C3 Glomerulopathy (C3G) ICD-10-CM Code Recommendation

The focus of this code revision request is to recognize C3 glomerulopathy (C3G) and its subtypes with specific ICD-10 coding.

Supported by the clinical consensus reached by an international group of experts in renal pathology, nephrology, complement biology, and complement therapeutics

Richard J. Hamburger, M.D.

Professor Emeritus of Medicine, Indiana University

Renal Physicians Association

(Pickering, Matthew C. *et al.* C3 glomerulopathy: consensus report. *Kidney International*, 84(6):1079-1089, 2013)

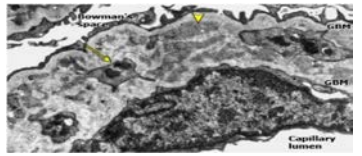
Classification of Glomerulonephritis: Limitations

- **Historically, glomerular diseases defined/classified by light microscopy histopathology**
- **Multiple etiologies of a glomerular disease can present as the same histopathologic manifestation with each requiring different therapeutic interventions**
- **Current approach, if possible, is to define a glomerular disease state by etiology; not the histopathological manifestation of the disease which our current classification system is based on.**
- **Therefore: must look at changing current classification to allow us to better classify and track these rare and complex glomerular diseases in search of optimal therapeutic interventions**
- **This is the case for C3 Glomerulopathy (C3G) we are bringing before this committee today**

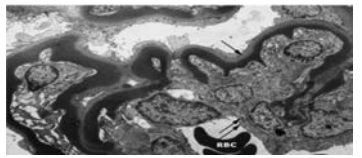
MPGN: Classification Old vs New

- Old:
  - Based on presence of ultra-structural appearance and location of electron dense deposits
  - Type I,II, III
  - Developed prior to use of Immunofluorescence (IF) in Kidney Biopsy
- New:
  - Based on presences of immunofluorescence microscopy
    - Immunoglobulins (Ig)
    - And/or C3

Classical Overview of MPGN



MPGN Type I
Deposits in mesangium and sub-endothelial space



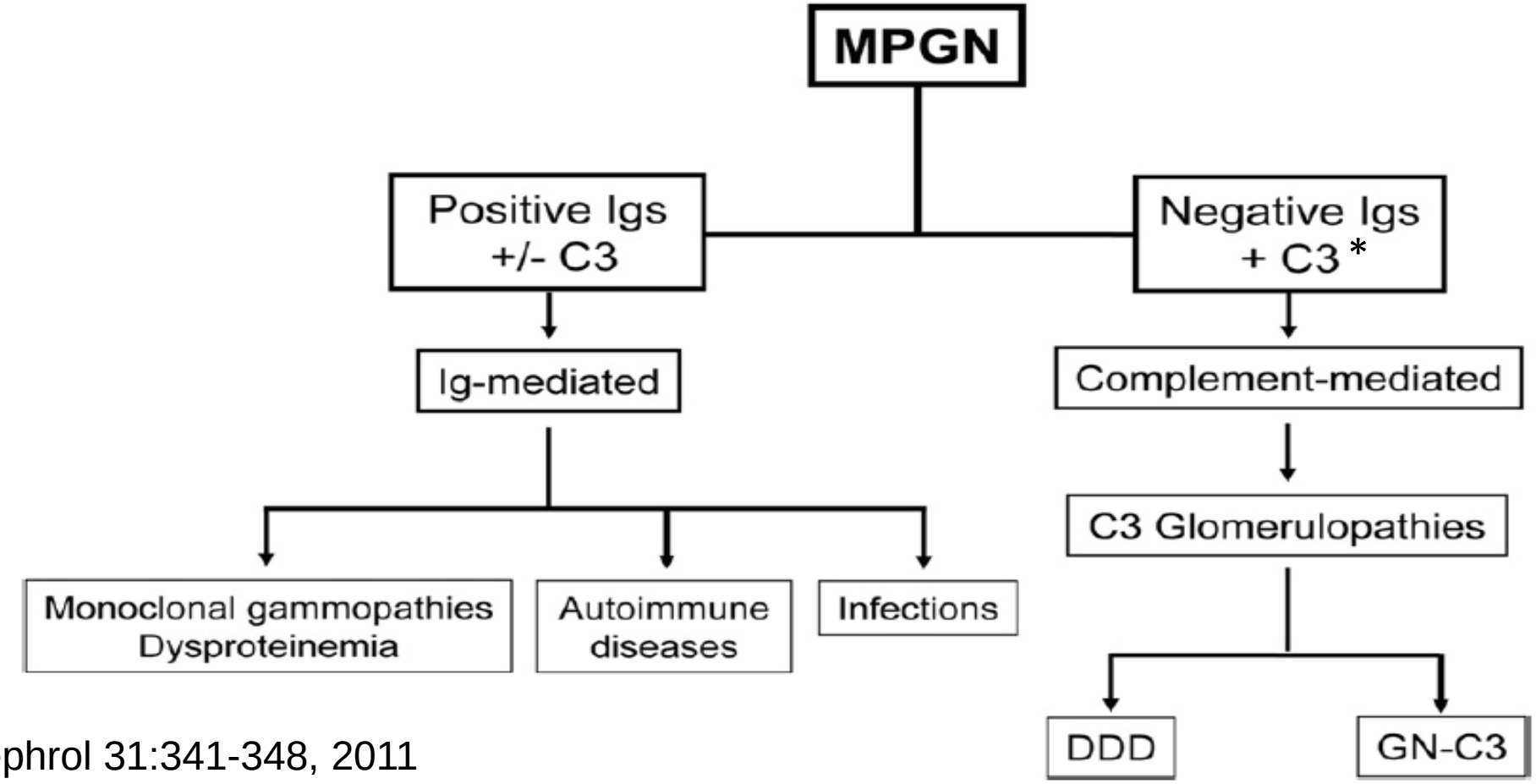
MPGN Type II
Intra-membranous dense ribbon-like deposits

