is the major protein responsible for keeping the fluid component in the blood vessels. The lower the albumin, the more likely fluid will leak out of the blood vessels into the tissues. |

| Common Complement Tests | What Is Measured |
|---|---|
| **C3** | The central protein of the complement system, acting as the convergence point for all three activation pathways. Low C3 or high C3a or C3b are signs of an overactive complement system. |
| **C4** | A key protein in the classical and lectin pathways. A low C4 can be a sign of an overactive classical complement pathway. |
| **sC5b-9** | Soluble form of C5b-9 which is generated during activation of the terminal complement pathway. Elevated levels indicate ongoing complement activation. |
| **C3 Nephritic Factor (C3Nef)** | An autoantibody (immunoglobulin) that binds to the central enzyme (C3 convertase) in the alternative complement pathway and causes persistent C3 consumption and prolonged complement activation. |
| **C5 Nephritic Factor (C5Nef)** | An autoantibody (immunoglobulin) that binds to the other major enzyme (C5 convertase) in the alternative complement pathway and causes persistent C5 consumption, activity of the terminal complement pathway, and prolonged complement activation. |

| Common Complement Tests | What Is Measured |
|---|---|
| **C4 Nephritic Factor (C4Nef)** | An autoantibody that binds to the central enzyme in the classical and lectin pathways, leading to continuous, uncontrolled complement activity. |
| **Factor H (FH)** | The major regulator of the alternative complement pathway. It controls the amplification loop, preventing over-activation. |
| **Factor I (FI)** | A major regulator of all three pathways of the complement system. It prevents excessive complement activation. |
| **Properdin** | Acts as a key positive regulator of the complement system's alternative pathway. |
| **CH50 / AH50** | Tests assess the overall activity of the classical (CH50) or alternative (AH50) complement pathway. Reduced activity can indicate overactivation (due to consumption of complement factors). They are also used for monitoring complement inhibitor treatment. |

### Genetic and Acquired Factors Driving Complement Dysregulation

These diseases are characterized by the overactivation of the complement system, which can be caused by genetic abnormalities or acquired autoantibodies.

Genetic abnormalities in the complement pathway are occasionally found in patients with C3G. These variants often lead to a loss of regulation, causing persistent activation of the complement pathway and ultimately resulting in kidney damage.

A genetic test involves sending a blood sample to a lab that specializes in complement genetics. However, finding a genetic variant does not necessarily mean that the patient will develop kidney disease. Often, genetic studies identify variants of uncertain significance. These are gene differences in the population whose function is unknown. They may have no function at all, including in relation to the disease.

| Genetic Testing | What Is Measured |
|---|---|
| **C3, CFH, CFI, CFB, CFHR1-5** | Genes most commonly associated with a complement-mediated disease. Sometimes the doctor may decide to look at the whole genome. |

In addition to genetic factors, the body may produce proteins that act against complement proteins, known as acquired autoantibodies. The most common of these in C3G and IC-MPGN are nephritic factors C3, C4, and C5 (see the table of complement tests). These autoantibodies may cause excessive complement activation. Prolonged activation leads to inflammation and progressive damage to the glomeruli of patients with C3G or IC-MPGN.

### Biopsy

A kidney biopsy is necessary for diagnosing C3G and IC-MPGN. During the procedure, a small sample of kidney tissue containing glomeruli is removed. The sample is then sent to a specialized laboratory, where a renal pathologist examines it.

To make an exact diagnosis, the pathologist must have experience diagnosing C3G and IC-MPGN. The following techniques will be used:

- **Light microscopy (LM):** This technique uses several different stains to evaluate the general appearance of various structures in the biopsy tissue.
- **Immunofluorescence (IF):** This technique reveals the presence of C3 or immunoglobulin staining and the intensity of the staining.
- **Electron microscopy (EM):** This technique is used to visualize structural changes and the location of complement proteins and/or immunoglobulin deposits. EM helps differentiate between C3G disease types. However, EM is not always performed and is not required for a C3G or IC-MPGN diagnosis.

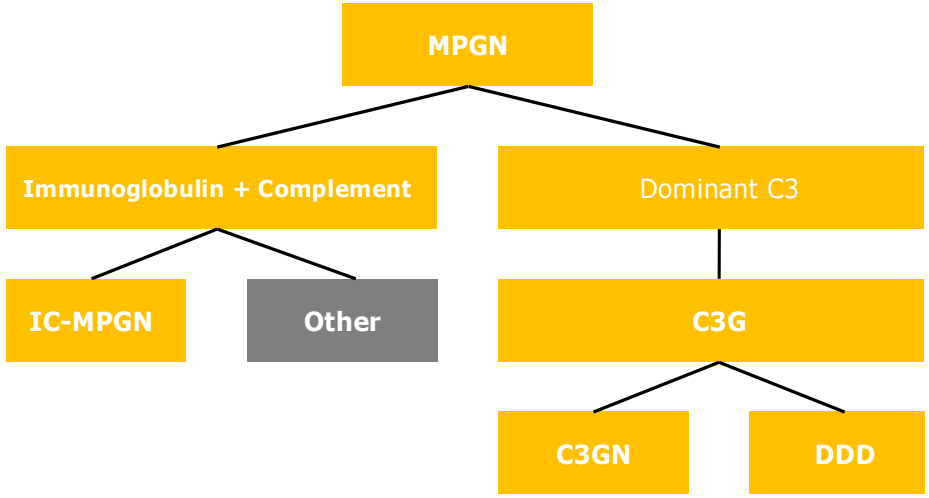
If the biopsy shows C3 staining that is twice as strong as any other fluorescent stain, the pathologist will call it „C3-dominant glomerulonephritis," which may suggest C3G. However, it is important to note that up to 30% of patients with postinfectious glomerulonephritis (PIGN) may also have „C3-dominant glomerulonephritis." This can be confusing. The distinction between C3G and PIGN can only be made after infection has been ruled out as the cause of the biopsy results.

A C3G diagnosis can be further classified by electron microscopy as dense deposit disease (DDD), which is characterized by sausage-shaped, thick intra-membranous deposits, or C3 glomerulopathy (C3GN), which involves mesangial and capillary wall deposits of lesser intensity.

If a membranoproliferative pattern of injury is present along with immunoglobulin staining (instead of C3 dominant staining), immune-complex membranoproliferative glomerulonephritis (IC-MPGN) can be diagnosed.

A biopsy is performed by a nephrologist or radiologist in a hospital while the patient is under general or local anaesthesia. It is important to avoid strenuous activities for one to two weeks after the biopsy and to contact the hospital if you experience bleeding, fever, or changes in your urine.

Biopsies may be repeated to monitor progression and the effectiveness of treatment.




**Overview of Diagnoses Based on Biopsy Results**

# Disease Management

*Katrine Maiggard and*
*Prof. Dr. Marina Vivarelli*

The management of C3G and IC-MPGN varies depending on each patient's individual needs. These needs are defined by disease activity and progression, among other factors.

It is important for everyone living with these diseases to undergo ongoing disease monitoring. This is because both C3G and IC-MPGN can flare up and become active without obvious symptoms.

Therefore, when living with C3G or IC-MPGN, taking medication and monitoring disease progression becomes normal routines, as does planning and prioritizing interactions with nephrologists and other healthcare professionals. Additionally, lifestyle changes such as limiting sodium intake, managing protein consumption, and prioritizing rest may help maintain health and stability.

C3G and IC-MPGN can progress silently, meaning patients do not experience symptoms. This is why monitoring key markers of progression in the blood and urine is important. Regular follow-up appointments with a medical professional can facilitate the early detection of flares and prevent the decline of kidney function and other possible complications.

The frequency of these appointments depends on the severity of the disease. The level of proteinuria and the patient's other laboratory values are decisive factors.

If the patient is doing well, appointments may be scheduled twice a year. Otherwise, they should see a nephrologist more frequently.

A full assessment is important during monitoring and includes blood tests to measure relevant markers, such as creatinine and eGFR levels, as well as complement activation. Regular urine tests are also important for measuring proteinuria and hematuria.

Patients should undergo periodic eye examinations to rule out drusen, which is commonly associated with C3G and IC-MPGN. They should also be evaluated by a specialist who can recognize partial lipodystrophy, a rare disorder involving progressive subcutaneous fat loss.

*All patients are advised to check their proteinuria level every month, regardless of how well they are doing. This test is important for promptly detecting relapses, which can occur at any stage of the disease. Early detection often makes relapses much easier to manage.*



# Treatment

*Hyo Jin Heinz and*
*Prof. Dr. Fadi Fakhouri*

Treatment of C3G and IC-MPGN is rarely straightforward, and many patients undergo a period of trial and error. These diseases are rare and vary widely, so responses to therapy differ from person to person. Weighing potential benefits against side effects is important, so patients have the best possible opportunity to live healthy, fulfilling lives.

This makes shared decision-making between nephrologists and patients an important part of care.

**Reducing and maintaining low proteinuria levels while stabilizing or improving estimated glomerular filtration rate is key.**

**The treatment has two main goals:**

- ***Slow kidney damage***
- ***Stabilize kidney function***

Since there is no single cure for C3G or IC-MPGN, therapy must be customized to each patient's needs. Most patients start with supportive care, which includes medications to control blood pressure and reduce protein loss in the urine. Lifestyle changes, such as following a low-sodium diet and avoiding kidney-toxic medications, become part of daily life.

