Pathology of Kidney Disorders
Components of Glomerulus:

- Capillary basement membrane
- Mesangium
- Bowman capsule
- Cells
  - Endothelial
  - Epithelial
  - Mesangial
Anatomy of Kidney

Color Atlas of Human Anatomy, 3rd Ed.
McMinn, RME, et al editors
Mosby Year Book Co.,
St. Louis, 1993
Anatomic Compartments

- Glomerulus
- Tubules
- Blood vessels
- Interstitium
- Collecting system
- (Callices & Pelvis)
Kidney Functions:

- Excretion metabolic waste/drugs.
- Water/fluid balance.
- Electrolyte balance.
- Acid-base balance.
- Blood pressure.
- Erythropoietin secretion.
Anatomy of Kidney

Note the positions of Glomerulus, Loop of Henley, PCT, DCT, CT, Cortex, Medulla, Pelvis.
GFR → Renin → Angiotensin → Blood Pressure

JGA
Filtration Membrane:
Normal Kidney:
Kidney Diseases

- Developmental disorders
- Glomerular diseases
- Tubulo-interstitial diseases
- Urinary stones
- Obstructive uropathy
- Tumors
Congenital Anomalies:

- Agenesis – Potter syndrome
- Ectopia
- Fusion
- Dysplasia
- Simple cysts
- Polycystic kidney disease
Horse Shoe Kidney
Double Ureter:
Polycystic kidney disease

• Autosomal dominant (adult) (1:1,000)
• Autosomal recessive (infantile (1:30,000)
• Medullary cystic disease complex (1:10,000)
• Medullary sponge kidney
• Acquired cystic renal disease
Autosomal Dominant PKD

- Common kidney disease (1:1,000)
- 10% of all transplant/dialysis patients
- ADPKD-1 gene (polycystin) mutation 85%
- Bilaterally enlarged kidneys (>3,000g)
- Symptoms appear in adult life
- Renal failure 5-10 years thereafter
ADPKD:
ADPKD Associated Conditions

- Liver cysts (30%)
- Splenic cysts (10%)
- Pancreatic cysts (5%)
- Cerebral aneurysms (20%)
- Diverticulosis coli
Kidney Disorders – clinical.

A  Asymptomatic hematuria/proteinuria
N  Nephrotic syndrome
N  Nephritic syndrome
U  Urolithiasis
R  Rapidly progressive glomerulonephritis
I  Interstitial and tubular diseases
C  Chronic renal disease
“To be a great champion you must believe you are the best. If you’re not, pretend you are.”

– Muhammad Ali
Glomerular Disorders:
Nephritic

- Hematuria
- Proteinuria
- Hypoalbuminemia
- Oliguria ($\text{GFR} \downarrow$, $\text{Cr} \uparrow$, $\text{BUN} \uparrow$)
- Edema (salt and water retention)
- Hypertension

Nephrotic

- Proteinuria ("nephrotic range" $>3.5\text{g/24h}$)
- Hypoalbuminemia
- Edema
- Hyperlipidemia
- Lipiduria
# Acute Post Strepto. GN:

<table>
<thead>
<tr>
<th>Synonyms</th>
<th>Acute proliferative glomerulonephritis, acute post-infectious GN.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>Peak incidence in children (3-14). Sporadic, mostly winter and spring.</td>
</tr>
<tr>
<td>Clinical</td>
<td>Acute nephritic syndrome post-strept pharyngitis or pyoderma. Other infections.</td>
</tr>
<tr>
<td>Lab:</td>
<td>Nephritic urine with RBC casts. Evidence of streptococcal infection or serologic evidence of recent infection. Decreased serum complement.</td>
</tr>
<tr>
<td>Path:</td>
<td>Enlarged, hypercellular glomeruli with endothelial and mesangial cell proliferation. Acute inflammation. IgG and C3 in very coarsely granular pattern along GBMs. Discrete, subepithelial “hump-like” deposits.</td>
</tr>
<tr>
<td>Clinical Course:</td>
<td>Children - Excellent prognosis. Adults - Worse prognosis, some develop progressive disease.</td>
</tr>
</tbody>
</table>

