C3G

A life-altering rare disease driven by the complement system[1,2]

Diagnosing C3G can be complex. Accurate biopsy analysis is crucial to setting your patients on the right path.[2-4]

C3G, complement 3 glomerulopathy.

Patient portrayal.

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C3G IS A RARE KIDNEY DISEASE THAT CAN RESULT IN TRANSPLANT OR DIALYSIS[1,5]

AFFECTS THOSE WHO SHOULD BE THRIVING

- ✓ C3G is a rare type of glomerular disease that affects fewer than 5 people per million in the United States[1]
- ✓ The incidence of C3G is higher in children and young adults (20 to 30 years of age) than in the elderly (>65 years of age)[6]
- ✓ Unlike CKD, patients with C3G often present as children and young adults, which can place a significant burden on their outlook for the future[6]
- ✓ Patients struggle with burdens like proteinuria, fatigue, and anxiety about their futures[7,8,*]

RISK OF DIALYSIS, TRANSPLANT, AND RECURRENCE

Approximately

50%

of patients With C3G

progress to kidney failure in just 10 years from diagnosis and require dialysis or transplant[4,5,9]

"What's most difficult is knowing time is not on my side . . . I know that a healthy diet, exercise, and following doctor's orders will not stop the progression of this disease."[8]

— Real patient with C3G

*Based on patient insights.
CKD, chronic kidney disease.

Patient portrayal.

DYSREGULATION OF THE COMPLEMENT SYSTEM DRIVES KIDNEY INJURY AND PROGRESSION[2]

COMPLEMENT-MEDIATED DISEASE

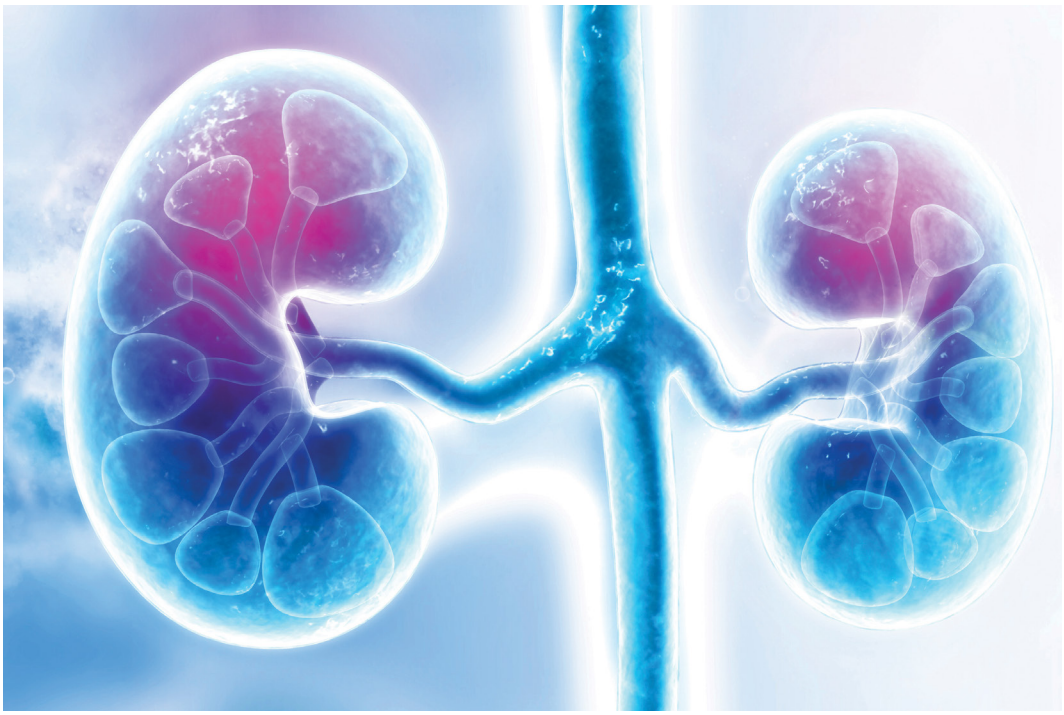
Dysregulation of the alternative complement pathway is the primary driver of C3G.[5,10]

Alternative pathway dysregulation leads to C3G deposition in the glomeruli potentially leading to glomerular inflammation and injury, which can lead to proteinuria, hematuria, chronic kidney disease, and potential kidney failure.[10,12]

