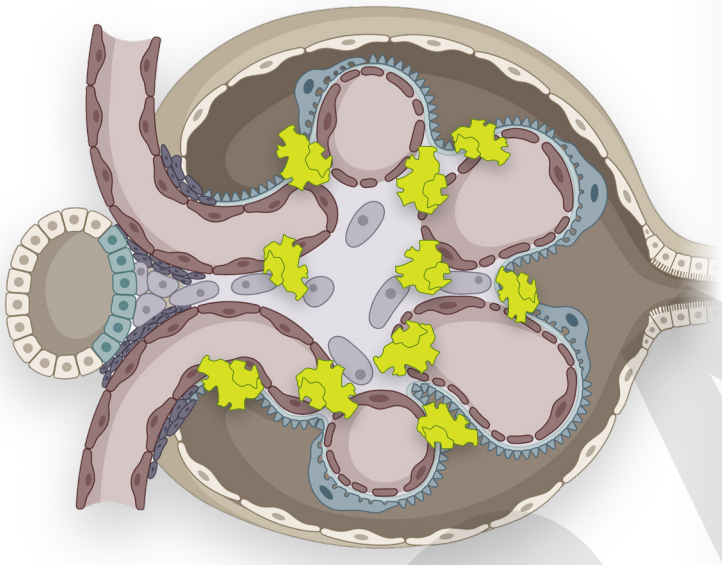
Diagnostic Approach to C3 Glomerulopathy (C3G)

A stepwise, exclusion-based approach to confirming diagnosis

C3 Glomerulopathy (C3G):

A group of kidney diseases characterized by predominant C3 deposition on kidney biopsy with minimal or absent immunoglobulin deposition, resulting from dysregulation of the alternative complement pathway. [1]




Podocyte


Mesangial cell


Endothelial cell


C3 deposit


Glomerular Basement Membrane

1 Kidney biopsy revealing C3 deposits on IF microscopy

C3 dominant staining on kidney biopsy (IF) [1,2]

2 Rule out PIGN if suspicion

Kidney biopsy findings may resemble those seen in acute C3G

PIGN: Low C3 levels; normalizes within 8-12 weeks [1,3,4]

3 Rule out MGRS

Assess for paraproteinemia especially in patients ≥ 50 years old [1,5]

IF: Detection of monoclonal Ig deposits (single Ig class, belonging to a single IgG subclass and single light-chain isotype) [5,6]

4 Assess for retinal drusen

Ophthalmologic assessment at diagnosis should be done for this extra-renal complication that can cause vision loss or impaired vision, similar to age-related macular degeneration [7,8]

5 EM to differentiate DDD and C3GN

Not required for diagnosis of C3G, but essential in identifying patterns that distinguish between C3GN from DDD [9]

6 Lab tests for complement dysregulation

Functional assays [5]	CH50, AP50
Quantification of complement components and regulators [5]	C3, C4
Measurement of complement activation [5]	sC5b9
Complement antibodies [5]	Nephritic factors (C3NeF, C5NeF, C4NeF), Anti-FH, Anti-FB, Anti-C3b
Gene variants [5]	C3, CFH, CFI, CFB, CFHR1-5 MLPA

**Adapted from Ref. 5*

Abbreviations: Anti-C3b, anti-complement component 3b antibody; Anti-FB, anti-factor B antibody; Anti-FH, anti-factor H antibody; AP50, alternative pathway hemolytic complement activity; C3, complement component 3; C3G, C3 glomerulopathy; C3GN, C3 glomerulonephritis; C3NeF, C3 nephritic factor; C4, complement component 4; C4NeF, C4 nephritic factor; C5NeF, C5 nephritic factor; CFB, complement factor B; CFH, complement factor H; CFHR1-5, complement factor H-related genes 1 through 5; CFI, complement factor I; CH50, total hemolytic complement activity; DDD, dense deposit disease; EM, electron microscopy; FH, factor H; FI, factor I; IF, immunofluorescence; Ig, immunoglobulin; IgG, immunoglobulin G; MGRS, monoclonal gammopathy of renal significance; MLPA, multiplex ligation-dependent probe amplification; MPGN, membranoproliferative glomerulonephritis; PIGN, post-infectious glomerulonephritis; sMAC, soluble membrane attack complex.