Introduction
### Minimal Change GN:

<table>
<thead>
<tr>
<th>Synonyms</th>
<th>Nil disease, lipoid nephrosis, foot process disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>80% of nephrotic syndrome in children (1-8 yrs.), mostly male. Adults in 2nd-3rd decade.</td>
</tr>
<tr>
<td>Etiology</td>
<td>Idiopathic. Loss of net negative charge on capillary basement membrane.</td>
</tr>
<tr>
<td>Lab Features:</td>
<td>Selective proteinuria. No specific laboratory findings.</td>
</tr>
<tr>
<td>Pathology</td>
<td>LM - Normal. IF - Negative. EM - Focal fusion/loss of foot processes.</td>
</tr>
<tr>
<td>Clinical Course:</td>
<td>Spontaneous remission in 25-40%. Complete remission in 65-70% of patients. Steroid resistant patients may progress to FSGS.</td>
</tr>
</tbody>
</table>
### Membranous GN:

<table>
<thead>
<tr>
<th>Synonyms:</th>
<th>Epimembranous, extramembranous GN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td>40-60 Years, 50% of adult nephrotic syndrome.</td>
</tr>
<tr>
<td><strong>Etiology:</strong></td>
<td>Immune complex disease. Idiopathic in most patients, associated with infections, drugs, carcinomas, and heavy metals.</td>
</tr>
<tr>
<td><strong>Clinical:</strong></td>
<td>Nephrotic syndrome in 80%, asymptomatic proteinuria in 20%. Microscopic hematuria.</td>
</tr>
<tr>
<td><strong>Lab:</strong></td>
<td>Non-selective proteinuria ± hematuria.</td>
</tr>
<tr>
<td><strong>Path:</strong></td>
<td>Diffuse, uniform BM thickening with subepithelial projections (“spikes”). Diffuse, coarsely granular IgG and C3 deposits along basement membranes. Electron-dense subepithelial deposits.</td>
</tr>
<tr>
<td><strong>Clinical Course:</strong></td>
<td>Excellent prognosis in children. Some adults develop ESRD. Exclusion of other diseases is required.</td>
</tr>
</tbody>
</table>

Introduction
### Membranoproliferative GN

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Children and young adults (5-25 years).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Etiology</strong></td>
<td>Chronic immune complex GN. Associated with chronic infections, SLE, cancer, cirrhosis, heroin abuse, etc.</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td>Nephrotic syndrome in 50%, acute nephritic syndrome in 20%. Recent history of URI in 50%. Hypertension and/or renal insufficiency.</td>
</tr>
<tr>
<td><strong>Lab</strong></td>
<td>Hypocomplementemia of classic and alternate pathways. C3 nephritic factor (C3NEF). Circulating immune complexes.</td>
</tr>
<tr>
<td><strong>Path:</strong></td>
<td>Diffuse proliferative GN with thickening of the glomerular capillary walls, and GBM splitting (“tram-tracking”). Diffuse, coarsely granular C3 and IgG deposits along GBMs. Electron-dense subendothelial deposits.</td>
</tr>
<tr>
<td><strong>Clinical Course:</strong></td>
<td>Progressive deterioration of renal function ± short remissions. ESRD within 10 years in 50% of children and 80% of adults.</td>
</tr>
</tbody>
</table>

**Introduction**
### Causes of nephrotic syndrome

<table>
<thead>
<tr>
<th>Disease</th>
<th>Children(%)</th>
<th>Adults(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal change GN</td>
<td>75</td>
<td>20</td>
</tr>
<tr>
<td>Membanous GN</td>
<td>5</td>
<td>40</td>
</tr>
<tr>
<td>MPGN I</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Other GN</td>
<td>5</td>
<td>20</td>
</tr>
</tbody>
</table>
Chronic renal failure (uremia)

- General symptoms – weakness, fatigue
- Cardiovascular – hypertension, pericarditis
- G.I. – nausea, vomiting, diarrhea
- CNS – lethargy, confusion, coma
- Muscles – twitching, weakness
- Bones – osteodystrophy
- Metabolic – acidosis, P↑K↑, BUN↑, Cr↑.
- Endocrine - parathyroids↑
Chronic Renal Failure: ESKD
CRF - ESKD with transplant:
Diabetic kidney diseases

