Kidneys with Kait

Kaitlyn R. McCranie
October 31, 2014
Overview of Kidney Pathology

We ARE covering

• Vocab
• Nephritic Syndromes
• Nephrotic Syndromes
• Cancers
• Pyelonephritis
• Renal Failure
• Necrosis
• Cysts

You will cover oyo

• Terms like “osteodystrophy”
• Casts
• Stones
• Some congenital defects
Vocab Review

**Focal** is *a few*. A few glomeruli are involved.

**Diffuse** is *Da whole thing*. All glomeruli are involved.

**Proliferative** is *plenty* of cells. Hypercellular.

**Membranous** is *massive* amounts of membrane. Thickened GBM.

**Primary Glomerular Disease**—just the glomerulus

**Secondary Glomerular Disease**—glomerulus, plus!
More Vocab

- **Azotemia**—high nitrogen levels in your blood
- **Pyuria**—urine containing pus
- **Oliguria**—decreased urine output
<table>
<thead>
<tr>
<th>Nephritic</th>
<th>Nephrotic</th>
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<tbody>
<tr>
<td><strong>Inflammatory</strong> process</td>
<td>Immunosuppression</td>
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<td>Hematuria</td>
<td><strong>Proteinuria</strong> (&gt;3.5 g/day), frothy</td>
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<td>Mild proteinuria (&lt;3.5 g/day)</td>
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<td>Edema</td>
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<td>Hypertension (salt retention)</td>
<td>Hyperlipidemia</td>
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In general...

Presentation
• Most common in certain populations
• Clinical picture

Histo
• LM– light microscope
• H & E– that stain that makes everything pink
• IF– immunofluorescence
• EM– electron microscope

Treatment
Complications
Nephritic

- Acute poststreptococcal glomerulonephritis
- Rapidly progressive glomerulonephritis
- Diffuse proliferative glomerulonephritis
- Berger’s disease
- Alport’s syndrome
Acute poststrep Glomerulonephritis

Presentation
• Arises after group A strep infection (impetigo/strep throat)
• Kids—coca cola colored urine, oliguria, HTN, periorbital edema, 2-3 weeks post infection

Histo
• H&E—Hypercellular, inflamed glomeruli
• IF—immune complex deposition, granular
• EM—subepithelial humps

Treatment—supportive

Complications
• Kids—renal failure (1%)
• Adults—rapid progressive glomerulonephritis (25%)
Normal Glomerulus

http://www2.palomar.edu/users/ggushansky/histology/pages/kidney%20glomerulus%203.tif.htm
Post Strep Glomerulonephritis-- H&E—Hypercellular, inflamed glomeruli
Acute Post Strep GN

immune complex deposition, granular appearance
Post Strep Glomerulonephritis

subepithelial humps

http://quizlet.com/9083341/renal-path-just-pics-flash-cards/
Rapidly Progressive Glomerulonephritis

Presentation
• Renal failure in weeks to months
• Can be caused by Goodpasture’s (linear IF), PSGN (granular IF), Wegener’s granulomatosis, microscopic polyangiitis, Churg-Strauss (negative IF)

Histo
• H &E—crescents (made of fibrin and macrophages) in Bowman’s space
• IF—linear, granular, none

Pathoma, 2014, pg 130-131
Rapidly Progressive Glomerulonephritis
crescents in Bowman’s space
Rapidly Progressive Glomerulonephritis

Linear, from Goodpasture’s syndrome

Granular, Post Strep GN
Diffuse Proliferative Glomerulonephritis

Presentation

- SLE, vasculitis syndrome, infectious processes
- More than 50% glomeruli
- Abundant mesangial, epi/endothelial cells
- Proliferation of inflammatory cells
- Hematuria, proteinuria, active urine sediment, azotemia
Berger’s disease/IgA Nephropathy

Presentation
• Most common nephropathy worldwide
• IgA deposition in mesangium
• Kids—episodic gross hematuria, RBC casts, post mucosal infection

Histo
• IF—Mesangial IgA deposition

Complications
• Renal failure
IgA Nephropathy

Mesangial IgA deposition

http://cjASN.asnjournals.org/content/1/6/1179/F3.expansion
Alport’s syndrome

Presentation

• Genetic disorder → defective type 4 collagen
• Results in thinning and splitting of GBM
• Only symptom is hematuria

Complications

• Can also have sensory hearing loss, ocular disturbances, family history
Nephrotic