COMPLEMENT DRIVES KIDNEY INJURY

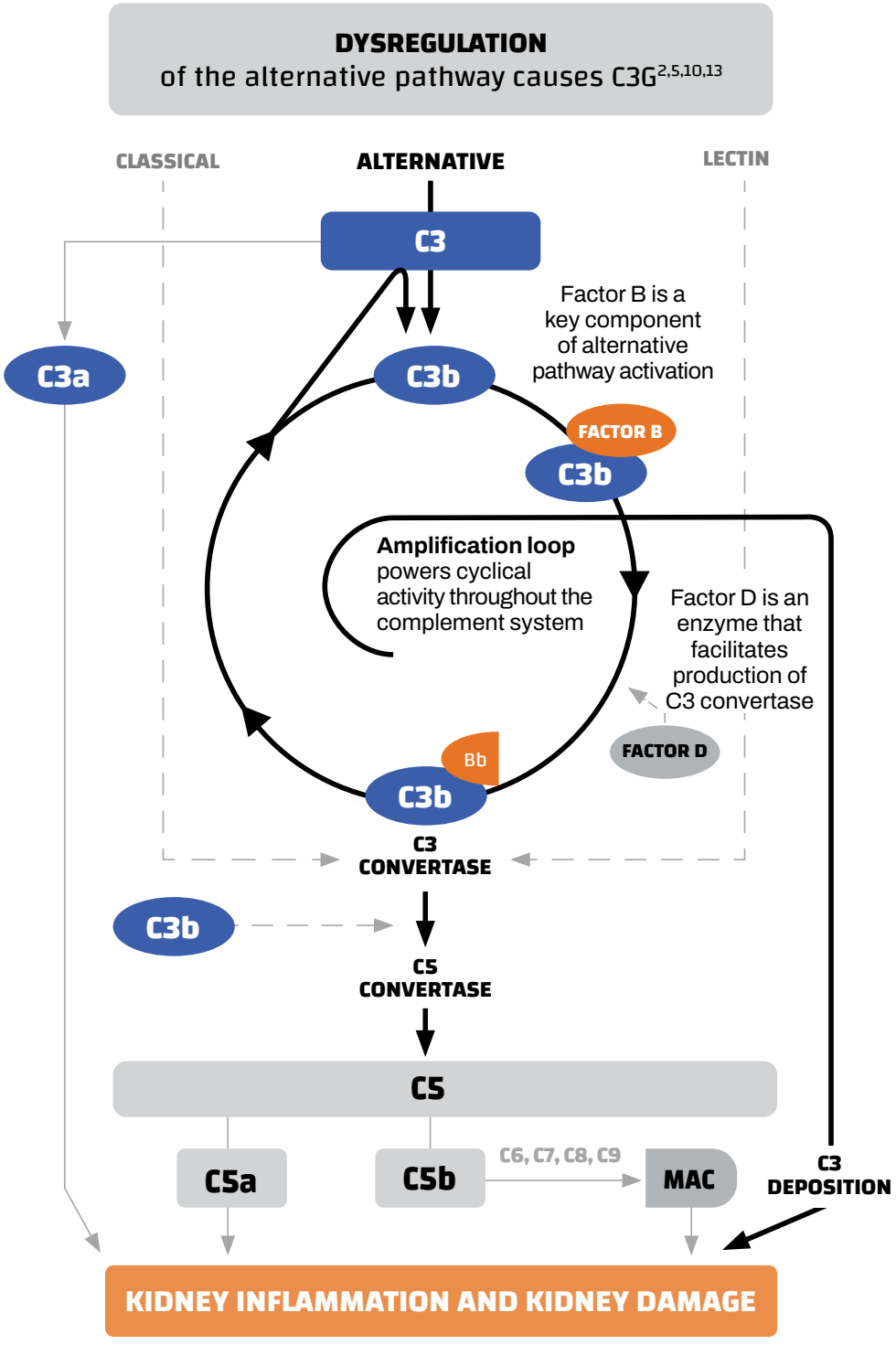
C3 deposits in the glomerular mesangium and along capillary walls can cause persistent inflammation and injury.[10,12]

Scarring of the glomeruli can cause irreversible damage and a decline in kidney function.[2]



C3, complement 3.

DYSREGULATION OF THE ALTERNATIVE COMPLEMENT PATHWAY IS THE PRIMARY DRIVER OF C3G[12]



C3 deposition, as well as its breakdown products in the glomeruli, causes glomerular inflammation and injury.[10]

IN C3G, BIOPSY ANALYSIS IS ESSENTIAL AND REVEALS COMPLEMENT ACTIVITY[2]

ACCURATE, CONFIRMATORY DIAGNOSIS OF C3G REQUIRES URINALYSIS, SEROLOGY, AND BIOPSY[2]

Common differential diagnoses with similar presentation to C3G can include PIGN, IC-MPGN, and MGRS.[2,4,14,15]

A biopsy is necessary for a pathologist to evaluate C3 accumulation, as well as glomerular inflammation and injury.[4,5,9]