- Glomerulosclerosis
- Arteriolosclerosis → Hypertension
- Pyelonephritis
- Papillary necrosis
Diabetic glomerulosclerosis

- Diabetes BM thickening Proteinuria → renal failure (leading cause of mortality in DM)
- nonenzymatic glycation (?), BM synthesis ↑, leaky.
- Pathology:
  - Diffuse global thickening of BM
  - Nodular sclerosis (K-W)
  - Arteriolosclerosis
  - Trapping of serum proteins
- Clin: Proteinuria (in 50% diabetics)
- ESKD (30%)
Diabetic Glomerulosclerosis

Hyaline nodules
Diabetic Glomerulosclerosis

KW lesion…
Benign Nephrosclerosis:

Leathery Granularity due to minute scarring
Renal Artery stenosis - Atrophy

Leathery Granularity
Benign Nephrosclerosis
IgA Nephropathy (berger)

- Most common form of GN
- Young adults (15-30 years)
- IgA deposits in mesangium, varied severity
- Asymptomatic microscopic hematuria (40%)
- Bouts of macro hematuria (40%)
- Nephrotic syndrome (10%)
- Renal failure (10%)
Nephrosclerosis - Hypertension

**Benign**
- sustained mild hypertension.
- hyaline arteriolosclerosis
- arterial fibrosis
- glomerular hyalinization, tubular atrophy

**Malignant**
- BP>125 mm/Hg, retinal hemorrhage, papilledema, renal dysfunction
- fibrinoid necrosis of arterioles
- microthrombi
Thrombotic microangiopathy

- Morphologic finding in several diseases
- microangiopathic hemolytic anemia
- HUS, TTP, Malignant nephrosclerosis
- Systemic sclerosis
Renal infarcts

- Thromboemboli
- Mural thrombi
- (M.I., atrial fibrillation)
- Endocarditis
- Aortic thrombi (atherosclerosis)
- Cholesterol emboli
Renal Infarcts:
Renal Infarct:
Renal Infarct:
Acute Tubular Necrosis:

- Common cause of acute renal failure
- “Dirty” brown casts in urine
- Oliguria → anuria → polyuria
  - Azotemia
  - Acidosis, K↑
  - Fluid retention
- Recovery 1-2 weeks
Acute Pyelonephritis

- Bacterial infection (E. coli 80%)
- Ascending / hematogenous
- Lower UTI precedes renal infection
- Fever, flank pain, neutrophilia
- Leukocyte casts in urine
- Healing - recurrence → chronic pyelonephritis
Septicemia-Microabscess
Septicemia-Microabscess
Acute Pyelonephritis with papillary necrosis (diabetes)
Septicemia-abscess
Pyelonephritis – Predisposing Cond.

U  Urolithiasis
R  Reflux (vesico-ureteric)
I  Infections of lower UT
N  Neoplasms (ureteric, vesical, prostatic)
E  External compression (e.g.) pregnancy retroperitoneal fibrosis
Chronic Pyelonephritis Pathology

- Destruction of renal tissue and fibrosis
  - Cortical scars
  - Loss of papillae
  - Ectasia of calices
  - Hydronephrosis
- Irregularly shrunken small kidney
- Chronic inflammatory infiltrates
- Tubular atrophy with casts ("thyroidization")
Drug induced renal disorders:

1. Acute tubular necrosis (toxic)
   Gentamycin, mercury, contrast agents.

2. Acute tubulointerstitial nephritis (allergic)
   – methicillin, thiazides.

3. Analgesic nepropathy (Phenacetin)
   chronic tubulointerstitial nephritis with papillary necrosis.
Urolithiasis – Stones:
Urolithiasis:

- 1-5%, environment, males, pelvis
- Renal colic, dull ache in loins
- Urinary tract infection recurrent.
- Factors affecting:
  - Urine pH, Infection, Metabolic,
  - Pyrophosphates and citrate inhibit.
Urolithiasis – stones:

- Calcium oxalate (or phosphate): 75%
- Magnesium ammonium phosphate (struvite, or "triple phosphate"): 12%
- Uric acid: 6%
- Cystine: 1%
- Other: 6%

Infection
Hypercalcemia / Hypercalciuria

**Primary** (increased intestinal absorption of Ca)
- Idiopathic (most common)
- Milk-alkali syndrome
- Vitamin D excess
- Sarcoidosis

**Secondary** (release of Ca from bones)
- Renal osteodystrophy
- Hyperparathyroidism
- Osteolytic metastases (e.g. breast cancer)
- Paraneoplastic syndromes (PTrP)
Urolithiasis:
Staghorn Calculus:
Urolithiasis with hydronephrosis:
Hydronephrosis:
Urolithiasis – sites of impaction
Hydronephrosis
- Urolithiasis
Causes of Obstructive Uropathy

PELVIS
- Calculi
- Tumors
- Ureteropelvic stricture

URETER-INTRINSIC
- Calculi
- Tumors
- Clots
- Sloughed papillae
- Inflammation

URETER-EXTRINSIC
- Pregnancy
- Tumors (e.g., cervix)
- Retroperitoneal fibrosis

VESICOURERETAL reflux

BLADDER
- Calculi
- Tumors
- Functional (e.g., neurogenic)

URETHRA
- Posterior valve stricture
- Tumors (rare)

PROSTATE
- Hyperplasia
- Carcinoma
- Prostatitis
### Urolithiasis:

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Common, male predominance.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etiology</td>
<td>Environmental, metabolic, infectious.</td>
</tr>
<tr>
<td>Clinical Features</td>
<td>Develop silently until episode of renal colic. Cause obstruction, pain, infection, hydronephrosis, and hydroureter.</td>
</tr>
<tr>
<td>Lab</td>
<td>Gross or microscopic hematuria. Chemical analysis to identify type of stone. Characteristic radiographic findings.</td>
</tr>
<tr>
<td>Path</td>
<td>Calcium phosphate or oxalate - Hard, sharp. Uric acid - Smooth. Staghorn - Cast of calyceal system.</td>
</tr>
<tr>
<td>Clinical Course</td>
<td>May recur. Complications are the problem.</td>
</tr>
<tr>
<td>Treatment</td>
<td>Surgery, lithotomy, or ultrasonic lithotripsy to remove stone. Treatment of metabolic process, if indicated. Adequate hydration.</td>
</tr>
</tbody>
</table>
“The weak can never forgive. Forgiveness is the attribute of the strong.”

—Mohandas Gandhi
% Renal tumors

- **Benign**
  - Adenoma, oncocytoma, angiomyolipoma, fibroma (rare!)

- **Malignant:**
  - Renal cell carcinoma (common – adults)
  - Wilms tumor (childhood)
  - Transitional cell carcinoma of renal pelvis
Renal Papillary Adenoma

- Papillary
- Common
- Histopathology similar to renal Cell Carcinoma.
- < 3cm – benign
- > 3cm - malignant
- All tumors considered malignant until proved otherwise.
Oncocytoma (DCT epithelia, benign)
## Wilm’s Tumor

<table>
<thead>
<tr>
<th><strong>Synonyms</strong></th>
<th>Nephroblastoma.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td>Most common renal tumor of childhood. Peak age - 2.5 - 3.5 years.</td>
</tr>
<tr>
<td><strong>Etiology</strong></td>
<td>Embryonic renal tissue (metanephric blastema). Genetic abnormalities.</td>
</tr>
<tr>
<td><strong>Clinical Features</strong></td>
<td>Palpable abdominal mass. Abdominal pain, fever, anorexia, nausea/vomiting. Hematuria.</td>
</tr>
<tr>
<td><strong>Lab</strong></td>
<td>No specific clinical laboratory findings. Diagnosis by radiographic techniques.</td>
</tr>
<tr>
<td><strong>Path</strong></td>
<td>Gross: Solitary/multiple cystic mass, sharply delineated. Soft, bulging, gray-white with focal hemorrhage and necrosis. Micro: Triphasic mesenchymal stroma, tubules, and solid areas (blastema). Primitive glomeruli, skeletal muscle, cartilage, bone, etc. (embryonic tissues)</td>
</tr>
<tr>
<td><strong>Clinical Course</strong></td>
<td>5-yr. Survival 80%. Metastases to lung, liver, bone, brain.</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Prompt resection with chemotherapy ± radiotherapy.</td>
</tr>
</tbody>
</table>
Renal Cell Carcinoma

