Robbins pp. 526-533

Objectives: Know the clinical and pathological findings in acute pyelonephritis, reflux nephropathy, drug induced acute interstitial nephritis, analgesic nephropathy, and acute tubular necrosis.

Two major categories: 1) inflammatory involvement of the tubules and interstitium (interstitial nephritis) and 2) ischemic or toxic tubular injury, leading to acute tubular necrosis and acute renal failure.

## Tubulointerstitial Nephritis

### Acute Pyelonephritis

*Pyelo* means pelvis. The renal pelvis is prominently involved. Common. Suppurative. Caused by bacterial infection.

UTI stands for urinary tract infection. Involves lower (cystitis, prostatitis, urethritis) or upper (pyelonephritis) urinary tract, or both. Extremely common.

Pathogenesis: *E. coli* most common, then *Proteus, Klebsiella, Enterobacter*, and *Pseudomonas.*

Two routes:

1. Ascending. Most common.
   Predisposing factors: urethral instrumentation, females with short urethra and trauma to urethra during sexual intercourse (honeymoon cystitis), bladder obstruction (eg. due to benign prostatic hypertrophy, pregnancy, or uterine prolapse) or dysfunction, incompetence of the vesicourethral orifice (vesicoureteral reflux or VUR), intrarenal reflux. Diabetes increases the risk of serious complications of UTI's.
2. Hematogenous

Morphology: Review on p.528 Neutrophils in interstitium and tubules.

Clinical Course: Costovertebral angle pain, chills, fever, malaise. Pyuria, bacteriuria.

Complications: Pus in renal pelvis = pyonephrosis. Necrotizing papillitis or papillary necrosis. Sepsis. Renal failure.

### Chronic Pyelonephritis and Reflux Nephropathy

(I personally hate the term chronic pyelonephritis and very seldom use it. I'll explain why in lecture.)
Chronic pyelonephritis: a morphologic entity in which interstitial inflammation and scarring of the renal parenchyma is associated with grossly visible scarring and deformity of the pelvicalyceal system.

Two forms: 1) chronic obstructive pyelonephritis and 2) reflux nephropathy (chronic reflux-associated pyelonephritis)

Morphology: Uneven scarring – upper and lower poles especially affected. Why?

- Uneven interstitial fibrosis and an inflammatory infiltrate of lymphocytes, plasma cells, and occasionally neutrophils.
- Tubular atrophy. "Thyroidization."
- Chronic inflammatory infiltration and fibrosis of the calyceal mucosa and wall.
- Arteriosclerosis.
- Focal segmental glomerulosclerosis.

Clinical Course. Present late. Renal failure, hypertension. (Proteinuria if associated with FSGS.)

Drug-induced Interstitial Nephritis

1. Acute Drug-Induced Interstitial Nephritis. Synthetic penicillins (methicillin, ampicillin), other synthetic antibiotics (rifampin), diuretics (thiazides ), nonsteroidal anti-inflammatory agents (phenylbutazone), and miscellaneous drugs (cimetidine). Occurs two weeks after exposure to drug. Findings may include fever, eosinophilia, hematuria, mild proteinuria, leukocyturia (including eosinophils), rising serum creatinine or acute renal failure. IgE and cell-mediated immune reactions.

   Morphology: Review on p. 530.

2. Analgesic Nephropathy. Chronic interstitial nephritis and renal papillary necrosis. Ingestion of mixtures of phenacetin, aspirin, acetaminophen, caffeine, or codeine. Dose related. Chronic renal failure, hypertension, and anemia. Increased incidence of transitional cell carcinoma of the renal pelvis.

   Morphology. Review on p. 531.

**Acute Tubular Necrosis**

Clinicopathologic entity characterized morphologically by destruction of tubular epithelial cells and clinically by acute suppression of renal function. Most common cause of acute renal failure. What are other causes? ATN reversible

Ischemic ATN: hypotension and shock, hemolytic transfusion reactions
Nephrotoxic ATN: heavy metals (mercury), solvents (carbon tetrachloride), drugs gentamicin), radiographic contrast agents.

Pathogenesis: See figure 14-17

Morphology: See p. 532

Clinical Course. Initiating phase, maintenance phase, recovery phase.

Review Questions.

1. A 24 year old female presents with fever, chills, and costovertebral angle pain. Urinalysis shows pyuria and bacteriuria. What is your leading diagnosis? What are some predisposing factors? What is the most likely organism?

2. A 40 year old male presents with hypertension and an elevated serum creatinine. A careful drug history uncovers the fact that he takes 10-12 Goody's headache powders a day. You investigate and find out that Goody's headache powder contains aspirin, acetaminophen, and caffeine. What is the most likely cause of his renal failure? What does his kidney look like? What are potential complications?

3. A 40 year old male is treated with methicillin for a staphylococcal wound infection after surgery. He develops acute renal failure 2 weeks later. What would the kidneys look like? What might you see in the urinary sediment to help you with the diagnosis?

4. A two year old child is diagnosed with vesicourethral reflux by voiding cystourethrogram after a history of recurrent episodes of pyelonephritis. He is unfortunately lost to follow-up. You see him several years later when he has an elevated creatinine and nephrotic range proteinuria. What do his kidneys look like?

5. After an earthquake in Turkey a thirty year old woman is pulled from the rubble of a building with massive crush injuries. She develops acute renal failure. What do her kidneys look like? What is the usual course of this disease? What is the most important prognostic factor?