Classification of Glomerular Diseases

Podocyte
- Focal Segmental Glomerulosclerosis*
- Membranous Nephropathy*
- Minimal Change Disease*
- Poststreptococcal GN†
- HIV-Associated Nephropathy*
- Diabetic Nephropathy*

Glomerular Basement Membrane
- Alport Syndrome
- Goodpasture Syndrome

Glomerular Endothelial Cell
- Poststreptococcal GN†
- Preeclampsia
- Thrombotic Microangiopathy
- Vasculitis

Glomerular Endothelial and Mesangial Cells
- Membranoproliferative GN‡
- Systemic Lupus Erythematosus‡

Mesangial Cell
- Diabetes Mellitus*
- Fibrillary Glomerulopathy*
- Henoch-Schönlein Purpura
- IgA Nephropathy
- IgM Nephropathy
- C1q Nephropathy
- Systemic Lupus Erythematosus

*Classically presents with the nephrotic syndrome.
†Often presents with the nephrotic syndrome.
Classification of pathologic and clinical manifestations of glomerular injury

**Histopathologic name**

- Minimal Change Disease
- Focal Segmental Glomerulosclerosis
- Nodular Glomerulosclerosis
- Membranous Nephropathy
- Membranoproliferative GN
- Mesangio proliferative 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)
Classification of pathologic and clinical manifestations of glomerular injury

Histopathologic name

**Minimal Change Disease**
- Glomerulosclerosis
- Nodular Glomerulosclerosis
- Membranous Nephropathy
- Membranoproliferative GN
- Mesangiproliferative 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)

Nephritic

Nephrotic
Case Bella

• Bella is a 19 year old high school student referred for proteinuria. She developed edema to thighs 3 wks ago. She has been previously healthy. She takes no medications.
Case Bella

- **Exam**: BP 101/63, exam normal except for 2+ pitting lower extremity edema bilaterally
- **Labs**: urine prot 4+, alb 2.2, cholesterol 498, creat 0.6
Case Bella

- Patient started on prednisone 60 mg daily. Returns 1 wk later – edema resolved and urine protein is down to trace.
- **Diagnosis:**
Case Bella

• Patient started on prednisone 60 mg daily. Returns 1 wk later – edema resolved and urine protein is down to trace.

• **Diagnosis**: Minimal Change Disease
Minimal change disease

• Definition:
Minimal change disease

• **Definition:** Histopathologic lesion with normal glomeruli on light microscopy and diffuse foot process fusion on electron microscopy, associated with nephrotic syndrome.
Minimal Change Disease

• **Pathogenesis:**
  – leading hypothesis: immune dysfunction/T cell activation leads to release of a cytokine
  – the cytokine ("permeability factor") targets podocytes disrupting GBM charge barrier and causing proteinuria
Minimal Change Disease, LM

Appears normal
Minimal Change Disease, LM

Proximal tubular epithelial cells filled with lipid and protein ("lipoid nephrosis")
Minimal Change Disease, EM

Normal

MCD
Minimal Change Disease
Case follow-up

• Patient was treated with a 4 months prednisone taper with complete resolution of proteinuria. However, 1 mo after stopping prednisone, her proteinuria increased to 3+, which indicated a relapse. Started on CellCept again with resolution of proteinuria after 1 wk. Pt then treated with CellCept x 1 year. She remains in complete remission
MCD recap
MCD recap

- Abrupt onset nephrotic syndrome
- Preferentially children, young adults
- Very responsive to steroids
- Relapsing course
- Excellent prognosis
Minimal Change Disease
Minimal Change Disease
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)
Case Laurent

- Laurent is a laboratory technician who has diagnosed himself with nephrotic syndrome.
Case Laurent

- He is a 45 year old African American male w h/o HTN, who developed progressively increasing lower extremity edema for the past 6 mo
Case Laurent