Depending on the severity and activity of the disease, nephrologists may add immunosuppressive therapies. In the past, these therapies were limited to non-specific immunosuppressive medications without documented effect on complement dysregulation, with varying efficacy and side effects. However, new targeted complement therapies are becoming available that provide significantly improved opportunities to manage disease activity.

## Medications Commonly Used To Treat C3G and IC-MPGN

**Medicines that Protect Kidney Function and Reduce Proteinuria**

- Renin-angiotensin-aldosterone system inhibitors (RAAS inhibitors), Angiotensin-Converting Enzyme inhibitors (ACE inhibitors), Angiotensin II Receptor Blockers (ARBs).
- In patients at risk for progressive kidney disease these medications are used to lower blood pressure, reduce protein in the urine, and slow kidney damage, starting at diagnosis, based on protein levels and blood pressure.
- Inhibitors of sodium-glucose cotransporter 2 (SGLT2-inhibitors), like dapagliflozin and empagliflozin, helps protect the kidneys by blocking sugar from being absorbed in the kidneys.

**Targeted Therapies with Complement Inhibitors**

Two of these therapies, iptacopan and pegcetacoplan, are new and have recently been approved by the FDA and the EMA. They are designed to block the overactivation of the complement system by targeting specific complement proteins.

- Iptacopan/Fabhalta is an oral complement factor B inhibitor, approved by the EMA and the FDA to treat C3G. Clinical trials for IC-MPGN are ongoing.
- Pegcetacoplan/Empaveli/Aspaveli is a C3 complement inhibitor administered via subcutaneous infusion twice per week. It has been approved by the EMA and the FDA to treat C3G and IC-MPGN.
- Eculizumab/Soliris and ravulizumab/Ultomiris are administered as infusions given every second week (eculizumab) or every second month (ravulizumab) to block the terminal complement cascade. Eculizumab and ravulizumab can help some patients with C3G and IC-MPGN, though the products are approved for other conditions. Efficacy of eculizumab and Ravulizumab has not been shown in prospective randomized trials.

**Unspecific Immunosuppressive Therapies**

These help control the immune system when it mistakenly attacks the body's tissues. Suppressing the immune system can make it harder for the body to fight infections.

- Corticosteroids, such as prednisone, dexamethasone and hydrocortisone, are strong anti-inflammatory drugs used to manage overactive immune conditions. They are typically prescribed for the shortest time needed, to avoid complications
- Mycophenolate mofetil/CellCept or mycophenolate sodium/Myfortic, helps control the immune system by preventing certain immune cells from growing and is used to treat autoimmune diseases.
- Cyclophosphamide is sometimes used when other treatments do not work, and there is a strong risk of rapid kidney damage. It helps reduce inflammation and can slow disease progression, but it requires careful administration and monitoring, due to increased risks of infections, infertility, malignancies, etc.

The side-effect profile of medications that have been on the market for a long time is well established. For the new products, the long-term efficacy and side-effects need to be established (see chapter on Networks and Evidence). Some medications are not safe during pregnancy and breastfeeding.

**This is why dialogue and close collaboration with your doctor are always crucial.**

**When a patient reaches the end-stage of renal disease, they require dialysis or a transplant to survive.**

### Dialysis

Dialysis is a procedure that cleanses waste from blood. During this process, excess water and toxins are filtered out of the blood and removed from the body. While machines can perform some of the filtering functions of the body, they cannot replace the important tasks of producing hormones and enzymes.

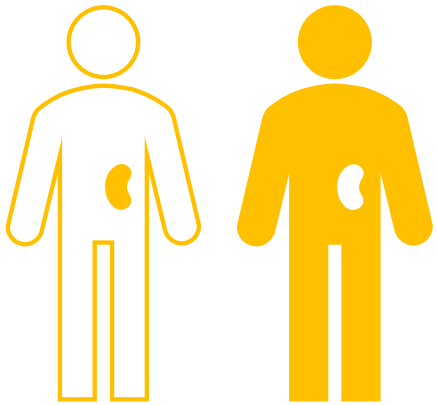
There are generally two forms of dialysis: hemodialysis (HD) and peritoneal dialysis (PD). With PD, the abdominal lining is used for daily filtering at home, while with HD, a machine is typically used three to five times weekly at a center.

### Kidney Transplantation

Although dialysis is lifesaving, it can be hard on the body and is associated with risks and challenges. Therefore, kidney transplantation is the best option for most people with end-stage renal disease. For patients with C3G or IC-MPGN, there is a high risk of the disease recurring in the transplanted kidney. Thus, continued monitoring and specialized care are critical.

### Beyond Medical Treatment

The emotional impact of living with a rare kidney disease extends beyond medical treatment. Uncertainty and isolation are common, especially when symptoms change or the future feels uncertain. Many patients find support through peer communities, advocacy groups, and education, which make them feel more informed and less alone. From the patient's perspective, successful disease management is ultimately defined not only by lab results, but also by preserving quality of life, resilience, and hope while living with a lifelong condition.



# Diet and Nutrition

*Enrique Gordillo and*
*Dr. Louise Havkrog Salomo*

A balanced diet is vital for everyone's health and wellbeing. For people living with kidney disease, a renal diet can help to reduce proteinuria and metabolic acidosis, manage blood pressure, and improve metabolic health. Therefore, a renal diet can ease the strain on kidneys affected by C3G and IC-MPGN. Furthermore, it can help to prevent cardiovascular, renal and metabolic complications, even in individuals without existing kidney disease.

The kidneys play a vital role in processing nutrients, balancing fluids, maintaining the body's acid–base balance, and filtering metabolic waste products, such as urea and creatinine from everything we consume. One of the most important dietary recommendations for people with kidney disease is to reduce salt intake, limit sugar and consumption of saturated fat, and restrict food additive (E-number) intake. It is also advisable to avoid highly processed foods, as these often contain high levels of salt, sugar, unhealthy fats, and additives. These include energy drinks, sausages, chips, sweets, ice cream, and mass-produced bread.

To avoid processed foods, patients are encouraged to prepare their own meals using fresh ingredients and natural spices. When preparing these meals, they should focus on eating more vegetables and less meat, particularly processed meat. Plant-based protein is generally associated with a lower dietary acid load and reduced uremic toxin generation, potentially through favorable modulation of the gut microbiota. The lower a patient's kidney function, the more restricted their diet usually needs to be. Nevertheless, it remains important to eat a varied and nutritious diet.

To minimize frustration, adopting an 80/20 approach can be helpful. This involves following a kidney-friendly diet 80 percent of the time and allowing for more flexibility for the remaining 20 percent.

Meal planning can be a challenge for people trying to follow a kidney friendly diet. Without planning, one may find himself reaching for processed snacks throughout the day. Preparing homemade snacks and planning meals in advance can help you stay on track.

As some kidney-friendly recommendations can result in repetitive and uninspiring food, the pleasure associated with eating can be negatively impacted. Cookbooks and recipes developed in collaboration with nephrologists, nutritionists, and skilled chefs can make adopting a renal diet a positive culinary experience for those affected and their families.

***It is recommended that you maintain an ongoing dialogue with your treating nephrologist regarding diet and nutrition, as well as undergoing regular blood and urine tests as part of your overall care.***

# Enrique

*A personal story*

Our journey began when we started trying to figure out why our son was not growing properly. Lab tests revealed low C3 levels and high proteinuria. A biopsy confirmed the diagnosis a couple of months later. This early diagnosis was crucial for my son.

However, his first nephrologist simply told us that C3G is difficult to manage and has a poor prognosis. He suggested that we learn more about it online. We were devastated. We felt alone, and we did not understand what we read. Every conversation with physicians only served to confuse us further. His nutritionist treated him as if he were in the end stages of renal failure and forbade him from eating almost anything. Over time, we realized that most doctors had no experience with this condition.

This confusion damaged my relationship with my wife because we interpreted things differently.

We switched to the best pediatric nephrologist in our area, who had experience treating C3G patients. We joined C3G patient groups. I attended the 2022 annual nephrology conference in Spain. We started correlating lab test results with daily life to better understand the disease. We contacted pharmaceutical companies and found CompCure. We are no longer alone, and I want to help others on this journey.

# The C3G and IC-MPGN Journey

*Lindsey Fuller & Adrian Ley*

**In this section, patients and caregivers describe what it is like to go through the different stages of the disease, and how to manage common challenges while preserving kidney function and maintaining a normal daily life. This section is based on the authors' personal experiences and input from other affected individuals during interviews and focus groups.**

While the journey with C3G or IC-MPGN varies vastly from patient to patient, it tends to be complex, with several stages that pose a variety of challenges. In addition to the impact on kidney function, complications related to other organs may also appear. All of this can be difficult to take in and handle.

A proportion of people living with C3G and IC-MPGN are diagnosed early through screening programs or health checks. It is common to experience symptoms for a long time before the actual diagnosis is made.
It happens that patients receive a wrong, or unspecific diagnosis, which may lead to unspecific and sub-optimal care. Some patients feel caught in a roundabout, where they reach end-stage-renal disease and need dialysis or transplantation; whereafter the disease recurs and dialysis is needed again.

