Introduction to Glomerular Disease

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Glomerulus
Capillary loops are covered with podocytes from outside and lined with fenestrated endothelium from inside.
Podocytes
Permeability barrier
Glomerular Filtration
Albumin is negatively charged and is not filtered due to charge barrier
Normal foot processes

Effaced foot processes

Podocytes with normal foot processes
Podocytes with effaced foot processes
Kidney biopsy

Light microscopy (LM)

Electron microscopy (EM)

Immunofluorescence microscopy (IF)
## LM stains

<table>
<thead>
<tr>
<th>Stain</th>
<th>Utility</th>
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<tbody>
<tr>
<td>Hematoxylin and eosin stain (H and E)</td>
<td>General evaluation, cellular characteristics, type of inflammation</td>
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<tr>
<td>Periodic acid-Schiff stain</td>
<td>Glomerular cell number, basement membrane, mesangium, tubular basement membrane, hyaline (red color)</td>
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<tr>
<td>Silver methenamine (Jones)</td>
<td>Basement details (black color)</td>
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<td>Masson’s trichrome</td>
<td>Extracellular glomerular matrix and tubular basement membranes (blue or green)</td>
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<tr>
<td>Congo red</td>
<td>Amyloid</td>
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<tr>
<td>Von kossa</td>
<td>Calcification</td>
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<tr>
<td>Acid fuschin-orange G</td>
<td>Protein deposition (immune complex)</td>
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<tr>
<td>Sirius red</td>
<td>Fibrosis</td>
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</tbody>
</table>
General evaluation

Cells

Types of inflammation
Structure (cell number, GBM, TBM, mesangium)
Silver

GBM
Trichrome Blue

Connective tissue - fibrosis
Congo Red

Amyloid
Congo Red

Amyloid
IF

The immunofluorescence staining panel includes IgG, IgM, IgA, C3, C1q, kappa, lambda, and albumin, C4d is routinely performed on renal transplant biopsies.
Granular signal in capillary loops distribution
Linear signal in capillary loops distribution
Granular signal in mesangial distribution, “pruned bush”
Pathology Terms for Glomerular Disease

• **Focal**: <50% glomeruli involved

• **Diffuse**: >50% glomeruli involved
Is this process focal or diffuse?
Pathology Terms for Glomerular Disease

**Segmental**: involving only segment of the glomerular tuft

**Global**: involving the entire glomerulus
Is this process segmental or global?
Mechanisms of glomerular injury

- Immune
- Non-immune
Immune mechanisms of glomerular injury: immune deposits
Immune mechanisms of glomerular injury: immune deposits
Immune mechanisms of glomerular injury
Immune mechanisms of glomerular injury

• Antibody to a resident glomerular antigen
• Antibody to a planted glomerular antigen
• Circulating immune complexes
• Cell-mediated injury/Cytotoxic antibody
• Thrombotic injury and complement dysregulation
Resident glomerular antigen

Ex: Anti-GBM (Goodpasture) disease - unmasked antigen within GBM (and sometimes alveolar BM)
Anti-GBM disease
Ex: Post-strep GN - streptococcal proteins with affinity for GBM form *in situ* immune complexes, which activate complement
Circulating immune complexes

Ex: Lupus - subendothelial deposits disrupt glomerular barrier
Cell-mediated injury

Ex: Minimal Change Disease, FSGS
Immune cells produce toxic factor against podocytes
Thrombotic injury

Ex: Thrombotic Microangiopathy, Hemolytic Uremic Syndrome, Preeclampsia
Abnormal platelet aggregation causes endothelial injury and damages microcirculation
Mechanisms of glomerular injury

• Immune

• Non-immune
  – Deposition Diseases
  – Genetic Diseases
Deposition diseases

Ex: Amyloidosis, Diabetes
Genetic diseases

Ex:
Alport’s syndrome

Fabry’s disease
Manifestations of Glomerular Injury

- Proteinuria
- Hematuria
- Decreased GFR
Proteinuria
Proteinuria
Proteinuria

• Definition:
Proteinuria

- Definition: >150 mg protein/24 hour collection in adults
Proteinuria: Detection

Dipstick: detects albumin only
Proteinuria: Detection

Sulfosalicylic acid: can detect urine proteins other than albumin, like Bence Jones proteins.
Proteinuria: Quantitation

24 hour urine is the most accurate method; can also do a random urine protein/creatinine ratio
Proteinuria: Classification

• Isolated
• Nephrotic range
• Nephrotic syndrome
Nephrotic range proteinuria
>3.5 g albumin (1 egg)
Nephrotic Syndrome

1.
2.
3.
4.
Nephrotic Syndrome

1. Nephrotic-range proteinuria
2. Hypoalbuminemia
3. Edema
4. Hyperlipidemia (lipiduria)
Hematuria
Hematuria

Dysmorphic RBC
Hematuria

RBC cast
Nephritic syndrome

1.
2.
3.
4.
Nephritic syndrome

1. Decreased GFR
2. Hematuria (RBC casts are diagnostic)
3. Proteinuria (<3.5 gm/day)
4. Salt & water retention
RPGN

• Definition:
RPGN

• Definition: acute nephritic syndrome characterized by marked and progressive drop in GFR, histopathologically crescentic GN
Classification of pathologic and clinical manifestations of glomerular injury

**Histopathologic name**
- Minimal Change Disease
- Focal Segmental Glomerulosclerosis
- Nodular Glomerulosclerosis
- Membranous Nephropathy
- Membranoproliferative GN
- Mesangioproliferative GN
- Proliferative GN
- Crescentic GN

**Clinical name**
- Minimal Change Disease
- FSGS, HIV nephropathy
- Diabetic Nephropathy, Amyloidosis
- Membranous Nephropathy
- MPGN
- IgA Nephropathy
- Post-infections (Post-Strep) GN
- Rapidly Progressive GN (RPGN)