- He was seen by his PCP several times, and his medications were adjusted. However, in spite of proteinuria on UA, no diagnosis was made.
- **Medications**: verapamil and lasix
- **On exam**, his BP is 145/91, remainder unremarkable except for tight 4+ LE edema.
Case Laurent

• **Labs** 9 mo prior:
  – 2+ protein on UA
  – serum albumin 4
  – cholesterol 300, LDL 180

• **Current labs:**
  – serum albumin 2.8
  – cholesterol 396, LDL 270 and
  – creatinine 1.2
  – Urinalysis 4+ protein and a few granular casts
  – Urine protein/creatinine ratio 12
Case Laurent

• **Diagnosis:** Nephrotic syndrome
• Kidney biopsy was performed
Focal Segmental Glomerulosclerosis

• **Definition:**

![Normal Glomerulus](image1.png) ![Glomerulus with Focal Segmental Glomerulosclerosis (FSGS)](image2.png)
Focal Segmental Glomerulosclerosis

• **Definition:** Histopathologic lesion with sclerosis of some but not all (hence focal) glomeruli that involves a portion (segment) of the glomerular tuft.
Focal Segmental Glomerulosclerosis

• Ethiology and pathogenesis:
  – Primary:
    • presumed due to a circulating factor (?cytokine) that damages VEC
  – Secondary podocytopathies:
    • HIV, heroin abuse, sickle cell disease, massive obesity.
    • maladaptive response to nephron loss
  – Inherited podocytopathies:
    • linked to mutations of the VEC proteins nephrin, podocin etc
Secondary Focal Segmental Glomerulosclerosis

http://what-when-how.com/acp-medicine/glomerular-diseases-part-4/
Focal Segmental Glomerulosclerosis

- **Morphology:**
  - Sclerotic segments show basement membrane collapse, increased matrix, trapping of plasma proteins in glomerular capillary walls by light microscopy
  - Pronounced tubular atrophy and interstitial fibrosis
normal
Focal Segmental Glomerulosclerosis

segmentally collapsed
unaffected
Focal Segmental Glomerulosclerosis

Effacement of VEC in sclerotic and non-sclerotic segments by EM; no deposits.

GBM collapse and foot process fusion

less affected segment
Laurent
Case follow-up

- Patient was started on prednisone. Two weeks later he was admitted with bacteremia. His prednisone was tapered and he was started on cyclosporine. Patient was unable to tolerate medication, switched to CellCept. This medication was stopped after several months due to lack of efficacy.
Laurent
Case follow-up

• His proteinuria increased to 40 g/24 hrs, and serum creatinine progressively increased to 3. Patient failed other immunosuppressive medications, and had multiple infectious complications. He also had severe complications of nephrotic syndrome – resistant anasarca, deep venous thrombosis from hypercoagulable state, pericardial effusion, and chronic hypotension due to low plasma oncotic pressure.
Laurent
Case presentation

• He was started on dialysis to control edema, but could not tolerate fluid removal due to hypotension. After hospitalization that lasted 4 months, patient finally agreed to have bilateral renal artery embolization, a procedure called “chemical nephrectomy”. He is now hemodialysis-dependent, and has much improved clinically.
FSGS recap
FSGS recap

- Insiduous onset nephrotic syndrome
- Mostly adults
- Most common NS in AA
- Slow response to steroids
- Prognosis is determined by response to treatment
Now let’s see if you’ve been paying attention...
Patient has nephrotic syndrome, biopsy below. Which statement about this disease is INCORRECT:

A. It is the most common cause of nephrotic syndrome in children
B. It is characterized by sudden onset of florid nephrotic syndrome
C. It is poorly responsive to steroids
D. It can be caused by NSAIDs
Patient has nephrotic syndrome, biopsy below. Which statement about this disease is INCORRECT:

A. It is the most common cause of nephrotic syndrome in children
B. It is characterized by sudden onset of florid nephrotic syndrome
C. It is poorly responsive to steroids
D. It can be caused by NSAIDs
Classification of pathologic and clinical manifestations of glomerular injury