The goal is to prevent or slow the progression of the diseases or even reach full or partial remission, while maintaining healthy kidney function for as long as possible. This is becoming more attainable as our **understanding improves, and new therapies become available.**

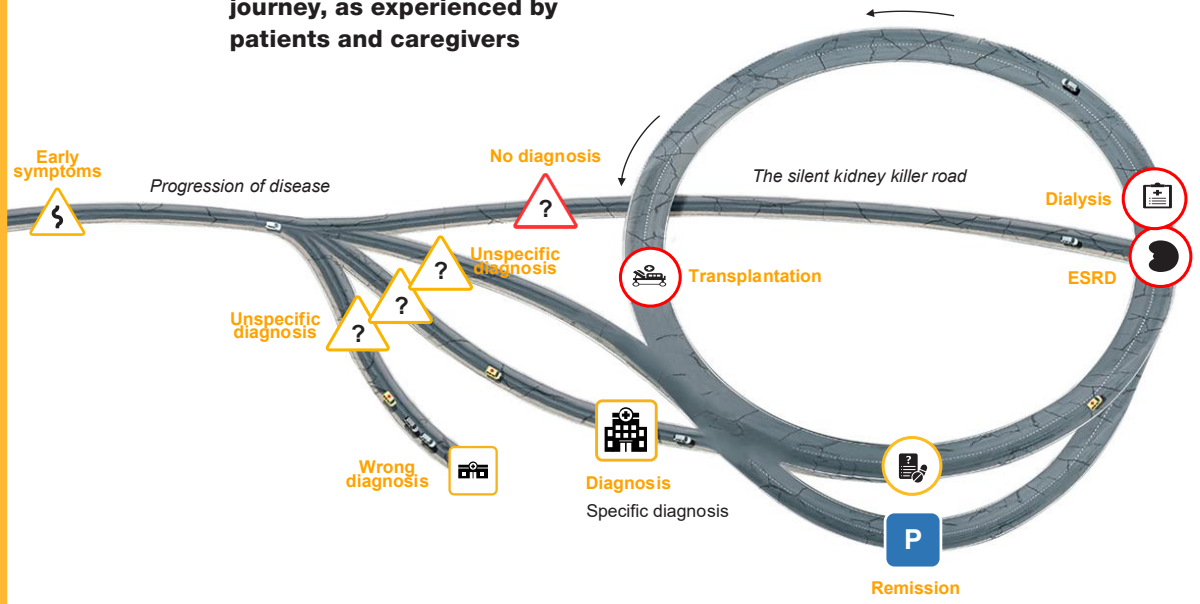
**Recommendations from patients on managing health and daily life with C3G and IC-MPGN:**

1. Consult nephrologists with specific expertise in C3G and IC-MPGN, either through the treating physician or directly, and as early as possible. The experts can support the treating nephrologist in developing a disease management plan targeted to your specific needs.
2. Consider and take care of the overall physical and mental health of yourself, your family, and other impacted people close to you.
3. Connect with other people in similar situations, e.g. through patient organizations, networks, or social media.

Many patients and families worry about the future and what to expect as the diseases progress. Since C3G and IC-MPGN manifest differently from person to person, it is difficult to generalize. Some individuals will go through all the stages described below, whereas others can stay in remission, meaning the disease is not active.

The emotional journey can be just as challenging as the physical aspects. The rarity of C3G and IC-MPGN can leave patients feeling isolated, and the unpredictable nature of the diseases can create ongoing anxiety about progression. Support from nephrology teams, patient communities, and mental health resources is crucial for long-term care.

**Illustration of the disease journey, as experienced by patients and caregivers**



### Early Symptoms

For most people, the journey with C3G or IC-MPGN begins unexpectedly. Early symptoms are often subtle or nonspecific, e.g., fatigue, swelling in the legs or around the eyes, foamy urine, or abnormal lab results found during a routine checkup.

In some cases, patients feel well and are surprised when urine tests show blood or protein, or when a blood test indicates that there could be an issue with the kidneys.

Because C3G and IC-MPGN are rare and can resemble other diseases, diagnosis is often delayed. It can take a long time to get referred to a nephrologist, who will order specialized blood tests and, most importantly, a kidney biopsy, which is required to make the diagnosis.

***The time it takes to diagnose and manage diseases has a strong impact on the prognosis.***

### Diagnosis

By the time they are diagnosed with C3G or IC-MPGN, many patients have active and progressed diseases. After a long journey where potential unclear, nonspecific, or wrong diagnoses can lead to suboptimal disease management, it can be a relief to finally get diagnosed. At the same time, the clarity of the diagnosis comes as a shock to most affected individuals. It may be difficult to accept the chronic and progressive nature of the disease. Gaining a sufficient level of understanding of the disease, while trying to navigate what may be a new reality and outlook, can also be overwhelming.

***A specific diagnosis is extremely important because it is necessary to receive optimal and disease-specific care.***

### Chronic Care

Patients in chronic care often describe it as a constant balancing act—trying to live a normal life while remaining aware of symptoms and lab results.

The time after diagnosis can be particularly challenging. Every patient is different, and there is no cure or treatment that works equally well for everyone. Therefore, it can be difficult to find the right treatment and customize a follow-up schedule to effectively monitor progression in each patient.



Periods of remission, where the disease is not active, can last months or even years. The objective of chronic care is remission, which can be spontaneous or driven by medication, called medicated remission. Flares, where the disease becomes increasingly active, are common and can be triggered by infections and other immune responses.

Living with C3G and IC-MPGN often means learning how to monitor stability versus activity. Regular blood and urine tests track kidney function, protein levels, and signs of inflammation. These tests are important because C3G and IC-MPGN can be unpredictable. Your nephrologist may recommend that you perform a urine test at least once per month using a dipstick at home. If there are persistent changes, contact the treating nephrologist.

It is not uncommon to experience new or recurring symptoms that may seem unrelated to the kidneys. Since C3G and IC-MPGN can impact other organs and mental health, it is important to note such symptoms and discuss them with the treating physicians, so that appropriate action can be taken.

***The objective of chronic care is to maintain kidney function and slow disease progression. Therefore, it is important to measure progression, e.g., through monthly proteinuria dipstick tests.***

### End-Stage Renal Disease

Despite best efforts, some patients gradually experience a decline in kidney function to a level where kidney replacement therapies are needed to survive. At this point, the focus shifts to preparing for advanced kidney care, including dialysis or transplantation.

There are different forms of dialysis, and the choice depends on medical factors, as well as individual circumstances. Many patients find dialysis to be time-consuming and physically and mentally demanding. Dietary and fluid restrictions, as well as additional medications, are also often necessary.

Although dialysis can be lifesaving by replacing essential kidney function, transplantation usually offers better long-term health. Not all medical centers perform transplants for patients with C3G or IC-MPGN, and in some cases, normalized C3 levels are required before transplantation.

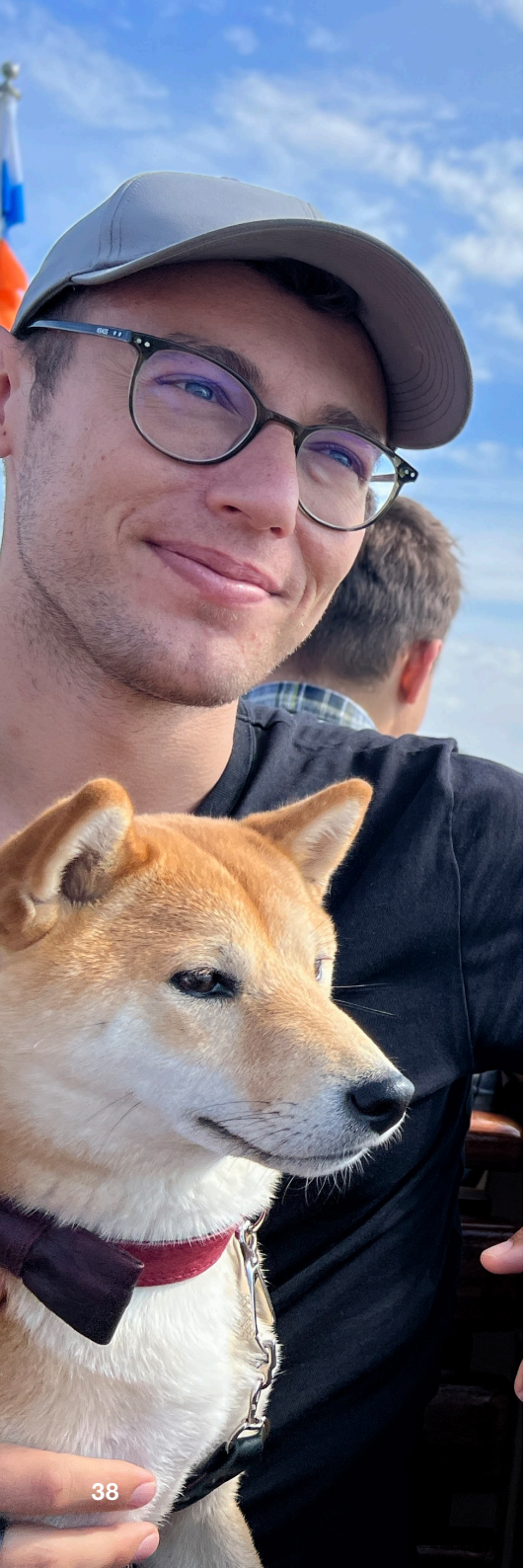
Due to the limited availability of organs, many patients face long waiting times for transplants from deceased donors. For some patients, receiving a kidney from a living donor can be an alternative. However, receiving such a gift from a healthy family member or friend is a profound decision — giving and receiving it can be a deeply personal and sometimes challenging experience for everyone involved.