- Membranous GN
- MCD
- Amyloidosis
- Diabetic GN
- FSGS
- MPGN
Membranous Nephropathy

Presentation

• Hep B or C, solid tumors, SLE, drugs
• Thick GBM—due to immune complex deposition, podocytes don’t like to get kicked off their GBM

Histo

• H & E—thick, pink GBM
• IF—granular, subepithelial deposits of immune complexes
• EM—spike and dome
Membranous Nephropathy

thick, pink GBM

Membranous Nephropathy

granular, subepithelial deposits of immune complexes

https://www.flickr.com/photos/roboonya/4954394994/
Membranous Nephropathy

spike and dome
Membranoproliferative Glomerulonephritis

Presentation
• Proliferation of GBM, inflammation
• Type 1—subendothelial deposits (HBV, HCV), more often associated with tram tracks
• Type 2—deposition within basement membrane (C3 nephritic factor)
• Can create nephritic/nephrotic/both

Histo
• H & E—tram tracking appearance
• IF—granular
Membranoproliferative Glomerulonephritis

tram tracking appearance

http://library.med.utah.edu/WebPath/RENAHTML/RENAL160.html
Membranoproliferative Glomerulonephritis

Granular

Deposition of IgG

Membranoproliferative glomerulonephritis

http://www.med.niigata-u.ac.jp/npa/Lectures/Images/Slides/MPGN/5MPGN_IF_L.gif
Draw a map!
Minimal Change Disease

Presentation
• Kids—idiopathic
• Hodgkin’s lymphoma
• Effacement of foot processes due to cytokine production
• Selective proteinuria (only albumin, not immunoglobulins)

Histo
• H & E—Normal glomeruli
• EM—Effacement of podocytes

Treatment
• steroids
Minimal Change Disease

Podocyte effacement

Normal Glomerulus  Glomerulus with MCD

http://www.unckidneycenter.org/kidneyhealthlibrary/minimalchange.html
Minimal Change Disease

Effacement of podocytes

Normal podocytes

Podocytes in MCD


Focal Segmental Glomerulosclerosis

Presentation
• Hispanic, Afr. Am
• HIV, heroin use, sickle cell disease

Histo
• H & E—segmental sclerosis of some glomeruli
• IF—negative
• EM—effacement of foot process

Treatment—none

Complications—Chronic renal failure
Focal Segmental Glomerulosclerosis

segmental sclerosis of some glomeruli

http://library.med.utah.edu/WebPath/RENAHTML/RENAL082.html
Focal Segmental Glomerulosclerosis

effacement of foot process
Systemic Amyloidosis

Presentation

- Amyloid deposits in mesangium leading to nephrotic syndrome

Histo

- Congo red staining with apple-green birefringence under polarized light
Systemic Amyloidosis

Congo red

Congo red with apple green birefringence

http://www.pathguy.com/lectures/imm-iii.htm
Diabetic Glomerulonephritis

Presentation

• Non enzymatic glycosylation of vascular basement membrane $\rightarrow$ hyaline arteriolosclerosis $\rightarrow$ increased pressure in glomerulus $\rightarrow$ pressure injury, sclerosis of mesangium
• Microalbuminuria
• Nephrotic syndrome

Histo

• H & E– Kimmelstiel-Wilson nodules
Diabetic Glomerulonephritis

Kimmelstiel-Wilson nodules
Think of them in Two’s!

MCD + FSGS = foot process effacement
MPGN + Membranous nephropathy = immune complex deposition
Diabetic nephropathy + amyloidosis = systemic diseases with protein deposits
In summary...

- **Nephritic Syndrome**
  - Acute post strep GN
  - Rapidly progressive GN
  - Berger disease (IgA glomerulonephropathy)
  - Alport syndrome

- **Nephrotic Syndrome**
  - Focal segmental GS
  - Membranous Nephropathy
  - Minimal change disease
  - Amyloidosis
  - Diabetic glomerulonephropathy

- Diffuse proliferative glomerulonephritis
- Membrano proliferative glomerulonephritis
Cancers

• Angiomyolipoma
• Renal Cell Carcinoma
• Wilms Tumor
Angiomyolipoma

- Blood vessel
- Smooth Muscle
- Fat

Hamartoma (tumor)

....in your kidney

Renal Cell Carcinoma

**Dfn:** Malignant tumor of the *tubule epithelium*

**Presentation**
- Triad: hematuria, palpable mass, flank pain
- Fever, weight loss
- Causes multiple *paraneoplastic syndromes* (EPO, renin, PTHrP, ACTH)
- May present with left side varicocele
- Yellow tumor grossly, clear cell carcinoma microscopically
Renal Cell Carcinoma