<table>
<thead>
<tr>
<th>Histopathologic name</th>
<th>Clinical name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal Change Disease</td>
<td>Minimal Change Disease</td>
</tr>
<tr>
<td>Focal Segmental Glomerulosclerosis</td>
<td>FSGS, HIV nephropathy</td>
</tr>
<tr>
<td>Membranous Nephropathy</td>
<td>Diabetic Nephropathy, Amyloidosis</td>
</tr>
<tr>
<td>Membranoproliferative GN</td>
<td>Membranous Nephropathy</td>
</tr>
<tr>
<td>Mesangiproliferative GN</td>
<td>MPGN</td>
</tr>
<tr>
<td>Proliferative GN</td>
<td>IgA Nephropathy</td>
</tr>
<tr>
<td>Crescentic GN</td>
<td>Post-infections (Post-Strep) GN</td>
</tr>
<tr>
<td></td>
<td>Rapidly Progressive GN (RPGN)</td>
</tr>
</tbody>
</table>
Membranous Glomerulonephropathy
Case presentation

• Jacob is a 25 yo previously healthy hospital security guard, who was referred for evaluation of proteinuria.
Membranous Glomerulonephropathy
Case presentation

• He noticed LE edema several weeks prior. He was hypertensive at 155/90. His serum creatinine was 0.9, alb 2.2, cholesterol 311 w LDL 173, Urine - 5g protein/24 hrs.
Membranous Glomerulonephropathy
Case presentation

- **Kidney biopsy** showed Membranous Glomerulopathy.

- **Clinical course**: patient was treated with an immunosuppressive regimen consisting of prednisone and cyclophosphamide for 6 months, and responded with markedly decreased proteinuria (0.5 g/24 hrs). He was seen in follow-up several years later and had trace proteinuria and normal creatinine.
Membranous Glomerulonephropathy

- **Definition:**
Membranous Glomerulonephropathy

- **Definition**: Histopathologic lesion characterized by glomerular basement membrane thickening due to immune complex entrapment, associated with nephrotic syndrome.
Membranous Glomerulonephropathy

Pathogenesis: A chronic immune-complex nephritis caused by:

- Ab directed against intrinsic GBM Ag PLA2R (primary)
- Circulating immune complex entrapment in the GBM (secondary)

Both activate complement, which damages podocytes and makes them leaky
Pathogenesis of primary membranous GN
Membranous Glomerulonephropathy

- **Pathology:** *light microscopy:* diffuse, uniform thickening of basement membrane with small subepithelial projections ("spikes") of basement membrane in capillary loops.
Membranous Glomerulonephropathy, LM
Membranous Glomerulonephropathy, LM

“Spike” formation on subepithelial (urinary) side of GBM, (silver stain)
Membranous Glomerulonephropathy, LM
Membranous Glomerulonephropathy, IF

- **Immunofluorescence microscopy**: diffuse, coarsely granular pattern to IgG along capillary loops.
Membranous Glomerulonephropathy, EM

Subepithelial electron-dense immune deposits
Membranous Glomerulonephropathy, EM
Now let’s see if you’ve been paying attention...
Patient has nephrotic syndrome and biopsy is depicted below. Which statement is INCORRECT:

A. It is the most common cause of idiopathic nephrotic syndrome in African American adults
B. It is characterized by slow and variable response to steroids
C. It can be associated with HIV
D. This disease does not affect podocytes
Patient has nephrotic syndrome and biopsy is depicted below. Which statement is INCORRECT:

A. It is the most common cause of idiopathic nephrotic syndrome in African American adults
B. It is characterized by slow and variable response to steroids
C. It can be associated with HIV
D. This disease does not affect podocytes
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
- Nephrotic
  - Minimal Change Disease
  - FSGS, HIV nephropathy
  - Diabetic Nephropathy, Amyloidosis
  - Membranous Nephropathy
  - MPGN
  - IgA Nephropathy
  - Post-infections (Post-Strep) GN
- Nephritic
  - Rapidly Progressive GN (RPGN)
Classification of pathologic and clinical manifestations of glomerular injury