Patients who have received transplants experience life differently than they did with their native kidney. Close follow-ups with experts are necessary to ensure the allograft's long-term survival. Patients often need to adopt a new lifestyle that includes special medications and diet. Careful disease management is essential, as C3G and IC-MPGN can recur after transplant.

***After a transplant, ongoing care and disease management are important to protect the new kidney, especially if C3G or IC-MPGN returns.***

**Summary**

Overall, the patient journey for those with C3G or IC-MPGN is one of early uncertainty, long-term management, and resilience. Although current treatments aim to slow down the progression of the disease, rather than cure it, ongoing research and new therapies offer hope for better outcomes and more stable futures.



# Adrian

*A personal story*

I still cannot fully explain what it truly means to live with IC-MPGN or C3G. And honestly, uncertainty is something many of us live with every day. But I can share what it does not mean.

I was diagnosed with C3G at 19. Later came an IgA diagnosis, and eventually it was confirmed as IC-MPGN. I am 32 now. I have had two kidney transplants, many treatments, setbacks, and moments where everything felt out of control. And yet, I live a good, full life.

In the beginning, the hardest part was not just the illness—it was the not knowing. I constantly asked myself the same questions many patients ask: What does this mean for my future? Will I be okay? Why is this happening to me? Did I do something wrong? That fear did not disappear overnight. Even today, uncertainty is still part of my life.

A lot went wrong in those early years, and I do not want to minimize that. Living with a rare disease can feel incredibly lonely, especially when doctors do not always have clear answers. But one important thing I have learned is this: when so much is unclear, there is also room for possibility. No two disease journeys are the same.

At 19, I went into kidney failure. I needed dialysis until my mother gave me one of the greatest gifts imaginable —one of her kidneys. After the transplant, I lived intensely and joyfully. I traveled, made memories, and felt hopeful again.

About three years later, my kidney function declined once more. At that time, treatment options were limited, and I had to return to dialysis. That moment broke something in me. It was one of the lowest points of my life and a painful reminder of how quickly everything can change.

At first, I went back to asking the same old questions. But eventually, something shifted. I started asking a different one: What options do I still have? If this was going to be part of my life, how could I still live well?

I tried different forms of dialysis, moved cities, and slowly rebuilt my life around my new reality. I traveled, connected with other patients, exercised, learned as much as I could, and focused on supporting my body. Dialysis did not stop my life; it changed it, but it did not end it.

During that time, I learned an important lesson: there are options for almost everything. Sometimes they are hard to see, and sometimes you have to search for them relentlessly—but they exist.

Years later, I received a call offering me another kidney. That moment is impossible to describe. By then, I was ready—physically and emotionally. I had accepted life as it was and found meaning in it. I was grateful for modern medicine, for the people who supported me, and for the life I was living.

Today, there are more treatment options, better diagnostics, and more knowledge than there were when I was first diagnosed. Things are still uncertain—but there is also progress, hope, and possibility.

Wherever you are right now, please know this: your disease does not define you. It is one part of your life, not the whole story. Connect with others who understand, ask questions, stay curious, and do not give up on the idea of a good life. It is still possible—even if it looks different than you once imagined.

# Mental Wellbeing

*Antonia King,*
*Hyo Jin Heinz*
*and Dirk Bethe*

Living with a rare kidney disease affects more than just the kidneys, lab results, and treatment plans. It also affects your thoughts, emotions, relationships, and sense of identity. If you have ever felt overwhelmed, isolated, or emotionally exhausted, it does not mean that you are weak. You are human and are responding to a very real and ongoing challenge.

Rare diseases often come with uncertainty. There are fewer answers and fewer people who truly understand. Sometimes there are long periods of waiting or explaining the condition over and over again. This uncertainty can fuel anxiety, sadness, or a constant feeling of being „on alert." Taking care of your mental wellbeing is essential to managing your health.

It is important to acknowledge that it is okay not to be okay all the time. A diagnosis can evoke grief for the life you expected, fear about the future, and frustration with limitations you did not choose. Having these feelings does not mean that you are failing to be positive or strong; it means that you are processing something difficult.

For many people, professional support is a vital part of that process. Speaking with a psychologist, counselor, or social worker who understands chronic illness can help you adjust to your diagnosis, manage anxiety or depression, and develop coping strategies that fit your life. ***Getting professional help is not a last resort; it is proactive care, just like seeing a nephrologist for kidney issues.***

Setting boundaries is another crucial aspect of maintaining mental wellbeing. Managing a rare kidney disease can require a lot of physical and emotional energy, so it is important to recognize your limits and protect your time and space. Saying no to extra commitments and designating rest periods are not selfish—they are acts of self-preservation. Clear boundaries prevent burnout, reduce stress, and allow you to focus on activities that support your health and healing.

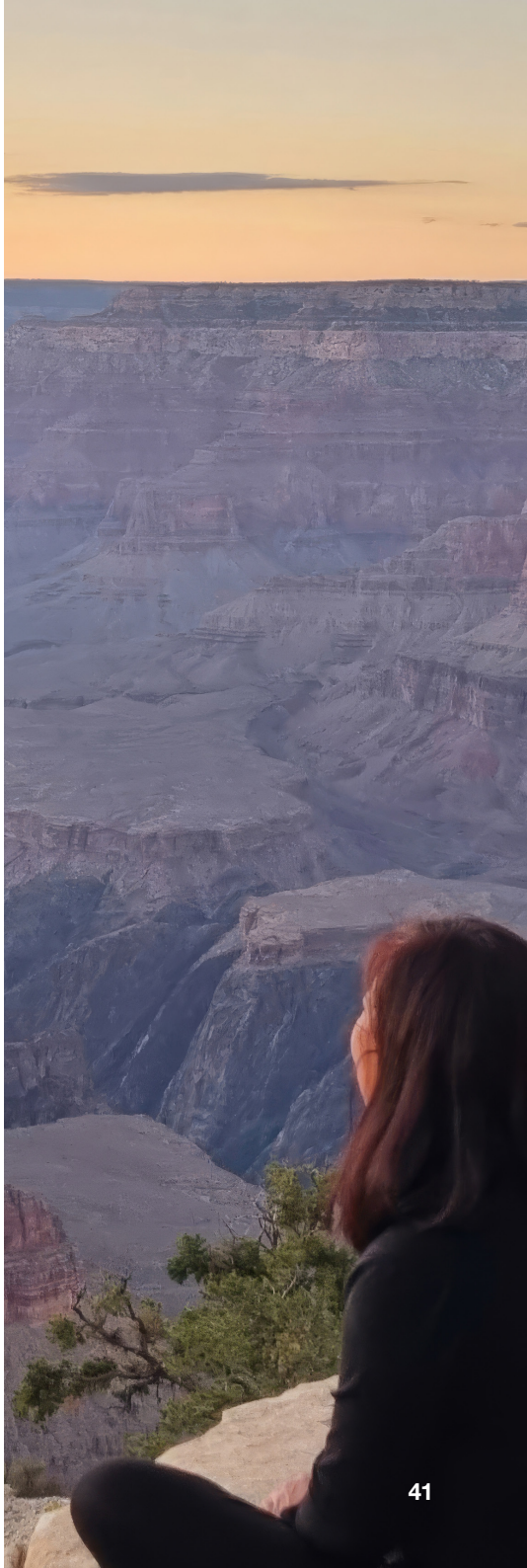
Your emotional and physical health are closely connected. Ongoing stress and emotional strain can affect sleep, energy levels, motivation, and even the effectiveness of treatments. Addressing mental wellbeing can improve quality of life and make day-to-day disease management feel more manageable.

A rare kidney disease affects not only you, but also the people who care about you. Family members and partners may feel scared, upset, helpless, or unsure of how to support you. Roles may change. Plans may change. Communication can become strained, especially when everyone is trying to „stay strong" for each other.

Open and honest conversations, when you are able to have them, can help protect relationships. Letting your loved ones know what you need—whether it is practical help, emotional space, or simply being listened to—can ease tension and reduce misunderstandings. It is also okay to recognize that your family members may need support of their own.

Connection matters. Having a space where you do not have to explain or minimize your experience, whether with a mental health professional, a peer support group, another patient, or a trusted friend, can be deeply grounding.

***Living with a rare kidney disease requires resilience, but being resilient does not mean facing everything alone. Taking care of your mental wellbeing and accepting help along the way, is part of caring for your kidneys, your relationships, and yourself.***



# The Role of and Impact on Caregivers

*Antonia King,*
*Tülin Sahin, and*
*Marianne Silkjaer Nielsen*

Caring for a loved one with a chronic illness can be deeply connecting, but it also carries emotional weight. Whether you are caring for a parent, partner, child, or another loved one, it takes extraordinary strength when you need to be alert and responsible day after day, all the time.