MPGN Type III
Deposits in the sub-endothelial and sub-epithelial space

Reclassification of MPGN Based on Underlying Pathogenesis

- ***Immunoglobulin-mediated disease***; Ig-Associated MPGN (IA MPGN)
  - Resulting from imbalances in classical complement pathway
- ***Non-Immunoglobulin disease***:
  - Resulting from imbalances in the alternate complement pathway
  - C3G: Dense Deposit Disease
  - C3 Glomerulonephritis (C3GN)

MPGN: New Classification based on Ig and/or C3 deposits by IF



Semin Nephrol 31:341-348, 2011

Kidney International, 84(6):1079-1089, 2013

* C3G is defined based on C3 intensity ≥2 orders of magnitude more than Ig

C3G

- Rare disease : incidence 1 to 3 / million population
- Natural history slowly being defined and appears fairly heterogeneous
- Variable clinical presentation
  - Asymptomatic hematuria and proteinuria with preserved kidney function to full nephrotic syndrome or rapidly progressive glomerulonephritis with acute kidney failure and need for renal replacement therapy
- Progression to end-stage renal disease (ESRD) is common
  - Up to 50 % of patients within 5 years of diagnosis in DDD patients (C3N)
  - Reportedly progressing twice as fast in C3GN patients

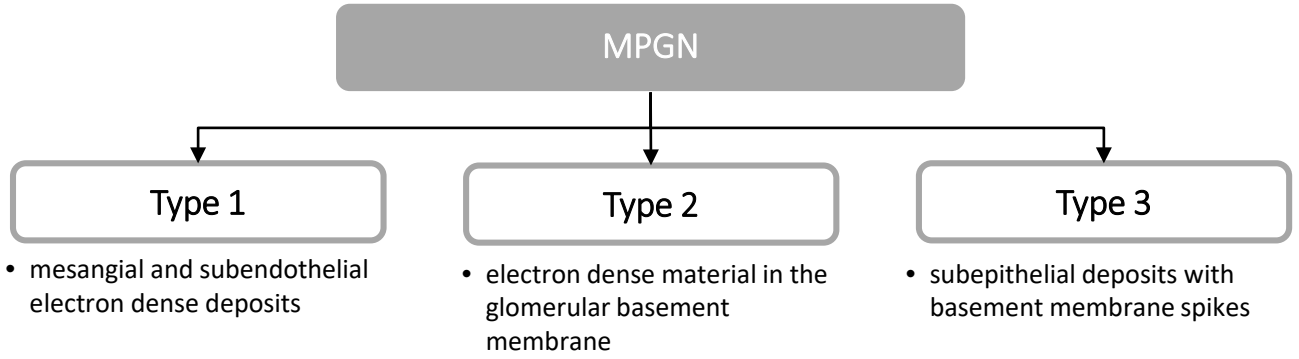
Kidney International (2018) 93, 977–985

Why is there a need for specific codes for C3G?