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

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

**Clinical Status**
- Nephrotic
- Nephritic
Membranoproliferative Glomerulonephritis Case presentation

• Jasper is a 48 year old Caucasian male with h/o polysubstance abuse.
Membranoproliferative Glomerulonephritis Case presentation

• He was admitted to the hospital with generalized swelling, hypertensive urgency and pulmonary edema. He was homeless, but is currently living at Rubicon drug treatment center.
Membranoproliferative Glomerulonephritis Case presentation

- His serum cr in 2, serum albumin is 2.5, urine protein to creatinine ratio is 10, UA showed proteinuria and hematuria. Further workup revealed that patient is positive for hepatitis C and cryoglobulins, and had low C4.
Membranoproliferative Glomerulonephritis Case presentation

- Kidney biopsy revealed membranoproliferative glomerulonephritis (MPGN), type I.
- Patient was not a candidate for treatment due to poor social situation and history of non-compliance. His renal function has deteriorated and he became dialysis-dependent within 6 months.
Membranoproliferative Glomerulonephritis

• Definition:
Membranoproliferative Glomerulonephritis

- **Definition**: histopathologic lesion characterized by mesangial proliferation and interposition into the glomerular capillary wall with double contours ("tram tracking") of GBM on light microscopy
Membranoproliferative Glomerulonephritis

- **Pathogenesis**: deposition of subendothelial immune complexes in glomerulus with abnormal activation of complement, production of “nephritic factors” and glomerular injury
MPGN Classifications

• By ultrastructural appearance
  – Type I (subendothelial deposits)
MPGN Classifications

- By ultrastructural appearance
  - Type II (Dense Deposit Disease)
  - Type III (subendothelial and subepithelial IC)
MPGN Classifications

• By IF appearance:
  – IC-mediated
  – Complement-mediated
  – Unrelated to IC or complement
MPGN Classification

MPGN
(Double contours & mesangial expansion)

C3 and Ig staining

- Infection
- Monoclonal gammopathy
- Autoimmune disease

C3 staining only

- Dense deposit disease
- GN with isolated C3

No staining

- Thrombotic microangiopathy
Mesangial interposition into GBM in MPGN
Membranoproliferative Glomerulonephritis

Light microscopy: glomerular hypercellularity and lobular simplification
Membranoproliferative Glomerulonephritis

Light microscopy: splitting of GBM ("tram-track") is characteristic
Membranoproliferative Glomerulonephritis (Type I)

Immunofluorescence: coarse granular staining of IgG and C3 along capillary loops
Membranoproliferative Glomerulonephritis (Type I), EM

**Normal GBM**

**Electron Microscopy:** subendothelial deposits with new formation of GBM (splitting)
Membranoproliferative Glomerulonephritis (Type I), EM, LM
Now let’s see if you’ve been paying attention...
Which statement regarding the disease with LM/IF below is INCORRECT:

A. This is the most common cause of primary nephrotic syndrome in Caucasian adults

B. 2/3 of patients will develop spontaneous or partial remission without treatment

C. Can be associated with solid tumors

D. EM would show reduplication of GBM with “tram tracking”
Which statement regarding the disease with LM/IF below is INCORRECT:

A. This is the most common cause of primary nephrotic syndrome in Caucasian adults
B. 2/3 of patients will develop spontaneous or partial remission without treatment
C. Can be associated with solid tumors
D. EM would show reduplication of GBM with “tram tracking”
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)
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)
IgA Nephropathy (Berger’s Disease)
Case presentation

- Alice is a 24 year old white female with history of hypertension, who is 16 wks pregnant. She is referred by her OB for proteinuria, hematuria and hypertension. Patient has a history of gross hematuria following upper respiratory infections.
IgA Nephropathy
Case presentation