There are no words to capture the pain of watching a loved one suffer. It is hard to see them struggle while longing for the things that once felt ordinary, such as independence, work, school, play, and the simple freedom to live without constant worries and limitations. You can offer your help, but your loved one may not always accept it.

You may see the person you care for change, physically, emotionally, or mentally due to illness. The roles within your relationship may shift. These changes can evoke feelings of grief alongside love and commitment. You may feel lonely sometimes, and at the same time, you may also experience a deeper connection with your loved one as you navigate through this journey together. Maybe you will also gain new opportunities to learn and to adopt deeper perspectives on what is important in life.

Adjusting to a new and radically different reality can leave people vulnerable in many ways. Emotional exhaustion, uncertainty, and grief can impair judgement, making one more susceptible to manipulation, gaslighting, exploitation, and abuse. Maintaining structure and healthy boundaries can provide stability.

**To create a more normal and supportive life for our loved ones, we must nurture that possibility for ourselves as well.**

The person receiving care often becomes the center of a caregiver's world. Other family members may sometimes feel overlooked, and caregivers themselves may easily place their own needs last. Over time, caregiving becomes far more difficult when your own wellbeing and that of the wider family are neglected. Prioritizing yourself can also foster a culture where caregiving becomes more of a shared responsibility.

Please know that your feelings are valid, and you also do not have to be alone as a caregiver. Asking for help and connecting with others, who share similar experiences, can be a lifeline that provides you and your loved one understanding, strength, coping strategies, and unexpected joy and gratitude.

For patients, having a trusted and loving caregiver by their side makes all the difference.

# Tülin

*A personal story*

***While patients carry diseases, care-givers, families, and close friends also bear some of the consequences.***

This story is a reflection of what families affected by kidney disease go through. It is a story I am encouraged to share by Esther, a young girl who lives with IC-MPGN. Her story let to the establishment of CompCure - a proof that a family, and a community, can make a difference together.

My mother's story began with a car accident when I was an infant. The family survived, but my mother suffered traumatic injuries. She developed chronic pain, which was managed with analgesic medicine. Silently, however, this medication impaired her kidney function. For decades, she carried this with remarkable strength. Everything changed February 6, 2023, the day of the devastating earthquake in Türkiye. While the country was waking up to unimaginable loss, we were in a hospital receiving another life-altering message: a tumor in my mother's kidney required immediate surgery. That day, my life split into two parallel realities. As a daughter I was at the hospital, facing my mother's condition. As a UNICEF ambassador in Türkiye, I supported the victims of the earthquake.

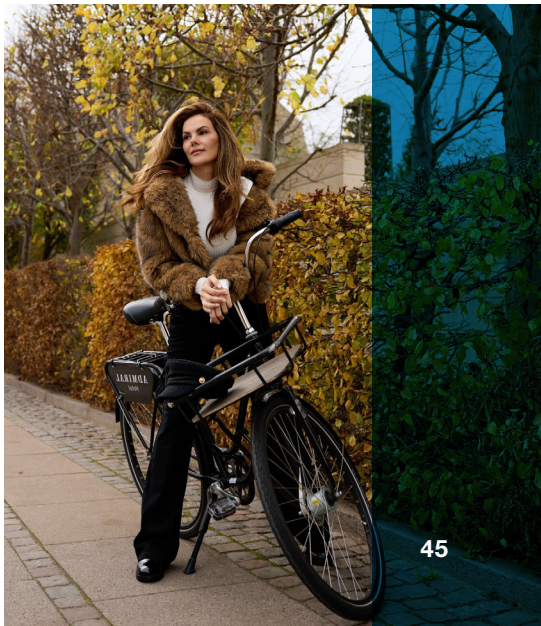
When dialysis became part of our lives, grief and responsibility existed side by side. Dialysis is not just a treatment; it becomes a lifestyle that reorganizes itself around time, machines, and survival. I planned everything around it - my job, my travels, my child's schooling, every day. Some days were good, others were difficult. We adapted, as families do.

Then came another shock. While on dialysis, my mother suffered a brain hemorrhage, bringing her to the brink of death. It was traumatic. I held onto the belief that things would turn out well, and they did. My sibling and I were both ready to donate a kidney. But as a mother, she would not accept the idea of taking something so vital from her children - until the day we discussed that she might not be able to see her granddaughter grow up. It was the hardest conversation I ever had. Sometimes love requires more courage than gentleness.

With support from doctors, she eventually agreed, and six months later, she finally received her kidney transplant. I felt an overwhelming sense of relief. I believed the hardest part was over. However, healing has its own timeline.

In the months that followed, I still found myself remaining alert, still planning according to the dialysis schedule, and waiting for something to go wrong. I could not understand this until my doctor explained that after such a long period of constant vigilance, the body does not immediately realize that the crisis has passed. My body was only just beginning to process everything we had lived through. Healing can only begin once the treatment is over.

Sometimes, a daughter becomes the mother, not by choice, but by love. I did not just witness this journey. I also lived it. I became her strength when she had none. And in many ways, I became her mother, so she could remain mine.



# Building a Functional Life

*Antonia King and*
*Hyo Jin Heinz*

Living with C3G or IC-MPGN can feel overwhelming, especially because it is rare, unpredictable, and often misunderstood. Many patients are diagnosed suddenly, during a health crisis, or after years of unexplained symptoms. Along with the physical impact, C3G affects work, relationships, mental health, and how patients see their futures.

There is no single "right" way to live with C3G or IC-MPGN—but there are ways to build a meaningful, functional life that respects your limits while protecting your independence and sense of purpose.

C3G and IC-MPGN force patients to rethink what "normal life" means. Fatigue, brain fog, swelling, infections, hospital visits, medications, and uncertainty can all interrupt daily routines. Functional living does not mean pushing through at all costs—it means learning how to live with the disease, not constantly against it.

Some days, functionality means working, exercising, and socializing. Other days, it means resting, managing symptoms, or simply getting through the day safely. Both are valid. Living well with C3G or IC-MPGN often requires pacing, flexibility, and letting go of guilt when our bodies say "not today."

### Employment: Challenges and Possibilities

Work is one of the biggest concerns for many people with rare kidney diseases. Employment provides income, structure, social connection, and identity—but it can also be a source of stress.

**Common challenges include:**

- Chronic fatigue and reduced stamina
- Frequent medical appointments or hospitalizations
- Medication side effects (such as brain fog or infection risk)
- Fluctuating kidney function
- Pressure to "perform" consistently

Despite this, many people with C3G do work—full time, part time, freelance, or in modified roles. The key is finding work that fits your health, not forcing your health to fit the job.

**Helpful strategies may include:**

- Flexible or remote work
- Reduced hours or job sharing
- Roles with predictable schedules
- Employers willing to provide accommodations
- Career changes that prioritize your health

If you are able and comfortable, learning about disability rights and workplace accommodations in your country can be empowering. Asking for adjustments is not a failure; it is a survival skill.

### When Work Is Not Possible

For some people, working is not realistic for periods of time—or at all. This can be emotionally difficult, especially in societies that tie self-worth to productivity.

If this is your situation, it does not mean your life has less value. Managing a chronic, rare disease is work in itself. Navigating healthcare systems, managing medications, and protecting your health takes time, energy, and resilience.

Accessing disability benefits, financial support, or social services can be complicated and frustrating, but these systems exist because people deserve stability when health limits employment. Asking for help is not giving up—it is choosing sustainability.

### The Importance of Support Systems

No one should live with a rare kidney disease alone. Support systems—formal and informal—make a huge difference. These may include:

- Family and friends who understand your limitations
- Patient organizations and online communities
- Social workers or patient advocates
- Mental health professionals familiar with chronic illnesses
- Employers or educators who are flexible and informed

Connecting with other patients can be especially powerful. Sharing experiences with people who get it reduces isolation and provides practical knowledge that textbooks cannot offer.

C3G and IC-MPGN are unpredictable. Plans may change. Treatments evolve. Life paths shift. But a meaningful life is still possible—one shaped by adaptability, personal awareness, and support.

# Antonia

*A personal story*

I was diagnosed with C3G when I was a 15-year-old student. I was a competitive swimmer and needed a check-up, during which my general practitioner discovered that I had proteinuria.

This led to years of different treatments, which ended in end-stage renal disease and dialysis before I received a transplant.

Throughout my illness, I was always afraid of losing a ‚normal' life. Would I be able to work a normal job? Would there still be room for love, friendship, and living life to the fullest?

This fear of losing my ‚normal' life became my main motivation. It drove me to study during the day while undergoing dialysis at night. It led me to earn my degree in social work and my master's in psychosocial counseling. Today, I work in a family counselling office, and I deeply value the work I am able to do there.

Although I love what I do, working alongside healthy colleagues can be challenging. I am always a bit different. I try to organize my life around treatments, appointments, and energy levels. Some days I lose concentration during important meetings or have to deal with sudden physical crashes.

It is hard for others to understand these challenges because the disease is not visible.

I have learned to communicate openly about my limitations and have found a supportive and understanding team.

Some time ago, I decided to reduce my working hours and work part-time. Although this decision comes with a financial burden, it enables me to manage my health and energy levels more effectively.

Additional support, such as flexible working hours and disability benefits, helps me to maintain my quality of life. Most importantly, I have learned that I do not have to be the same as everyone else. It is okay to take breaks and set priorities.