- VHL gene
- Smoker
- Sporadic
- Hooligan (or just any young person with this genetic mutation)
- Hereditary

http://media-1.web britannica.com/ebmedia/60/131160004FC5A76F7.jpg
Wilms’ Tumor

- Most common in kids
- Malignant tumor from blastema
- Large unilateral flank mass, hematuria, HTN (secondary to renin elevation)
- WT1 mutation, often in syndromes, like WAGR

http://path.upmc.edu/cases/case201/images/image02.jpg
Transitional Cell Carcinoma

• Malignant tumor arising in urothelial lining of renal pelvis, ureter, bladder or urethra
• Painless hematuria in older adults

Two paths
• Papillary – low grade → high grade → invade
• Flat – starts as high grade → invades
Transitional Cell Carcinoma

Papillary form

Flat form

Pyelonephritis

• Acute
  – ascending infection of kidney
  – Fever, flank pain, WBC casts, leukocytosis
  – *E. coli, Klebsiella, Enterococcus faecalis*

• Chronic
  – Fibrosis and **tubular atrophy** due to recurring infections
  – Kids with vesiculoureteral reflux
  – Adults with obstruction (BPH, cervical cancer)
Acute Renal Failure (ARF!)

- **Presentation** – within days, azotemia, oliguria
- **Prerenal** – decrease in blood flow to the kidney (cardiac failure)
- **Postrenal** – decreased outflow of urine due to outflow obstruction in some area beyond the kidney (ureters, bladder...)
  - Longstanding damage results in tubular damage, so they no longer function
- **Intrarenal** – injury/necrosis of interstitial/tubular epithelial cells
  - Most common cause of ARF
  - Brown granular casts in urine
  - Acute Interstitial Nephritis—drug induced inflammatory response
  - Acute Tubular Necrosis
# Acute Renal Failure

<table>
<thead>
<tr>
<th>Type of Failure</th>
<th>Cause</th>
<th>GFR</th>
<th>Nitrogenous waste</th>
<th>Urine production</th>
<th>BUN:Cr</th>
<th>Tubule function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prerenal</td>
<td>Decrease in blood flow to the kidney</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
<td>Normal</td>
</tr>
<tr>
<td>Postrenal</td>
<td>Decrease in outflow of urine</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>Initially ↑ Later ↓</td>
<td>Normal initially, lost over time</td>
</tr>
<tr>
<td>Intrarenal</td>
<td>Injury/necrosis of tubular epithelial cells</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
<td>lost</td>
</tr>
</tbody>
</table>
A quick word on
Acute Interstitial Nephritis

Presentation
• Rash, fever, oliguria, eosinophils in urine
• Drug induced – NSAIDS, PCN, diuretics

Histology
• Hypersensitivity reaction resulting in inflammatory infiltration of tubular interstitium

Complications—renal papillary necrosis
Necrosis

• Acute tubular necrosis—brown granular casts
  – Ischemia (prerenal azotemia)
  – Nephrotoxic (toxic agents)
• Renal papillary necrosis—gross hematuria, flank pain
  – Chronic analgesic abuse
  – DM
  – Sickle cell
  – Severe acute pyelonephritis
Chronic (End-stage) Renal Failure

Causes
- Top three—HTN, DM, glomerular disease

Presentation
- Uremia (azotemia)
  - Nausea, anorexia, pericarditis, platelet dysfunction, encephalopathy with asterixis, deposition of urea crystals in the skin
- Salt and water retention → HTN, hyperkalemia, metabolic acidosis
- Anemia (lack of EPO from renal peritubular interstitial cells)
- Hypocalcemia (lack of vitamin D conversion, hyperphosphatemia)
- Renal osteodystrophy
Renal Cysts

- Polycystic Kidney Disease
  - Autosomal Recessive
  - Autosomal Dominant
- Medullary Cystic Disease
- Dialysis cyst
- Simple cysts
PKD– Polycystic Kidney Disease

• Inherited defect
• Bilateral enlargement due to cysts
• Cysts in both renal cortex and medulla

Two Types
• Autosomal Recessive—infants
• Autosomal Dominant—young adults
Medullary Cystic Kidney Disease

- Cysts in medullary collecting ducts
- Shrunken kidneys due to parenchymal fibrosis
- Presentation—worsening renal failure
Dialysis Cyst