References

Illustration adapted from "Renal corpuscle (cross-section)," by BioRender.com (2026). Retrieved from https://app.biorender.com/biorender-templates

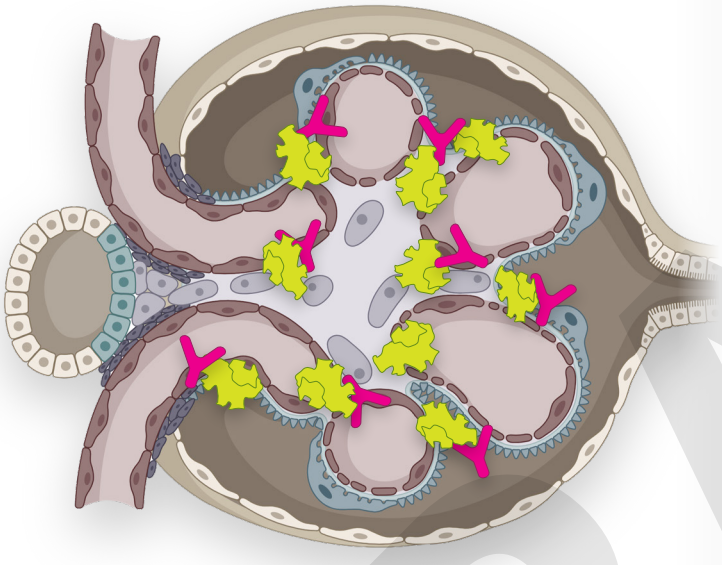
C3G
C3 Glomerulopathy Canada

Diagnostic Approach to Primary Immune-Complex Membranoproliferative Glomerulonephritis (IC-MPGN)

A stepwise, exclusion-based approach to confirming diagnosis

Primary IC-MPGN:

Membranoproliferative glomerulonephritis (MPGN) in which other underlying causes have been excluded and complement dysregulation contributes to disease pathophysiology.




Podocyte


Mesangial cell


Endothelial cell


C3 deposit


Glomerular Basement Membrane


Immune deposit

1 Kidney biopsy revealing C3 deposits and immunoglobulin deposits on IF

C3 deposits ≥ 2 orders of magnitude greater intensity than other common immune reactant, and immunoglobulin deposition, such as IgG and or IgA, IgM, C1q deposits [1,2,10,11]

2 Rule out chronic infections, autoimmune etiologies, and malignancy

Autoimmune diseases (SLE); chronic infections (HBV/HCV, endocarditis, shunt nephritis, schistosomiasis, mycoplasma pneumoniae, malaria); monoclonal gammopathies (cryoglobulinemia, proliferative glomerulonephritis with monoclonal IgG deposits)

3 Rule out MGRS if evidence of monoclonality

Assess for paraproteinemia [1,5]

Pronase digestion: Apply pronase digestion treatment followed by staining to assess for monoclonality and reveal masked immunoglobulins [12]

IF: Detection of monoclonal Ig deposits (single Ig class, belonging to a single IgG subclass and single light-chain isotype) [5,6]

4 Assess for retinal drusen

Ophthalmologic assessment at diagnosis should be done for this extra-renal complication that can cause vision loss or impaired vision, similar to age-related macular degeneration [7,8]

5 Lab tests for complement dysregulation

Functional assays [5]	CH50, AP50
Quantification of complement components and regulators [5]	C3, C4, FH, FI
Measurement of complement activation [5]	sC5b9
Complement Antibodies [5]	Nephritic factors (C3NeF, C5NeF, C4NeF), Anti-FH, Anti-FB, Anti-C3b
Gene variants [5]	C3, CFH, CFI, CFB, CFHR1-5 MLPA

Abbreviations: Anti-C3b, anti-complement component 3b antibody; Anti-FB, anti-factor B antibody; Anti-FH, anti-factor H antibody; AP50, alternative pathway hemolytic complement activity; C1q, complement component 1q; C3, complement component 3; C3NeF, C3 nephritic factor; C4, complement component 4; C4NeF, C4 nephritic factor; C5NeF, C5 nephritic factor; CFB, complement factor B; CFH, complement factor H; CFHR1-5, complement factor H-related genes 1 through 5; CFI, complement factor I; CH50, total hemolytic complement activity; FH, factor H; FI, factor I; HBV, hepatitis B virus; HCV, hepatitis C virus; IC-MPGN, immune-complex membranoproliferative glomerulonephritis; IF, immunofluorescence; Ig, immunoglobulin; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; MGRS, monoclonal gammopathy of renal significance; MLPA, multiplex ligation-dependent probe amplification; MPGN, membranoproliferative glomerulonephritis; SLE, systemic lupus erythematosus; sMAC, soluble membrane attack complex.

References

Illustration adapted from "Renal corpuscle (cross-section)," by BioRender.com (2026). Retrieved from https://app.biorender.com/biorender-templates

C3G
C3 Glomerulopathy Canada