Creating a life that feels as normal as possible within the limits of my health is my greatest achievement in living with C3G. I do not know what the future will bring, but I trust that I will always find a way.

# Family Planning

*Lindsey Fuller and*
*Prof. Dr. Em. Jack Wetzels*

**It is important to consult with specialists with experience in C3G and IC-MPGN before becoming pregnant.**

Family planning is an important and deeply personal consideration that raises special concerns for many people living with C3G or IC-MPGN. It is natural to have questions. Is pregnancy possible? Could pregnancy trigger a flare? Could a genetic abnormality be passed on to the baby?

Although these diseases are rarely passed from generation to generation, it can happen. In such rare cases, understanding inheritance patterns and speaking with a genetic counselor can provide clarity and help guide decisions. Advances in reproductive medicine also offer options to reduce risks and support informed decision-making.

You must be aware that pregnancy may increase the risk of flares, and some treatments are not safe during this time. Getting pregnant the first one to two years after diagnosis is not recommended.

It is essential to plan ahead with your nephrologist and to maintain a strong collaboration with all relevant healthcare professionals to monitor your health and the development of your baby closely throughout pregnancy.

Although there are challenges, many people with C3G or IC-MPGN go on to have successful pregnancies and healthy children.

- Medications may not only impact female patients. Some medications can impact both males and females, causing negative effects on fertility, libido, and fetal health, including birth defects. It is important to discuss medications with your nephrologist to determine risk.
- Many patients and their partners may experience anxiety about making the commitment to have children under these circumstances. Uncertainties about future health, the ability to provide care, job stability, and finances can make this a difficult decision. The challenges are not only physical.
- Pregnancy after transplant is possible and may be more successful if kidney damage is less advanced.
- While difficult to consider, patients should be realistic about the risks of miscarriages, preeclampsia, and premature birth.
- Pregnancy may have complications, such as hypertension, declining eGFR, and permanent changes in kidney function, even if ultimately successful.
- Patients with hereditary genetic diseases who want to have healthy children should seek care from specialists in genetics and reproduction.
- Although your pregnancy may be normal and uneventful, even if you live with C3G or IC-MPGN, the risks may be higher. This means that you should consider the feasibility of things like required bed rest and extra medical appointments as part of your care.

# Advocating for Yourself and Others

*Antonia King and*
*Hyo Jin Heinz*

Staying informed about C3G and IC-MPGN is an act of self-care. It is essential for feeling empowered to advocate for yourself, your child, and others affected by these diseases.

Receiving a diagnosis can make you feel like you are losing control. Appointments, tests, unfamiliar terminology, and having other people make decisions that may significantly impact your life can be frustrating and intimidating. One of the most powerful ways to regain control is to educate yourself about your condition.

Being informed does not mean becoming a doctor or reading scientific papers every night. Rather, it means understanding the basics: where the condition comes from, how it may progress, which symptoms matter, and how the disease can be managed. This knowledge provides you with a language, and language provides you with a voice.

When you know what is happening in your body, it becomes easier to notice when something feels off, ask the right questions, and impact decisions related to your health. You will also find it easier to weigh risks and benefits with your care team instead of feeling like decisions are happening to you rather than with you. That is advocating for yourself, and it matters.

Patients who are engaged and informed often have better outcomes. They are more likely to follow treatment plans that they understand, catch side effects early, and feel confident speaking up. Confidence does not come from knowing everything; it comes from knowing enough to say, „I do not understand this yet," or „This is not working for me."

There is also an emotional side to being informed. Fear often thrives in the unknown. Learning about your condition can replace some of that fear with clarity and realism. It can help you distinguish myths from facts and worst-case scenarios from actual probabilities. While knowledge does not erase uncertainty, it makes it more manageable.

Most importantly, remember this: you are the expert on your own experience. Doctors bring medical training, and you bring your lived reality. When these two forms of expertise converge, care improves.

Start small. Use reputable sources. Write down your questions. Bring a trusted person to appointments if you can. Give yourself grace—learning takes time.

Being informed is not about being „difficult" or demanding. It is about honoring your body, your time, and your right to be an active participant in your care. This is not only empowerment but also compassion toward yourself.



**About CompCure**

CompCure is a non-profit association, seeking to improve outcomes in complement-mediated kidney diseases through global cross-functional collaboration, evidence generation, advocacy, and support to patients and their treating physicians.

CompCure was founded by parents of a girl who lives with IC-MPGN. The association is managed by a multidisciplinary team consisting of nephrologists, scientists, patient-representatives, and other experts in complement-mediated kidney diseases.

**www.compcure.org**
**info@compcure.org**

**CompCure**

**LinkedIn**

**Facebook**

**Instagram**

**YouTube**

# Zina

*A personal story*

It started in 2019. My ankles and eyelids were swollen all summer.

Since it was a very hot summer, we assumed it was due to the heat.

However, during my first week of high school, we decided to see a doctor. I took a urine test for protein, and the results were very high. I needed to go to the hospital.

The hospital staff wanted to take a blood sample, but I was reluctant, because I am afraid of needles. After spending two weeks in two different hospitals, though, that fear was gone.

Every day, I asked if I could go home, and every day they said, „Yes, tomorrow." After ten IV lines, hundreds of blood tests, and one biopsy, I was finally diagnosed with C3 glomerulopathy. The message was clear: there was no cure.

Over the past six years, I have undergone six different treatments.

Because of my illness, I have always felt different from other people my age. I was always more tired and had to go to the hospital often. I did not want to be different or tired all the time. I wanted to be able to do everything others my age could do. Then I realized that I could do those things, just at my own pace.

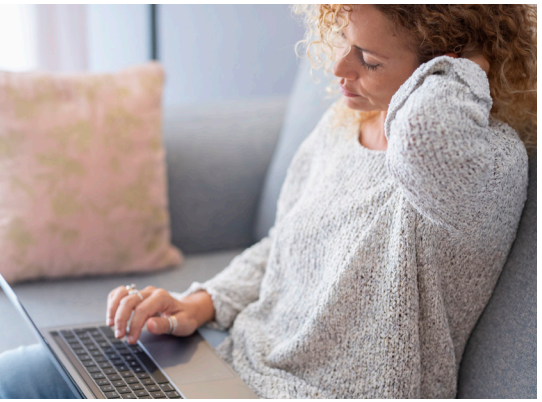
The most important lesson I have learned and want to share with others living with kidney disease, is to not be so hard on yourself.

# Community and Self-Help

*Oksana Paulsen and Lindsey Fuller*

Living with C3G or IC-MPGN is often associated with frustrations and significant life changes. This can lead to feelings of isolation, loneliness, and grief.

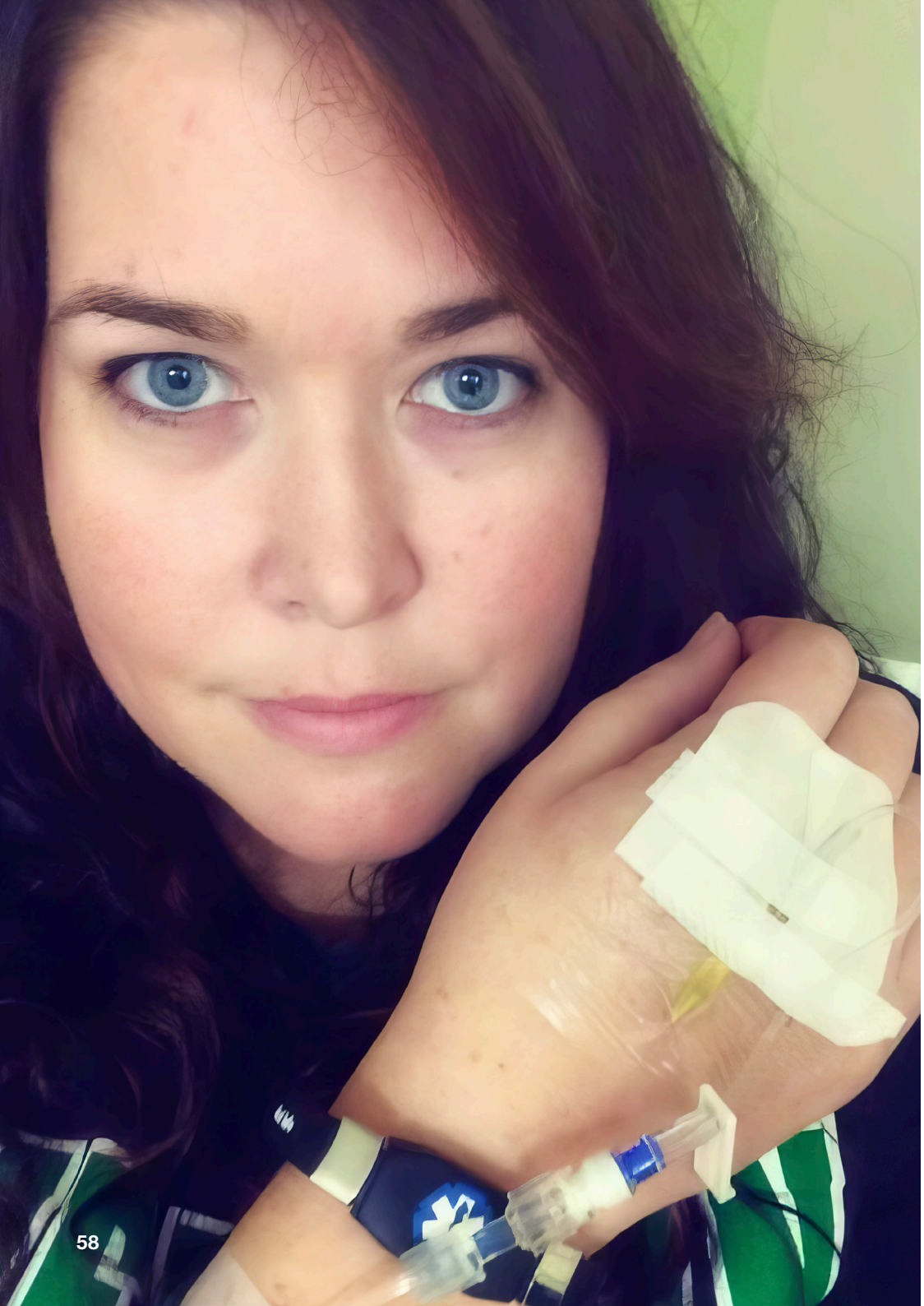
The conditions may change everyday life into a new reality with unpredictable health challenges, time-consuming medical appointments, and changing treatments. This can result in absence from school, work, or social activities. Uncertainty about the future and how to handle health challenges that could be associated with the diseases, add additional layers of concerns and stress to people living with the diseases.