- Kidney is shrunken due to end stage renal failure
- Cysts develop on shrunken kidney after prolonged dialysis
- Develop in the cortex or medulla
- Increased risk for renal cell carcinoma
- May present with hematuria
Simple Cyst

- Relatively common, benign
- Cysts are almost always in cortex
Resources


• The vast images of the internet, as cited internally
Kidney Stones

High concentration of solute

Low urine volume

Precipitation of solute as a stone

Presentation:
Hematuria
“Colicky” (on and off)
unilateral flank pain

Passed within hours or with surgery

Pathoma, 2014, pg 132
## Kidney Stones

<table>
<thead>
<tr>
<th>Composition</th>
<th>Frequency</th>
<th>Causes</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| Calcium Oxalate/Calcium Phosphate  | Most common (adults) | • Idiopathic (or not) hypercalcemia  
• Crohn’s disease            | HCTZ (Ca\(^{2+}\) sparing diuretic)                                    |
| Ammonium Magnesium Magnesium Phosphate | 2\(^{nd}\)    | • Urease producing organisms (*Proteus vulgaris* and *Klebsiella*)  
• Alkaline urine                | • Aka struvite  
• Staghorn calculi (nidus for UTI)  
• Surgically removed            |
| Uric Acid (radiolucent)            | 3\(^{rd}\)     | • Hot, dry climate  
• Low urine volume  
• Acidic pH  
• Hyperuricemia (eg in gout, leukemia, myeloproliferative d/o) | • Hydration  
• Alkalinization (KHCO\(_3\))  
• Allopurinol (if they have gout) |
| Cystine                            | Rare (mostly kids) | • Cysteinuria (genetic defect: tubule can’t resorb cysteine) | • Staghorn calculi  
• Hydration  
• Alkalinization |

*Pathology, 2014, pg 133*
Casts

- Formed in the DCT
- Precipitated out into urine
Fun activity: fill in the rest of the tale yourself!

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<thead>
<tr>
<th>Composition</th>
<th>Conditions</th>
<th>Diseases</th>
</tr>
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<tbody>
<tr>
<td>RBC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBC</td>
<td>• Inflammatory cells entering tubule as inf ascends from bladder</td>
<td>• Pyelonephritis</td>
</tr>
<tr>
<td>Hyaline</td>
<td>• Low urine flow&lt;br&gt;• low pH&lt;br&gt;• high concentration of urine</td>
<td>• Normal&lt;br&gt;• Nonspecific</td>
</tr>
<tr>
<td>Waxy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Granular cell</td>
<td>• Breakdown of cellular casts&lt;br&gt;• Inclusion of immunoglobulins&lt;br&gt;• Inclusion of plasma proteins</td>
<td>• Chronic renal disease&lt;br&gt;• Strenuous exercise&lt;br&gt;• Acute Tubular Necrosis</td>
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# Prototypes

<table>
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<tr>
<th>Term</th>
<th>Disease</th>
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<td>Focal</td>
<td>Focal segmental glomerulosclerosis</td>
</tr>
<tr>
<td>Diffuse</td>
<td>Diffuse proliferative glomerulonephritis</td>
</tr>
<tr>
<td>Proliferative</td>
<td>Mesangial Proliferative</td>
</tr>
<tr>
<td>Membraneous</td>
<td>Membraneous Glomerulonephritis</td>
</tr>
<tr>
<td>Primary glomerular</td>
<td>Minimal Change Disease</td>
</tr>
<tr>
<td>Secondary glomerular</td>
<td>Lupus!</td>
</tr>
</tbody>
</table>
Kidney Pathology Review II Outline

Kaitlyn R. McCranie

**Vocab Review**

**Focal** is a few. A few glomeruli of the kidney are involved.

**Diffuse** is *Da* whole thing. Over 50% of the glomeruli are involved.

**Proliferative** is plenty of cells. Hypercellular.

**Membranous** is massive amounts of membrane. Thickened GBM.

**Primary Glomerular Disease**—just the glomerulus (think Minimal Change Disease. The disease only effects the glomerulus)

**Secondary Glomerular Disease**—glomerulus, plus! (Think SLE. The disease effects the glomerulus, but also so, so much more)

**Azotemia**—high nitrogen levels in your blood

**Pyuria**—urine containing pus (see neutrophils in the urine, which defines the presence of pus)

**Oliguria**—decreased urine output

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Looking at the table on the previous page you can see some patterns emerge. Nephritic syndromes are characterized by inflammation and hypercellularity of the glomerulus which results in glomerular bleeding. If you have a bleeding glomerulus, you will have hematuria and RBC casts. Salt retention will lead to hypertension and periorbital edema.