C3-dominant staining

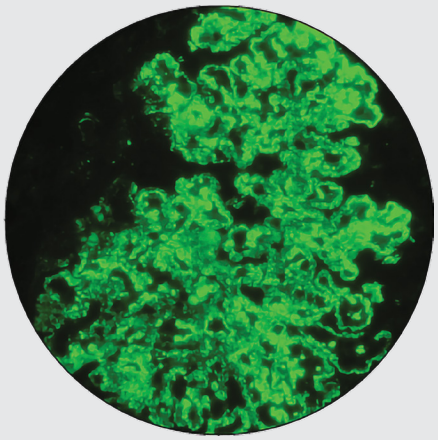


Image credit: Smith RJH, Appel GB, Blom AM, et al. C3 glomerulopathy - understanding a rare complement-driven renal disease. Nat Rev Nephrol. 2019;15(3):129-143. doi:10.1038/s41581-018-0107-2

IgG-dominant staining

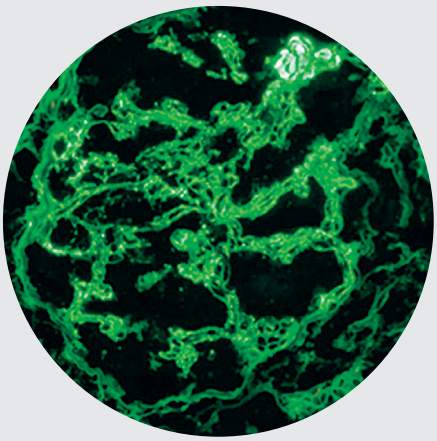


Image credit: Sethi S, Vriese ASD, Fervenza FC. Acute glomerulonephritis. Lancet. 2022;399:1646-1663. doi:10.1016/S0140-6736(22)00461-5

C3 ACCUMULATION IS SEEN AS[2,4]:

Intense staining of C3 at least 2 orders of magnitude greater than any other immune component **WITH** → Absence or low presence of immunoglobulin **AND** → Components of the classical complement pathway

Unresolved proteinuria and hematuria may be important indicators of C3G and should trigger expert biopsy analysis.[2]

IC-MPGN, immune complex membranoproliferative glomerulonephritis; IgG, immunoglobulin G; MGRS, monoclonal gammopathy of renal significance; PIGN, postinfectious glomerulonephritis.

CONFIRMING C3G DIAGNOSIS: POTENTIALLY DIFFICULT BUT NECESSARY[2]

Distinguishing C3G from other more common glomerular nephropathies, including postinfectious GN, can be a complex process.[2-4,16]

✓ This complexity can cause delays in diagnosis, which may result in loss of kidney function—especially if an undiagnosed patient with C3G experiences an infection that accelerates disease progression

> **"You can't plan for the future . . . you don't know where you'll be next year."[8]**
> *— Real patient with C3G*

Patient portrayal.

STEPS FOR CONFIRMATORY DIAGNOSIS OF C3G[2,4,14,17]

1

Lab Testing

- Hematuria
- Proteinuria
- Low C3 serum level
- Creatinine or kidney function assessment
- Genetic testing

2

Biopsy

- Percutaneous ultrasound-guided on left or right kidney

3

Light microscopy

- Non-diagnostic; does not rule out other forms of GN
- MPGN pattern of injury

Immunofluorescence

- Distinguishes C3G from other forms of MPGN patterns of injury
- C3-dominant: at least 2 orders of magnitude greater than any other immune component

Electron Microscopy

- Differentiates C3G subtypes, C3GN from DDD

C3G can be heterogeneous in clinical presentation and prognosis[1,2,9,18]:

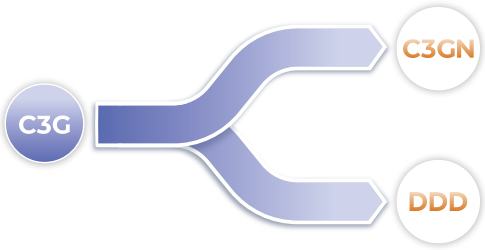
✓ **Patients may present with low to heavy levels of proteinuria and hematuria**

✓ **C3G can be acute, recurrent, or rapidly progressive**

C3GN, complement 3 glomerulonephritis; DDD, dense deposit disease; GN, glomerulonephritis; MPGN, membranoproliferative glomerulonephritis.