The diseases can also affect close relatives, partners, and friends. They may find it hard to see someone they love struggling with a serious condition they have never heard about. It can be difficult for others to understand what people impacted by C3G and IC-MPGN are really going through. Thus, misunderstandings, sub-optimal behaviors, disappointments, and conflicts can have a negative impact on relationships and the opportunities to get and give the support needed to optimally manage life with the diseases.

It can be extremely valuable to connect with others who are faced with the same conditions, questions, and challenges. Not only does it feel good to finally be understood; connecting with other patients and caregivers can also help you to take proactive steps to prevent or prepare for potential complications.

If you or someone you care for lives with C3G or IC-MPGN, you can join groups on social media or in-person patient and family meetings. You can find links to meetings and social media groups on CompCure's website.



# Lindsey

*A personal story*

I was a child who was often ill. I had many infections, most of which were not serious, but they were frequent and often difficult to treat effectively. When I was 12, a pattern of blood and protein in my urine was noticed and subsequently thoroughly investigated due to concerns that I might have inherited a predisposition to renal failure (my paternal grandfather had died of it and my father had received a kidney transplant which ultimately failed four times). However, no cause for my symptoms was found, and as my kidney function was normal, I was diagnosed with benign hematuria. We were assured that my family did not have a hereditary kidney disease and that I would most likely be fine. During that time, it was noted that both my father and I had low C3 levels, but no one knew what this meant or whether it was relevant. Around the same age, I began experiencing joint and muscle pain, which was also investigated, but no cause was identified.

When I was 23, I became pregnant with my son. My kidney symptoms intensified and I had to be closely monitored. I lost some kidney function during the pregnancy, but it remained within the normal range and stabilized after I gave birth. However, after my son was born, my joint pain, inflammation and fatigue worsened significantly, and I was eventually diagnosed with lupus. I had

my first kidney biopsy at the age of 27, which revealed PIGN. This diagnosis did not make sense at the time, as C3G had not yet been identified. There was no indication of lupus in the results of my kidney biopsy.

At my routine kidney appointment when I was 33, I learned that I had lost a significant amount of kidney function in the year since my last appointment. A month later, I took my nine-year-old son to his well-child examination, where blood and protein were found in his urine. These events prompted me to have my seven-year-old kidney biopsy re-evaluated, and I was diagnosed with C3G and macular drusen. Genetic testing followed, revealing a novel C3 variant.

# Importance of Expert Networks and Evidence

*Marianne Silkjaer Nielsen, Dr. Giulia Bassanese, and Prof. Dr. Franz Schaefer*

Diagnosing and treating rare kidney diseases can be challenging. Approximately 300 rare kidney disorders have been described, many of which are heterogeneous, which means that they present and progress differently. Efficacious therapeutic options are often limited, and evidence to guide treatment decisions remains scarce.

Fortunately, the situation is improving for C3G and IC-MPGN. Approved therapies are becoming available in many countries, and our understanding of the diseases continues to evolve. Registries are critical to facilitating this learning process. Registries are organized systems for the collection, storage, and analysis of data. They help us to understand how diseases develop in real life, how patients respond to different therapies over time, and how to define and develop optimal care, etc.

One of CompCure's focus areas is to contribute to a deeper understanding of C3G and IC-MPGN through our registry. The CompCure registry is a sub-registry of the European Rare Kidney Diseases Registry, the ERKReg, which is the largest registry for rare kidney diseases world wide. The ERKReg is the registry of the European Rare Kidney Disease Network (ERKNet), a network connecting healthcare providers across Europe to improve the understanding and care of rare and complex kidney diseases that require specialized treatment.

CompCure's registry collects patient data from all over the world. Because C3G and IC-MPGN are so rare, global collaboration is crucial to get enough data to optimally inform decisions. Without strong, representative datasets, uncertainty increases, and innovation becomes more difficult.

CompCure's registry is governed by a steering committee of internationally recognized multidisciplinary experts, including patients. The compass guiding decisions always points at the best possible solutions for patients. The registry's data is collected according to strict European data privacy legislation.

It can be difficult for any single nephrologist to have extensive experience with all rare kidney diseases. For this reason, collaboration and networks play an important role. Through CompCure's network and close partnerships with the ERKNet and other organizations, best practices for providing care for C3G and IC-MPGN are developed and shared. Advice on managing a patient with C3G, IC-MPGN, or another rare kidney disease, can be obtained through ERKNet. Additionally, CompCure's steering committee experts, and the authors of this book can be contacted.

CompCure and other organizations also provide support for diagnostic services as part of ongoing research. By collecting information in the registry, the experts which collaborate within CompCure and the ERKNet can review the diagnostic tests and treatments provided to patients. In case they notice that important clinical information or tests may be missing, or if there is a need for further evaluation, CompCure can provide feedback to the treating center. This collaborative "double-check" helps ensure that diagnoses are as accurate as possible, and it supports doctors in providing the best possible care for patients.

Please contact us if you have questions or are interested in learning more about participating in research and evidence generation.

# Research and Clinical Trials

*Marianne Silkjaer Nielsen,*
*Hyo Jin Heinz and*
*Dr. Giulia Bassanese*

Clinical trials are studies that test new treatments or new ways of using existing medications. In rare kidney diseases like C3G and IC-MPGN, clinical trials play a very important role because treatment options are still limited. Progress in developing new treatments depends on the participation of patients who choose to take part in clinical research. Because these diseases are so rare, the number of eligible participants is often small. For this reason, studies are conducted across multiple hospitals and across different countries, so that enough patients can participate and meaningful results can be obtained.

Patients consider clinical trials for several reasons, one of which is the possibility of accessing promising therapies before they become widely available. Another reason is the level of medical attention involved. Participants are usually monitored closely by experts, with regular laboratory tests and frequent contact with specialists experienced in these rare conditions. Some patients find reassurance in this careful monitoring. Others are motivated by the chance to advance knowledge for future patients with the same diagnosis. In rare diseases, each participant's contribution is especially valuable, because every piece of information helps researchers better understand the condition and develop more effective treatments.

However, participation is not the right choice for everyone. A clinical trial is research, so outcomes are not guaranteed. The treatment may or may not be effective, and unexpected side effects are possible. Studies may also require additional appointments, travel, or time commitments that could impact daily life. These practical aspects are just as important to consider as the medical ones.

Before joining a study, you will go through a process called informed consent. This means the research team will explain the study in detail, including its purpose, risks, benefits, and expectations, so you can decide whether to participate freely. You are always welcome to ask questions, take time to think about it, and discuss the decision with your family and doctor. It is important to note that joining a trial is voluntary, and you can leave at any time without affecting your regular medical care.

Many patients describe their experience as becoming active partners in research rather than merely receiving treatment. For some, this brings a sense of control in the face of an otherwise unpredictable disease. For others, however, the structured schedule can feel demanding. Experiences vary, and there is no single „right" decision.

Considering a clinical trial does not mean that you have exhausted all your options. Instead, it can be a way to explore new possibilities while contributing to progress in C3G and IC-MPGN research. The best choice is the one that fits your health situation, personal values, and daily life, and should be made with good information and support from your medical team.

# Hyo Jin

*A personal story*

Prior to my C3G diagnosis in 2023, I was a very active person who ran marathons, hiked mountains, and managed my busy family of five. Therefore, when I heard the diagnosis, I was simply devastated.

It all started with symptoms, like edema, foamy urine, and significant weight gain, about six months prior to the diagnosis. I visited several doctors to figure out what was wrong with me, until I finally went to a nephrologist who recognized the need for a biopsy.

I was supposed to stay in the hospital for one night but ended up staying for four. I wondered, ***what could be so bad that I would need to stay for four nights?*** But I put faith in my doctors, as they worked with other centers of expertise around the country to diagnose me.