- Reflect correct diagnosis for specific condition
- Better understand patient segmentation or disease prevalence by subtypes
- Allow for tracking outcomes and therapeutic selection
- Support for reimbursement

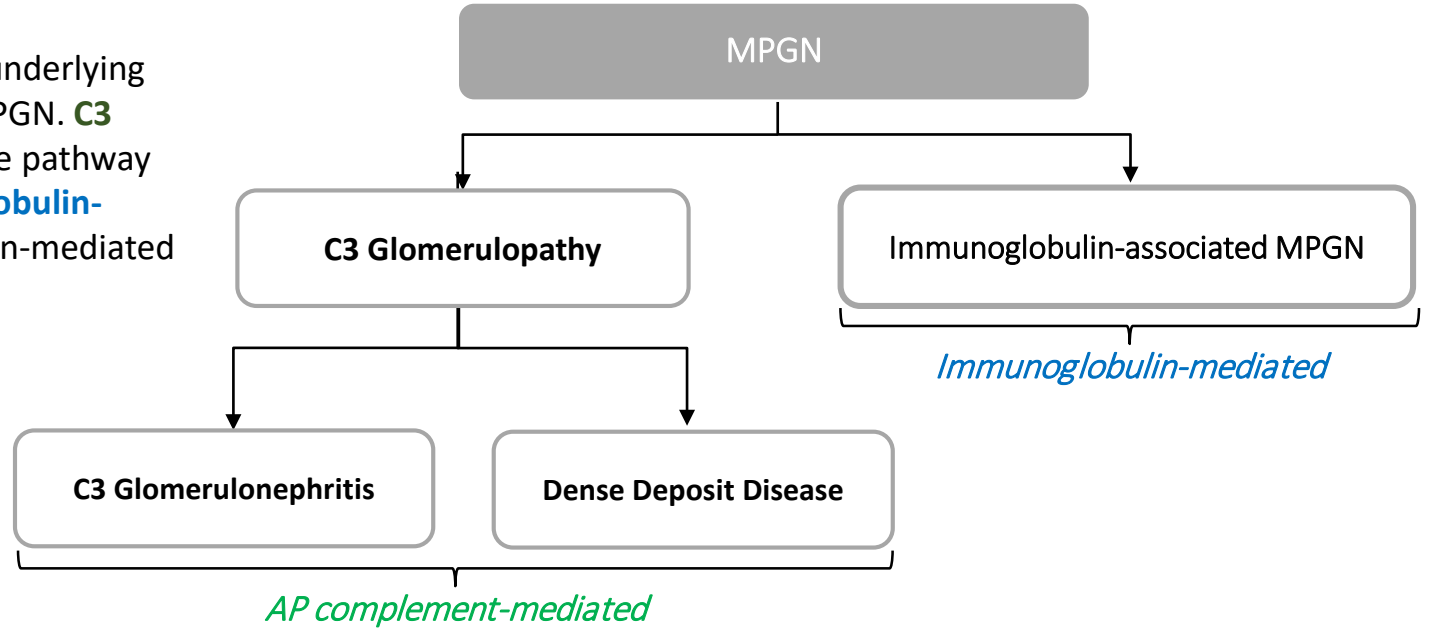
New Classification of MPGN: C3G and Immunoglobulin-associated MPGN

Traditional classification of MPGN was based on pattern and location density of deposits visible using electron microscopy evaluation of kidney biopsies



2013 Consensus Report

Current consensus classification is based on the underlying mechanism contributing to the pathology of MPGN. **C3 Glomerulopathy (C3G)** is considered an alternative pathway complement-mediated disease and **Immunoglobulin-associated MPGN (IA-MPGN)*** is an immunoglobulin-mediated disease



*IA-MPGN also referred to as Immune Complex MPGN

**C3G diagnosis requires isolated C3 staining on renal biopsy or a C3 intensity ≥ 2 orders of magnitude more than any other immune reactant