C3G IS MORE PROGRESSIVE THAN OTHER GNs, HIGHLIGHTING THE IMPORTANCE OF ACCURATE DIAGNOSIS[2]

PREVIOUSLY CLASSIFIED AS MPGN



C3G and its subtypes were previously classified as MPGN until being **reclassified as C3GN and DDD in the latest ICD-10-CM codes**.[19]

Patients can be diagnosed with 1 of 2 subtypes of C3G: DDD or C3GN.[2]

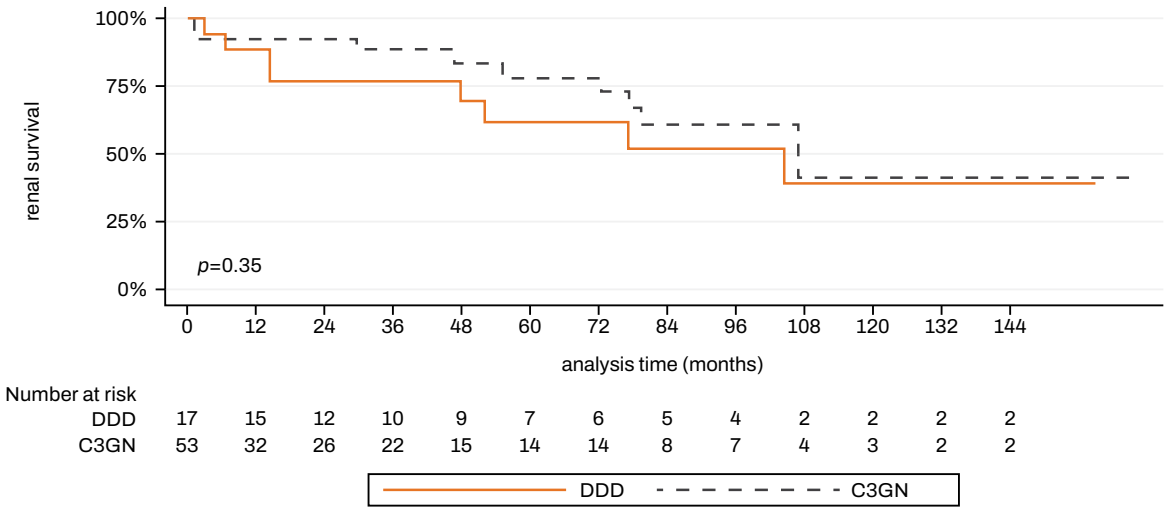
DDD is usually associated with pediatric cases and may progress more quickly than C3GN.[2]

REGARDLESS OF SUBTYPE

Studies have shown **~50% of patients with C3G progress to kidney failure** within 10 years.[4]

In a retrospective review of the renal biopsies of 80 patients with C3G, some patients progressed to kidney failure as early as 2-4 years.[9,*]

Kaplan–Meier analysis of renal survival by C3G subtype in a retrospective cohort[9]



Graph credit: Medjeral-Thomas NR, O'Shaughnessy MM, O'Regan JA, et al. C3 glomerulopathy: clinicopathologic features and predictors of outcome. *Clin J Am Soc Nephrol*. 2014;9(1):46-53. doi:10.2215/CJN.04700513

*All patients with kidney biopsies fulfilling criteria for C3 glomerulopathy from 2 quaternary renal centers within the United Kingdom and Ireland between 1992 and 2012 were retrospectively reviewed. Histologic, demographic, and clinical data and determined predictors of ESRD were recorded using the Cox proportional hazards model. Treatment details were inadequately documented in some cases. Patients' height from the time of original presentation were not available, prohibiting calculation of eGFRs in children.

eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification.

C3G

COMPLEMENT-DRIVEN, PROGRESSIVE, AND OFTEN IRREVERSIBLE[2,4,5]

C3G is a rare and progressive kidney disease that can result in transplant or dialysis[1,5]

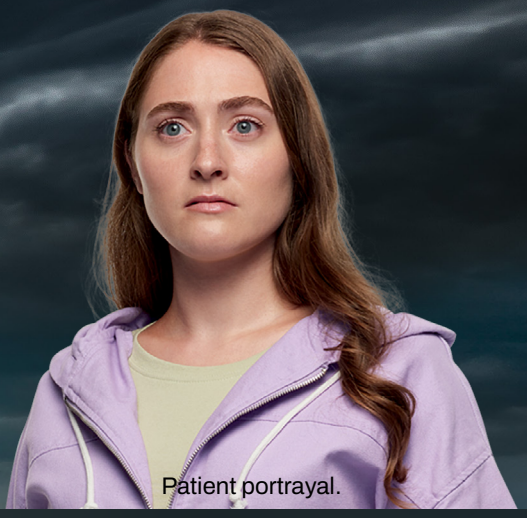
Dysregulation of the alternative complement pathway is the primary driver of C3G, causing kidney injury and progression[2]

Patients continue to face challenges due to their disease that impact their day-to-day lives, including fatigue and anxiety about their future* and kidney failure[4,7,8]

"We need a way to avoid a lifetime of dependence on a dialysis machine or a series of failed transplants."[8]

— Real patient with C3G

*Based on patient insights.



Patient portrayal.

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