Nephrotic syndromes are characterized by proteinuria. This is mainly a loss of albumin leading to decreased oncotic pressure within the blood. That in turn leads to edema. Another type of protein lost is gamma globulin: this results in immunosuppression. Antithrombin 3 is also lost in the urine. What do you think antithrombin does? Right. It inhibits clotting. So if you remove the inhibitor, you end up with a procoagulable state. Finally, if you think about the lack of protein in the blood, the body feels the need for some type of filler molecule, so you can picture it as the liver begins dumping lipids and cholesterol to compensate for the oncotic pressure. This results in a hyperlipidemia and fatty casts in the urine.

In general, try to focus on clinical presentations and less on immunofluorescence, since that is lower yield.

**Nephritic Syndromes**

**Acute Post Streptococcal Glomerulonephritis**

**Presentation**

- Arises after group A strep infection (impetigo/strep throat). The Grp A strep must have the M protein as a virulence factor to make glomerulonephritis possible.
- Kids– coca cola colored urine, oliguria, HTN, periorbital edema, 2-3 weeks post infection

**Histo**

- H&E—Hypercellular, inflamed glomeruli
- IF—immune complex deposition, granular
- EM—subepithelial (on top of basement membrane) humps

**Treatment**—supportive. Kids typically recover completely. Occasionally adults can progress to RPGN

**Complications**

- Kids—renal failure (1%)
- Adults—rapid progressive glomerulonephritis (25%)
Normal glomerulus. Note that the bowman’s space is open, the glomerulus is not hypercellular.

Post Strep GN glomerulus. Note the hypercellularity of the glomerulus itself resulting in a lack of space in bowman’s capsule.

Post Strep GN Immunofluorescence
Note: immune complex deposition, granular.

Post strep GN subepithelial humps
Rapidly Progressive Glomerulonephritis

Presentation

- Renal failure in weeks to months
- Can be caused by Goodpasture’s (linear IF), PSGN (granular IF), Wegener’s granulomatosis, microscopic polyangiitis, Churg-Strauss (negative IF)

Histo

- H &E—crescents (made of fibrin and macrophages) in Bowman’s space
- IF—linear, granular, none

Specifics

- Goodpastures—Linear pattern is caused by anti basement membrane antibody. Antibody to the collagen in alveolar and glomerular BM’s. Presents with hematuria, hemoptysis. Most often seen in young adult males
- PSGN—Granular pattern caused by immune complex deposition
- Diffuse proliferative GN—Granular pattern, most common renal disease in SLE
- Negative immunofluorescence means pauci immune. There’s not much to see on IF.

ANCA test

- Wegener’s granulomatosis—C-ANCA (cytoplasmic ANCA). You will see an ANCA antibody to the cytoplasm of a neutrophil. Presents with hemoptysis, RBC casts, nasalapharyngeal sx (sinus infections)
- Churg Strauss and microscopic polyangiitis are p-ANCA (perinuclear ANCA antibodies).
- Churg Strauss is associated with granulomatous inflammation, eosinophilia, asthma, whereas microscopic polyangiitis doesn’t have any of those.

RPGN—Crescents made of fibrin and macrophages
**Diffuse Proliferative Glomerulonephritis**

**Presentation**

- Caused by some sort of systemic inflammatory disease such as SLE, vasculitis syndrome (like Wegener’s granulomatosis), infectious processes
- More than 50% glomeruli (diffuse)
- Abundant mesangial, epi/endothelial cells (proliferative)
- Proliferation of inflammatory cells (glomerulonephritis)
- Hematuria, proteinuria, active urine sediment, azotemia, classic nephritic syndrome

**Berger’s/ IgA Nephropathy**

**Presentation**

- Most common nephropathy worldwide
- IgA deposition in mesangium
- Kids—episodic gross hematuria, RBC casts, post mucosal infection (such as gastroenteritis)
- Basically, you produce extra IgA in defense, which lodges in the mesangium and deposits as immune complexes → This leads to glomerular bleeding → resulting in hematuria

**Histo**

- IF—Mesangial IgA deposition

**Complications**

- Every episode is cumulative damage, so you could progress to renal failure

**Alport’s Syndrome**

**Presentation**

- Genetic disorder → defective type 4 collagen
- Most often (85% of the cases) this is X-linked, but it can also be autosomal recessive.
- Results in thinning and splitting of GBM
• Isolated (only symptom) hematuria

Complications

• Can also have sensory hearing loss, ocular disturbances, family history
• Complications are also due to disturbance of the basement membrane

Nephrotic Syndromes

Membranous Nephropathy

Presentation

• Hep B or C, solid tumors, SLE, drugs
• Thick GBM– due to immune complex deposition, podocytes don’t like to get kicked off their GBM. Immune complexes deposit under the podocyte. Podocyte responds by trying to put down additional basement membrane so it can sit down on its basement membrane.