• Her BP is 155/90, she has trace LE edema, and her UA shows 3+ protein and 20 rbc. Her renal function is normal. She is managed conservatively with labetalol for BP control and bed rest. Her proteinuria is monitored and remains stable throughout the pregnancy. She is delivered via C-section at 37 weeks gestation.
IgA Nephropathy
Case presentation

• 6 weeks post-partum her proteinuria remains unchanged at 3g/24 hrs. Kidney biopsy is performed and shows IgA nephropathy with 50% glomerulosclerosis and moderate interstitial fibrosis. She is started on ACE-I, fish oil and prednisone, but then lost to follow-up.
IgA Nephropathy

- **Definition:**

Mesangial IgA deposits
IgA Nephropathy

- **Definition**: Histopathologic lesion of a glomerulonephritis characterized by prominent IgA–containing immune deposits in the mesangium.
IgA Nephropathy

• **Pathogenesis:**
  
  – Error of IgA production and clearance
    
    • abnormally high production of mucosal and marrow IgA in response to an environmental Ag
    
    • abnormal glycosylation reduces plasma clearance of IgA by the liver
    
    • IgA deposition as immune complexes in the mesangium; there it activates complement.
IgA Nephropathy

IgA Nephropathy

LM: Mesangial hypercellularity and matrix expansion
IgA Nephropathy

- IF: mesangial IgA, diffuse and granular, in “pruned bush” pattern
IgA Nephropathy, LM, IF

© Elsevier 2005
IgA Nephropathy

EM: mesangial immune deposits
Now let’s see if you’ve been paying attention...
Which diagnosis can you suspect from the light microscopy below:

A. Membranous nephropathy
B. Minimal change disease
C. FSGS
D. Membranoproliferative Glomerulonephritis (MPGN)
Which diagnosis can you suspect from the light microscopy below:

A. Membranous nephropathy
B. Minimal change disease
C. FSGS
D. Membranoproliferative Glomerulonephritis (MPGN)
Classification of pathologic and clinical manifestations of glomerular injury

<table>
<thead>
<tr>
<th>Histopathologic name</th>
<th>Clinical name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal Change Disease</td>
<td>Minimal Change Disease</td>
</tr>
<tr>
<td>Focal Segmental Glomerulosclerosis</td>
<td>FSGS, HIV nephropathy</td>
</tr>
<tr>
<td>Nodular Glomerulosclerosis</td>
<td>Diabetic Nephropathy, Amyloidosis</td>
</tr>
<tr>
<td>Membranous Nephropathy</td>
<td>Membranous Nephropathy</td>
</tr>
<tr>
<td>Membranoproliferative GN</td>
<td>MPGN</td>
</tr>
<tr>
<td>Mesangioproliferative GN</td>
<td>IgA Nephropathy</td>
</tr>
<tr>
<td>Proliferative GN</td>
<td>Post-infections (Post-Strep) GN</td>
</tr>
<tr>
<td>Crescentic GN</td>
<td>Rapidly Progressive GN (RPGN)</td>
</tr>
</tbody>
</table>
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
- FSGS, HIV nephropathy
- Diabetic Nephropathy, Amyloidosis
- Membranous Nephropathy
- MPGN
- IgA Nephropathy
- Post-Strep Glomerulonephritis
- Rapidly Progressive GN (RPGN)

Clinical name
Acute Post-Streptococcal Glomerulonephritis
Case presentation

• Edward is transferred to VCU from outside hospital for acute glomerulonephritis. He is an 18 year old Caucasian male with h/o tonsillectomy at age 5.
Acute Post-Streptococcal Glomerulonephritis
Case presentation

- Ten days prior to admission he had strep throat with positive rapid strep test, and was started on augmentin by his PCP.
Acute Post-Streptococcal Glomerulonephritis
Case presentation