- Most common renal tumor
- Peak age – 60y M:F = 3:1
- Incidence increasing world wide
- Tobacco; Obesity, genetics (VHLgene, familial cases)
- Von Hippel-Lindau syndrome
  - Hemangioblastoma cerebellum retina
  - Bilateral renal cysts,
  - Clear cell type RCC – common.
RCC - Pathology

- Yellow orange tumor – Hypernephroma.
- Partially encapsulated
- Extends into renal vein
  - tubular clear cell (77%)
  - papillary (15%)
  - granular, chromophobe, sarcomatoid (5%)
Renal Cell Carcinoma:
Renal Cell Carcinoma:
Renal Cell Carcinoma:
RCC – Clinical Features:

- Classical triad (hematuria, flank pain, mass) (<10%)
- Hematuria (50%) most common symptom
- Metastases-hematogenous and local abdominal
- Paraneoplastic syndromes (PTH, Epo, amyloid)
- 5 year survival = 40%
# Renal Cell Carcinoma:

<table>
<thead>
<tr>
<th><strong>Synonyms:</strong></th>
<th>Hypernephroma, clear cell carcinoma.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence:</strong></td>
<td>5&lt;sup&gt;th&lt;/sup&gt; and 6&lt;sup&gt;th&lt;/sup&gt; decades, most common primary renal malignancy.</td>
</tr>
<tr>
<td><strong>Etiology:</strong></td>
<td>Cells of proximal convoluted tubule. Risk factors are smoking, obesity, analgesic abuse, APCKD.</td>
</tr>
<tr>
<td><strong>Clinical Features:</strong></td>
<td>Hematuria*, flank pain, palpable mass. Frequently metastasize (lungs, bone, skin, liver, brain).</td>
</tr>
<tr>
<td><strong>Lab:</strong></td>
<td>Gross or microscopic hematuria. Specific Dx by radiographic techniques.</td>
</tr>
<tr>
<td><strong>Path:</strong></td>
<td>Gross: Large yellow mass with hemorrhage and necrosis. Invade renal vein. Micro: Usually clear or granular cells with little anaplasia. Other histologic variants (&quot;great mimicker&quot;).</td>
</tr>
<tr>
<td><strong>Clinical Course:</strong></td>
<td>5-yr. survival 40%. Poor prognosis with metastases.</td>
</tr>
<tr>
<td><strong>Treatment:</strong></td>
<td>Chemotherapy, surgery, immunotherapy.</td>
</tr>
</tbody>
</table>
Wilms tumor

- Childhood tumor (2-5y) 98%< 10 years
- Most common tumor in childhood
- Sporadic, unilateral (90%)
- Bilateral more common in familial cases (20%)
- Familial syndromic (5%), nonsyndromic (5%)
- WAGR sy – Aniridia, genital abn, Mental Ret. WT1
- Beckwith Wiedemann sy - Hemihypertrophy – WT2
Wilms Tumor:
Transitional Cell Carcinoma:

- 5-10% of adult renal ca.
- Etiology: Analgesic abuse, dye, rubber etc..
- Multiple common.
- Malignant cells in urine
- Desquamated tissue may cause obstruction.
- Hematuria & pain.
Transitional cell Carcinoma:
Transitional cell Carcinoma:
Transitional cell Carcinoma:
Wilms Tumor Features:

- Lobulated tumors mass –encapsulated
- Histology: mixture of immature cells metanephric, stromal, tubular
- Chemotherapy + surgery = 5 years = 90%
- Children < 2 years better prognosis
“When you develop the habits of success, success will become a habit.”

http://SuccessNet.org