Histo

• H & E– thick, pink GBM
• IF– granular, subepithelial (under podocyte) deposits of immune complexes.
• EM–Spike and dome (spike is the valley between the domes)
Membranoproliferative Glomerulonephritis

Presentation

Membrano– thick capillary membrane, due to immune complex deposition

Proliferative— cytoplasm of mesangial cell extends to separate immune complexes in half, creating two lines, which is a “tram track”

• Proliferation of GBM, inflammation
• Type 1—subendothelial deposits (HBV, HCV), more often associated with tram tracks
• Type 2—deposition within basement membrane (C3 nephritic factor)
• Note on C3 nephritic factor— C3 is a piece of complement, C3 convertase makes C3a and C3b. C3 convertase is usually broken down rapidly so that it doesn’t make too much. This “C3 nephritic factor” is actually an antibody that stabilizes C3 convertase resulting in overactivation of complement, inflammation, and inflammatory damage
• Can create nephritic/nephrotic/both syndromes

Histo

• H & E— tram tracking appearance
• IF—granular

Tramtracking seen in MPGN

Draw a Map!

If you are able to sketch a quick map for yourself, it will be helpful in figuring out which disease has deposits in which locations. Remember:
Membranous GN has subepithelial deposits (below podocytes), Type 1 MPGN deposits are subendothelial, and Type 2 deposits are within the GBM.
**Minimal Change Disease**

**Presentation**

- Kids—idiopathic
- Hodgkin’s lymphoma (Reed Sternberg cells make lots of cytokines, which will lead to effacement)
- Effacement of foot processes due to cytokine production
- Selective proteinuria (only albumin, not immunoglobulins)

**Histo**

- H & E—Normal glomeruli
- EM—Effacement of podocytes

**Treatment**

- Steroids—Steroids decrease the immune response, reducing the number of cytokines

![MCD—EM—Count in from the lumen: endothelial cells, basement membrane, podocytes—FLATTENED!](image)

**Focal Segmental Glomerulosclerosis**

**Presentation**

- Hispanic, Afr. Am
- HIV, heroin use, sickle cell disease
- Type of nephrotic syndrome, basically looks like MCD but not responsible to steroids
- Focal—involvement of only some glomeruli in the kidney
- Segmental—just one segment of the glomerulus
• Glomerulosclerosis—dense pink deposition of collagen in basement membrane of glomerular segment

Histo

• H & E—segmental sclerosis of some glomeruli
• IF—negative, not driven by immune deposition
• EM—effacement of foot process

Treatment—none

Complications—Chronic renal failure

Systemic Amyloidosis

Presentation

• Amyloid deposits in mesangium leading to nephrotic syndrome
• Systemic disease of tons of amyloid being deposited

Histo

• Congo red staining with apple-green birefringence under polarized light

Diabetic Glomerulonephritis

Presentation

• Non enzymatic glycosylation of vascular basement membrane increases propensity of protein deposition → which leads to hyaline arteriolosclerosis of the vessel wall → decreasing lumen preferentially in efferent arteriole→ causing increased pressure in glomerulus→ increased filtration→ hyperalbumenuria→pressure injury→resulting in sclerosis of mesangium
• Microalbumenuria (you can find albumen in the urine)
• ACE inhibitors decrease hyperfiltration injury because they decrease the pressure
• Nephrotic syndrome
It might help you keep them straight in your mind, if you group them in pairs.

MCD + FSGS = foot process effacement

MPGN + Membranous nephropathy = immune complex deposition

Diabetic nephropathy + amyloidosis = systemic diseases with protein deposits

**Cancers**

**Angiomyolipoma**

The only thing you need to know about this is that it is a hamartoma tumor in your kidney made up of blood vessel tissue (angio), smooth muscle cells (myo), and fat cells (lipoma). This is associated with tuberous sclerosis (a tumor syndrome).