• He was referred for admission after he developed tea colored urine, and was found to have hematuria, proteinuria and HTN. Pt reports 20 lbs wt gain in 3 days w periorbital and upper body edema, and abdominal pain. He now denies any sore throat.
Acute Post-Streptococcal Glomerulonephritis
Case presentation

• **SH** is significant for tobacco, alcohol and marijuana use

• **Exam**: BP 175/77, ps 49. Young athletic wm in no acute distress. Lungs were clear and heart was regular, with 2/6 systolic murmur at base. Abdomen was soft, diffusely tender, with liver and spleen edges palpable. Trace LE edema. No rash.
Acute Post-Streptococcal Glomerulonephritis
Case presentation

• **Labs** showed cr 1.3, albumin 2.7, urinalysis 178 rbc and 25 wbc, 3+ protein and several red blood cell casts. ASO titer and streptozyme were positive. C3 complement level was low.

• **Diagnosis**: Acute post-streptococcal GN.
Acute Post-Streptococcal Glomerulonephritis

Case presentation

• Due to worsening renal function, we performed renal biopsy, which confirmed the above diagnosis. Patient was treated with diuretic and ace inhibitor. Patient’s condition improved and he was discharged with follow-up in renal clinic.
Acute Post-Streptococcal Glomerulonephritis
Case presentation

• His creatinine normalized after 1 mo. After 4 months, he was off antihypertensives, however his UA still showed 3+ blood and 2+ protein. He was lost to follow-up since that visit.
Acute Proliferative (Poststreptococcal, Postinfectious) GN

• **Definition:**

![Image of oral cavity with lesions](image1)

![Image of skin with lesions](image2)
Acute Proliferative (Poststreptococcal, Postinfectious) GN

- **Definition:** acute nephritic syndrome that develops following infection by nephritogenic strains of strep or other organisms.
Acute Proliferative (Poststreptococcal, Postinfectious) Glomerulonephritis

- **Pathogenesis**: Deposition of immune complexes in capillary loops, with complement (C3) activation. Implicated are “planted” antigens, like endostreptosin and nephritis-associated plasmin receptor.
Postinfectious Glomerulonephritis Capillary Viewed by Electron Microscopy (top right) and High Magnification Light Microscopy (bottom)

Normal glomerular capillary

Neutrophils

Hump-like Subepithelial Immune Complex Deposits
Acute Proliferative (Poststreptococcal, Postinfectious) GN

• **Pathology:** *light microscopy:* enlarged, hypercellular glomeruli with endothelial and mesangial cell proliferation. Neutrophils may be present. Crescents may be seen.
Acute Proliferative (Poststreptococcal, Postinfectious) GN
Acute Proliferative (Poststreptococcal, Postinfectious) GN

- **Immunofluorescence microscopy**: coarsely granular ("lumpy-bumpy") pattern along capillary loops.
Acute Proliferative (Poststreptococcal, Postinfectious) GN

- *Electron microscopy:* subepithelial "hump-like" deposits.
Acute Proliferative (Poststreptococcal, Postinfectious) GN
Now let’s see if you’ve been paying attention...
This IF staining pattern is most likely to be seen in:

A. RPGN
B. Membranous nephropathy
C. IgA nephropathy
D. FSGS
This IF staining pattern is most likely to be seen in:

A. RPGN
B. Membranous nephropathy
C. IgA nephropathy
D. FSGS
Classification of pathologic and clinical manifestations of glomerular injury

**Histopathologic name**

- Minimal Change Disease
- Focal Segmental Glomerulosclerosis
- Nodular Glomerulosclerosis
- Membranous Nephropathy
- Membranoproliferative GN
- Mesangioc proliferative 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)
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
Rapidly Progressive Glomerulonephritis
Case presentation

• Carlisle is a 50 year old Caucasian male who is transferred from outside hospital for rapidly progressive renal failure with hematuria and proteinuria.
Rapidly Progressive Glomerulonephritis Case presentation

- He was very fit and healthy until several weeks prior to admission, when he developed a protracted upper respiratory illness requiring several visits to PCP and emergency rooms and several courses of antibiotics.
Rapidly Progressive Glomerulonephritis
Case presentation

• He was finally admitted after he was found to have bilateral pulmonary infiltrates, gross hematuria and elevated creatinine. His condition deteriorated and he required mechanical ventilation for acute respiratory failure.