I immediately started traditional therapies, with a footnote to consider a clinical trial. ***Why would I consider a clinical trial when I had not even tried the traditional therapies? Was my condition so bad that that was the only option?*** Quite honestly, I used to think that clinical trials were only for people who had exhausted all their options, and they were the last resort. But in the end, there must have been a reason for it.

I researched clinical trial protocols and discussed them with my doctor. I asked about the risks, potential side effects, time commitment, etc., and after much consideration, I decided to participate. If the medication was not effective or even counterproductive, I could exit the trial at any time.

I entered the trial six months after my diagnosis. The first six months of the study constituted the double-blind phase, where nobody knew whether I was receiving a placebo or the real medication. Very quickly, I was confident I knew. I started feeling like my old self. I had more energy, and I could work out and even begin running again. And slowly, I began to hope again.

Four months later, I toed the starting line at the New York Marathon. My nephrologist gave me the green light, with a few caveats, to which I adhered diligently (e.g., taking walk breaks every 2 minutes). My only goals were to cross the finish line on my own two feet and to have fun. I have run eleven marathons, but this will remain the most memorable one for me. I was able to finish the marathon in under six hours and proved that having C3G could not stop me from living my life to the fullest.

# Glossary

**ACE Inhibitor:**
Used primarily to treat hypertension, heart failure, and protect kidneys in patients with diabetes or chronic kidney disease.

**Albumin:**
A protein made by your liver. Low albumin levels can be a sign of liver or kidney disease or another medical condition. It can lead to fluid leaking into tissue, called edema, and causing swelling.

**Albuminuria:**
The presence of the protein albumin in the urine. It usually indicates kidney damage or disease, because healthy kidneys normally prevent albumin from leaking into urine.

**ARB:**
Angiotensin Receptor Blockers (ARBs) are a class of blood pressure-lowering medications (e.g., losartan, valsartan) commonly used to treat chronic kidney disease, especially in diabetic patients, by slowing kidney damage. They work by blocking the angiotensin II hormone, which relaxes blood vessels and reduces kidney strain, lowering proteinuria (protein in urine).

**Autoimmune Disease:**
Occur when the immune system mistakenly attacks healthy body cells, causing chronic inflammation and damage to tissues and organs.

**Biopsy:**
A kidney biopsy is usually required to diagnose C3G and IC-MPGN. It is a procedure in which a small piece of kidney tissue is removed using a needle. This tissue contains tiny filtering units called glomeruli, which clean the blood. The sample is then examined by a kidney specialist (renal pathologist) using different laboratory techniques.

**C3:**
Complement component 3 (C3) is a vital blood protein that acts as the central hub of the complement system

**C3a:**
C3a in the kidneys refers to a small, pro-inflammatory protein fragment (anaphylatoxin) generated by complement system activation. It acts through C3a receptors (C3aR) on renal cells, often driving inflammation and fibrosis in conditions like lupus nephritis and diabetic nephropathy.

**C3b:**
C3b in the kidneys refers to the accumulation of an activated complement protein (part of the immune system) within the kidney's filtering units (glomeruli), which is the hallmark of C3 Glomerulopathy (C3G). This buildup causes inflammation, damages the glomeruli, and can lead to kidney failure.

**C5:**
Complement C5 is a key pro-inflammatory protein in the innate immune system that, when overactivated, drives kidney inflammation, fibrosis, and injury. It is cleaved into C5a (a potent inflammatory mediator) and C5b (part of the Membrane Attack Complex), acting as a major therapeutic target in renal diseases like diabetic nephropathy and atypical hemolytic uremic syndrome (aHUS).

**C5a:**
C5a is a highly potent, pro-inflammatory fragment of the complement system that acts as a powerful initiator of inflammation and tissue injury within the kidneys. Formed by the cleavage of complement component C5, C5a binds to receptors (C5aR1/C5aR2) on renal cells, driving inflammation, fibrosis, and damage in conditions like lupus nephritis and diabetic nephropathy.

**C5b:**
C5b is a component of the complement system that triggers the formation of the Membrane Attack Complex (MAC, or C5b-9). In the kidneys, uncontrolled activation leads to C5b-9 deposition, causing cellular damage, inflammation, fibrosis, and proteinuria in diseases like IgA nephropathy, Membranous Nephropathy, and C3 Glomerulopathy.

**Cell Proliferation:**
An increase in the number of cells.

**Creatinine:**
A waste product in the blood produced by the natural breakdown of muscle tissue and protein digestion. Kidneys filter creatinine from the blood and remove it through urine, making blood creatinine levels a primary indicator of kidney function.

**Dipstick Test:**
A diagnostic tool used to screen for health issues by dipping a specially treated, color-changing plastic strip into a urine sample.

**Edema:**
Swelling caused by excess fluid trapped in body tissues, often seen in the legs, ankles, or around the eyes.

**eGFR (estimated glomerular filtration rate):**
A blood test–based estimate of how well your kidneys are filtering waste from the blood. It is used to assess kidney function and stage kidney disease.

**Electron Microscopy:**
This technique is used to visualize structural changes and the specific location of complement protein and/or immunoglobulin deposits. EM helps differentiate C3G and IC-MPGN from post-infectious glomerulonephritis and other glomerular diseases.

**Flare:**
The disease becomes increasingly active and can be triggered by infections and other diseases.

**Genetic Variants:**
A permanent alteration in the DNA sequence of a gene, differing from the most common sequence. These

changes, also called mutations, can be inherited or acquired. Variants can be benign, pathogenic (causing disease), or of unknown significance.

**Glomeruli:**
Tiny filtering units in the kidneys. Each glomerulus is a small cluster of blood vessels that filters waste, excess fluid, and toxins from the blood to form urine.

**Glomerulonephritis:**
Inflammation of the kidney's filtering units (glomeruli). It can reduce kidney function and cause blood or protein to appear in the urine.

**Gut Microbiota:**
Vast, complex community of roughly 100 trillion microorganisms—including bacteria, viruses, and fungi—residing in the human digestive tract. Often considered a „hidden organ," it contributes to immune regulation, digestion, vitamin synthesis (such as vitamin K), and protection against pathogens.

**Hematuria:**
Presence of blood in the urine. It can be classified as:

- **Macroscopic (gross) hematuria** – Blood is visible to the naked eye; urine appears red or brown.
- **Microscopic hematuria** – Blood is not visible but detected under a microscope or with a urine test.

Both can indicate kidney, urinary tract, or bladder problems.

**Hepatitis:**
Inflammation of the liver, commonly caused by viral infections, alcohol abuse, toxins, or autoimmune diseases.

**Idiopathic:**
Meaning that the cause of the disease is unknown.

**IgA Nepropathy:**
IgA nephropathy (also known as Berger's disease) is a chronic autoimmune kidney disease that occurs when immunoglobulin A (IgA) antibodies build up in the glomeruli of the kidney, leading to kidney inflammation.

**Immunofluorescence:**
This technique shows whether there is C3 or immunoglobulin staining and, if so, how intense the staining is.

**Immunoglobulin:**
Also called antibodies; they are essential in protecting against bacteria, viruses, and fungi.

**Inflammation:**
The body's natural immune response to injury, infection, or irritation, designed to protect and heal damaged tissue.

**Lupus:**
A chronic, autoimmune disease where the immune system mistakenly attacks healthy tissues and organs, causing widespread inflammation and damage to joints, skin, kidneys, blood, heart, lungs, and brain.

**Membrane:**
A thin biological structure that acts as a selective barrier. In the kidney, the glomerular basement membrane plays a key role in filtering blood.

**Metabolic Acidosis:**
Serious condition where too much acid accumulates in the body's fluids (blood pH < 7.35) or when the body loses too much base (bicarbonate). It is caused by increased acid production, reduced kidney function, or severe bicarbonate loss. It is often caused by diabetic ketoacidosis, severe kidney disease, or shock.

**Metabolic Health:**
How efficiently your body processes food, uses energy, stores fat, and responds to hormones like insulin.

**Non-Specific Immunosuppressive Medication:**
Medicines that lower the activity of the immune system in a general way. They are used to treat autoimmune diseases or prevent organ rejection after transplantation, but they can make the body more vulnerable to infections.

**Pathogens:**
Microorganisms such as bacteria, viruses, fungi, or parasites that can cause disease by damaging cells, producing toxins, or triggering harmful immune responses.

**Protein:**
Essential macronutrients made of amino acids, acting as the building blocks for body structures like muscles, skin, and hair. They are complex, folded molecules that power chemical reactions (enzymes), carry oxygen (hemoglobin), and support immune function. Proteins are vital for growth, repair, and satiety.

**Proteinuria:**
Presence of excess protein in the urine. It usually indicates kidney damage or disease, since healthy kidneys normally keep protein in the blood.

**Remission:**
The disease is not active.

**Serology:**
The study and testing of blood serum to detect the presence of antibodies or antigens, often used to diagnose infections or immune responses.

**Tissues:**
Tissue is a group of cells that have similar structure and function together as a unit.

**Uremic Toxin Generation:** The production of harmful waste compounds that accumulate in the body when kidney function declines.

# Thank You

*Marianne Silkjaer Nielsen*

This guide has been a labor of love, written by those who would have wanted something like this as they navigated their journeys with C3G or IC-MPGN. It was written together with nephrologists and other experts, for those who are just beginning their journeys or need a 'friend' walking beside them.

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