**Renal Cell Carcinoma**

**Dfn:** Malignant tumor of the tubule epithelium

**Presentation**

- Triad: hematuria, palpable mass, flank pain (all three are rarely seen clinically, though. Mostly see hematuria)
- Fever, weight loss
- Causes multiple paraneoplastic syndromes (EPO, renin, PTHrP, ACTH are all made in the kidney)

**Overproduction of**

- EPO—reactive polycythemia (abnormal increase in blood cells)
- Renin—HTN
- PTHrelated Peptide—hypercalcemia
- ACTH—Cushings syndrome
• May present with left side varicocele (Varicocele—widening of the veins along the cord that holds up a man’s testicles. Carcinoma invades left renal vein and can block the spermatic vein on the left side. This would lead to a backup of blood that would widen the spermatic vein. This does not occur on the right side because the spermatic vein connects to the abdominal aorta rather than the renal vein)

• Likes to metastasize to the renal vein, can go to lungs and bone, lymph node

• Yellow tumor grossly, clear cell carcinoma microscopically

Important associations

• VHL gene— tumor suppressor gene, loss of it results in increased IGF-1 (Insulin like growth factor-growth promotion), HIF (transcription factor that increases Vascular Endothelial GF and Platlet Derived GF). So, if you lose the suppression of these growth factors, you would get overgrowth, aka a tumor.

• Sporadic form— typically a smoker, tumor is in the upper pole of the kidney, unilateral

• Hereditary form— Typically a young person, multiple tumors found bilaterally, (often due to Von Hippel-Lindau disease, an autosomal dominant disorder where VHL is broken)

Wilms Tumor

• Most commonly found in kids

• Malignant tumor from blastema (primitive kidney tissue→ it can develop glomeruli, tubules and stromal cells)

• Large unilateral flank mass, hematuria, HTN (secondary to renin elevation)

• WT1 mutation, often in syndromes, like WAGR (Wilms tumor, aniridia, genital abnormalitis, mental and motor retardation)

Other things

Pyelonephritis

Acute

• Bladder infection ascended to the kidney, typically. Increased risk of infection with reflux from bladder up to the kidney

• Fever, flank pain, WBC casts, leukocytosis

• E. coli, Klebsiella, Enterococcus faecalis
Chronic

- Fibrosis and tubular atrophy due to recurring infections (Tubular atrophy occurs because tubules have proteinaceous material deposited in them. On histology, it is reminiscent of thyroid follicles, so this can be called thyroidization of the tubule.)
- Kids with vesicoureteral reflux (When kid’s ureters plug in to the bladder at the wrong angle, so they get reflux of urine up the ureter into the kidney)
- Adults with obstruction to urine outflow (BPH, cervical cancer)

Acute Renal Failure

- **Presentation** –
  - within days (it is acute, after all)
  - azotemia (increase in nitrogenous waste in BLOOD)
  - increased BUN: creatinine ratio Because BUN can be resorbed into blood, but Cr can’t, there will be more BUN in the blood, but Cr will continue to be lost to the urine at the same rate (provided no tubule epithelial damage, since that is what allows BUN uptake). BUN: Cr ratio >15 (15 is normal)
  - oliguria (decreased urine output) increased Aldosterone \( \rightarrow \) resorb Na\(^+\) and water resulting in reduced urine output

- **Prerenal** – decrease in blood flow to the kidney (cardiac failure)

- **Postrenal** – decreased outflow of urine due to outflow obstruction in some area beyond the kidney (ureters, bladder…)
  - Longstanding damage results in tubular damage, so they no longer function

- **Intrarenal** – injury/necrosis of interstitial/tubular epithelial cells
  - most common cause of ARF
  - brown granular casts in urine (due to epithelial cell sloughing)
  - Acute Interstitial Nephritis—drug induced inflammatory response (to be discussed)
  - Acute Tubular Necrosis (to be discussed)
**Acute Interstitial Nephritis**

**Presentation**

- Rash, fever, oliguria, eosinophils in urine
- Drug induced – NSAIDS, PCN, diuretics

**Histo**

- Hypersensitivity reaction resulting in inflammatory infiltration of tubular interstitium

**Complications**—renal papillary necrosis
Types of Necrosis

• Acute tubular necrosis—brown granular casts
  – Ischemia, as a cause, is often resultant of prerenal failure, if present for a long enough time
  – Presents with increased BUN:Cr, hyperkalemia, metabolic acidosis, oliguria
  – Nephrotoxic agents also cause this (can be caused by aminoglycosides, heavy metals, myoglobinuria, ethylene glycol, radiocontrast dye, urate)