• Bronchoscopy was consistent with pulmonary hemorrhage.
Rapidly Progressive Glomerulonephritis
Case presentation

• His renal function deteriorated and he was started on hemodialysis.
• His C-ANCA were positive at high titer.
• Kidney biopsy was performed and showed crescentic pauci-immune glomerulonephritis.
• **Diagnosis**: Granulomatosis with polyangiitis, with alveolar hemorrhage and rapidly progressive glomerulonephritis.
Rapidly Progressive Glomerulonephritis

Case presentation

• **Clinical course**: He was treated with intravenous steroids, cyclophosphamide and plasmapheresis with gradual improvement in respiratory and renal function. He recovered completely.
Rapidly Progressive Glomerulonephritis

• **Definition:**

• **Ethiology:**
  1. Anti-GBM disease
  2. Immune complex-mediated crescentic GN (any GN that has gone severe - lupus nephritis, post-infectious GN, IgA nephropathy)
  3. Pauci-immune GN (vasculitic diseases –Granulomatosis with Polyangiitis, Microscopic Polyangiitis)
Rapidly Progressive Glomerulonephritis

• **Definition:** acute nephritic syndrome associated with rapidly deteriorating renal function (over weeks). Histopathologically this is crescentic GN.

• **Ethiology:**
  1. Anti-GBM disease
  2. Immune complex-mediated crescentic GN (any GN that has gone severe - lupus nephritis, post-infectious GN, IgA nephropathy)
  3. Pauci-immune GN (vasculitic diseases –Granulomatosis with Polyangiitis, Microscopic Polyangiitis)
Rapidly Progressive (Crescentic) Glomerulonephritis

http://what-when-how.com/acp-medicine/glomerular-diseases-part-3/
Rapidly Progressive (Crescentic) Glomerulonephritis, LM
Crescentic GN is a histopathologic equivalent for RPGN

• Type I – Anti-GBM disease
• Type II – Immune-complex GN
• Type III – Pauci-immune GN
Anti-GBM disease is caused when anti-GBM antibodies bind to capillary basement membranes and attract and activate white blood cells (such as neutrophils). This causes the white blood cells to attack vessel walls resulting in vessel wall inflammation (glomerulonephritis and alveolar capillaritis).

Blood vessel (capillary) wall  Neutrophil type of white blood cell

Inflammation of the vessel wall caused by white blood cells that have been stimulated by anti-GBM bound to capillary basement membranes (GBM)
Anti-GBM Disease
Anti-GBM Disease

- IF reveals linear (not granular) deposition of IgG and C3 along the GBM
- EM shows no deposits
Anti-GBM Disease
Anti-GBM Disease

- In some cases IgG and C3 may also bind the pulmonary alveolar capillary basement membranes, producing a syndrome *(Goodpasture’s syndrome)* of pulmonary hemorrhage and renal failure.
Crescentic GN type II, Immune-Complex-Mediated GN

- May be associated with any immune-complex type GN including SLE, IgA nephropathy, or postinfectious GN.
Immune-Complex-Mediated Crescentic GN

- IF will reveal a coarse, granular or “lumpy-bumpy” staining pattern. Treatment is directed at the underlying disease.
Immune-Complex-Mediated Crescentic GN

- EM usually shows deposits
Crescentic GN type III, Pauci-Immune GN

- **Pauci-immune GN** shows no antibodies or immune-type complexes in the kidney either by IF or EM. Diagnostic antibodies are in the plasma, and are called Anti-Neutrophil Cytoplasmic Antibodies (ANCA)

\[<\text{Image of C-ANCA and P-ANCA}>\]
Pauci-Immune GN

- Feature of Granulomatosis with Polyangiitis (GPA), Microscopic Polyangiitis (MPA), or other vasculitic diseases.
Pauci-immune GN

Inflammation of the vessel wall (vasculitis) caused by white blood cells that have been stimulated by ANCA.
## Crescentic GN (RPGN)

<table>
<thead>
<tr>
<th></th>
<th>Anti-GBM GN (I)</th>
<th>Immune-complex GN (II)</th>
<th>Pauci-immune GN (III)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pathogenesis</strong></td>
<td>Anti-GBM Ab to type IV collagen</td>
<td>Circulating immune complexes</td>
<td>Ab against neutrophils (ANCA)</td>
</tr>
<tr>
<td><strong>Clinical examples</strong></td>
<td>Goodpastures’ Disease</td>
<td>Severe Lupus Nephritis, severe Post-Strep GN</td>
<td>Granulomatosis with Polyangiitis, Microscopic Polyangiitis</td>
</tr>
<tr>
<td><strong>LM</strong></td>
<td>Crescents</td>
<td>Crescents</td>
<td>Crescents</td>
</tr>
<tr>
<td><strong>IF</strong></td>
<td>Linear IgG</td>
<td>Granular</td>
<td>Negative</td>
</tr>
<tr>
<td><strong>EM</strong></td>
<td>No deposits</td>
<td>Deposits</td>
<td>No deposits</td>
</tr>
</tbody>
</table>
Now let’s see if you’ve been paying attention...
Which statement regarding the disease depicted on electron micrograph below is INCORRECT:

A. This disease has poor prognosis
B. This disease is treated in supportive fashion with diuretics and antihypertensives
C. Light microscopy would show proliferative GN
Which statement regarding the disease depicted on electron micrograph below is INCORRECT:

A. This disease has poor prognosis
B. This disease is treated in supportive fashion with diuretics and antihypertensives
C. Light microscopy would show proliferative GN
Chronic Glomerulonephritis (CRGN)
Chronic Glomerulonephritis (CRGN)

Case presentation

- Emmett is a 25 year old student with history of HTN self-referred to renal clinic to have his “kidneys checked”.

![Image of Emmett]
Chronic Glomerulonephritis (CRGN) Case presentation

• He reports that he was seen by a private nephrologist in town 2 years prior and had a kidney biopsy, which showed “chronic changes”. He did not have insurance and could not afford to pay medical bills, therefore he has not followed up. He is not taking any medications.
Chronic Glomerulonephritis (CRGN) Case presentation

- Patient is asymptomatic
- PE: BP170/110, trace LE edema.
- Labs BUN 55, creatinine 6.2
- UA 3+ protein, 5 rbc's per hpf, and some broad granular casts.
- Renal ultrasound: 8.5 cm kidneys bilaterally with thin echogenic cortex.
- **Diagnosis**: chronic glomerulonephritis
Chronic Glomerulonephritis (CRGN)

- **Pathology:** kidneys are grossly shrunken, and microscopically show significant and widespread global glomerular sclerosis, with interstitial fibrosis and tubular atrophy, “end-stage kidney”.

Now let’s see if you’ve been paying attention...
Look at biopsy slides below. Which statement about this disease is INCORRECT:

A. Plasmapheresis should be started to remove circulating antibodies
B. This disease can be associated with pulmonary hemorrhage
C. This disease is associated with Antinuclear Cytoplasmic antibodies (ANCA)
D. This disease clinically presents as RPGN
Look at biopsy slides below. Which statement about this disease is INCORRECT:

A. Plasmapheresis should be started to remove circulating antibodies
B. This disease can be associated with pulmonary hemorrhage
C. This disease is associated with Antinuclear Cytoplasmic antibodies (ANCA)
D. This disease clinically presents as RPGN
THE END

YOU MADE IT!