• Renal papillary necrosis—gross hematuria, flank pain
  – Chronic analgesic abuse (phenacetin or aspirin use)
  – DM
  – Sickle cell
  – Severe acute pyelonephritis

Chronic (End Stage) Renal Failure

Causes

• Top three—HTN, DM, glomerular disease

Presentation

• Uremia (azotemia)
  – Nausea, anorexia, pericarditis, platelet dysfunction, encephalopathy with asterixis, deposition of urea crystals in the skin

• Caused by damage to any part of kidney
  – Glomerulus—Nephrotic syndrome, rapidly progressive glomerulonephritis
  – Tubule
  – Inflammatory
  – Damage to blood vessels

• Salt and water retention→ HTN, hyperkalemia, metabolic acidosis

• Anemia (lack of EPO from renal peritubular interstitial cells)

• Hypocalcemia (lack of vitamin D conversion, hyperphosphatemia)
• Renal osteodystrophy (due to the vitamin D malabsorption)

Cysts

Polycystic Kidney Disease

• Inherited defect
• Bilateral enlargement of kidneys due to cysts
• Cysts in both renal cortex and medulla

Two Types
• ARPKD: Autosomal Recessive—infants present with renal failure, HTN, portal hypertension
  – Present as if they have bilateral kidney agenesis—showing Potter’s sequence (results of oligohydramnios, which is not making urine in utero)
  – Associated with cyst in liver ➔ can result in congenital hepatic fibrosis ➔ which results in portal hypertension
• ADPKD: Autosomal Dominant—young adults (memory trick: ADult PKD)
  – genetic defect present at birth, but manifests in adulthood
  – HTN (inc renin), hematuria, worsening renal failure
  – Associated with berry aneurysm, hepatic cysts, mitral valve prolapse
  – Memory trick: cysts in kidney, liver, and brain (cystic dilatation of the vessel)

Medullary Cysts

• Cysts in medullary collecting ducts
• Shrunken kidneys due to parenchymal fibrosis
• Presentation—worsening renal failure
Dialysis Cysts

- Kidney is **shrunken** due to end stage renal failure
- Cysts develop on shrunken kidney after prolonged dialysis
- Develop in the **cortex or medulla**
- Increased risk for renal cell carcinoma
- May present with hematuria

Simple Cyst

- Relatively common, benign
- Cysts are almost always in cortex

Kidney Stones

- High concentration of solute
- Low urine volume
- Precipitation of solute as a stone
- Presentation: **Hematuria**
  - "Colicky" (on and off)
  - Unilateral flank pain
- Passed within hours or with surgery

Pathoma, 2014, pg 132
<table>
<thead>
<tr>
<th>Composition</th>
<th>Frequency</th>
<th>Causes</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium Oxalate/Calcium Phosphate</td>
<td>Most common (adults)</td>
<td>• Idiopathic (or not) <strong>hypercalcemia</strong>&lt;br&gt;• Crohn’s disease</td>
<td>HCTZ (Ca(^2+) sparing diuretic)</td>
</tr>
<tr>
<td>Ammonium Magnesium Phosphate</td>
<td>2(^{nd})</td>
<td>• <em>Urease</em> producing organisms (<em>Proteus vulgaris</em> and <em>Klebsiella</em>)&lt;br&gt;• <em>Alkaline</em> urine</td>
<td>• <em>Aka struvite</em>&lt;br&gt;• <em>Staghorn calculi</em> (nidus for UTI)&lt;br&gt;• <em>Surgically removed</em></td>
</tr>
<tr>
<td>Uric Acid (radiolucent)</td>
<td>3(^{rd})</td>
<td>• Hot, dry climate&lt;br&gt;• Low urine volume&lt;br&gt;• Acidic pH&lt;br&gt;• <strong>Hyperuricemia</strong> (eg in gout, leukemia, myeloproliferative d/o)</td>
<td>• Hydration&lt;br&gt;• Alkalization (<strong>KHCO(_3)</strong>)&lt;br&gt;• Allopurinol (if they have gout)</td>
</tr>
<tr>
<td>Cystine</td>
<td>Rare (mostly kids)</td>
<td>• <em>Cysteinuria</em> (genetic defect: tubule can’t resorb cysteine)</td>
<td>• <em>Staghorn calculi</em>&lt;br&gt;• <em>Hydration</em>&lt;br&gt;• <em>Alkalization</em></td>
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