DISEASES OF THE TUBULES AND INTERSTITIUM

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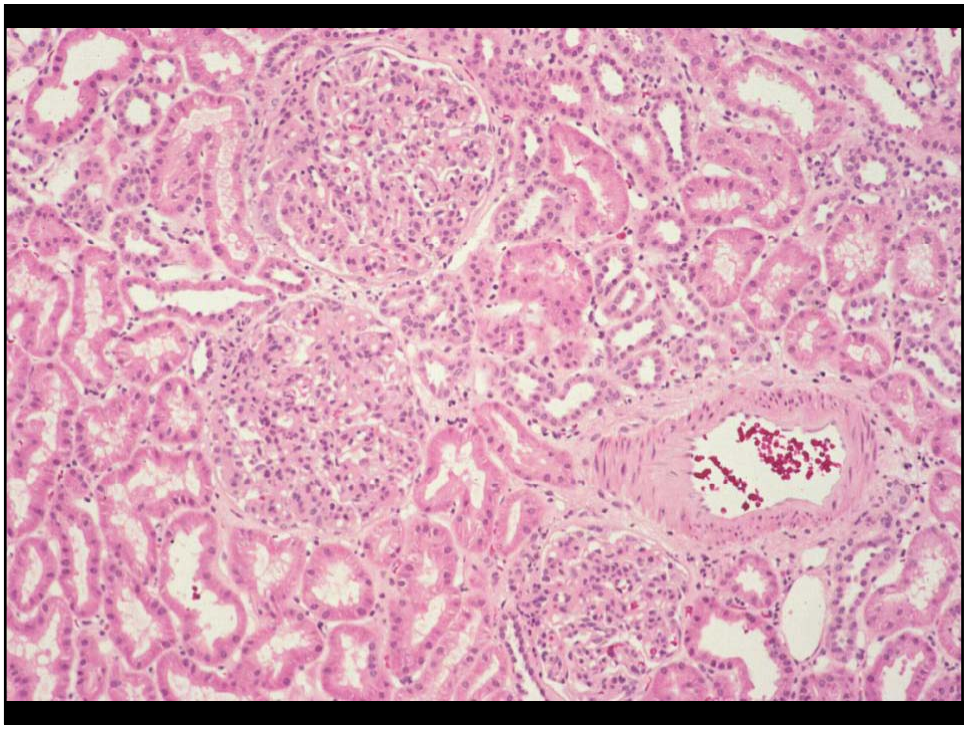
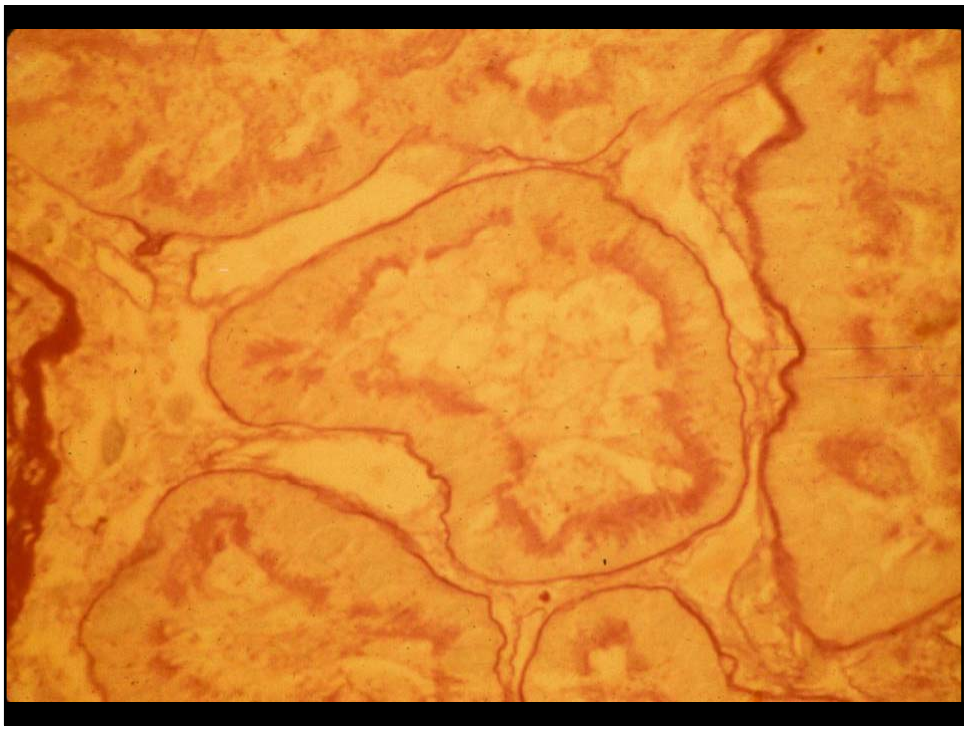
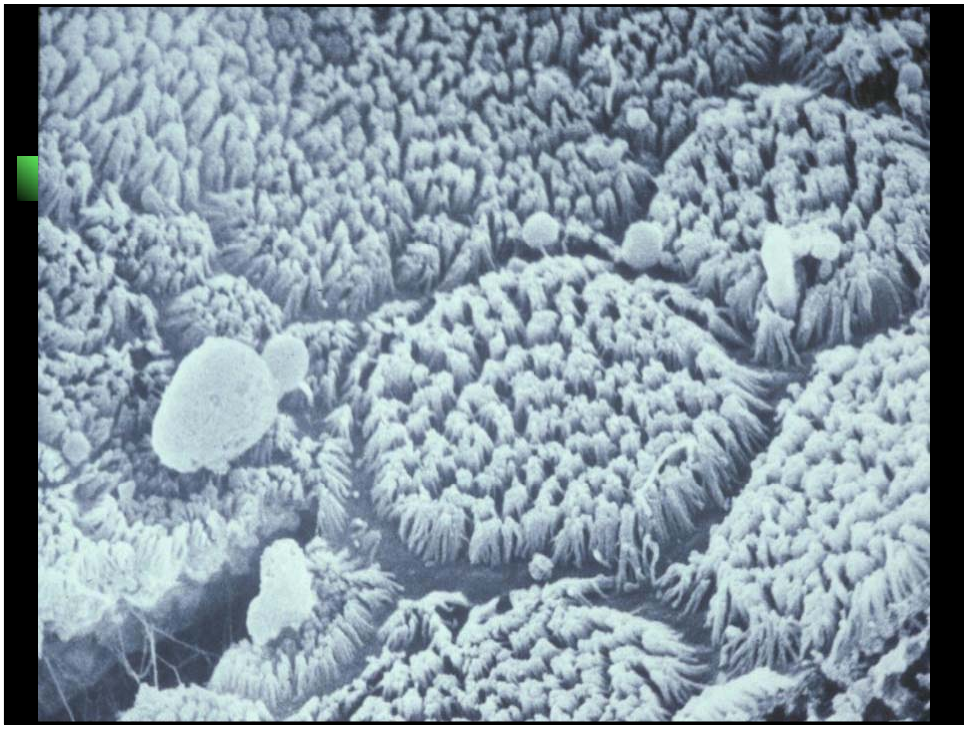
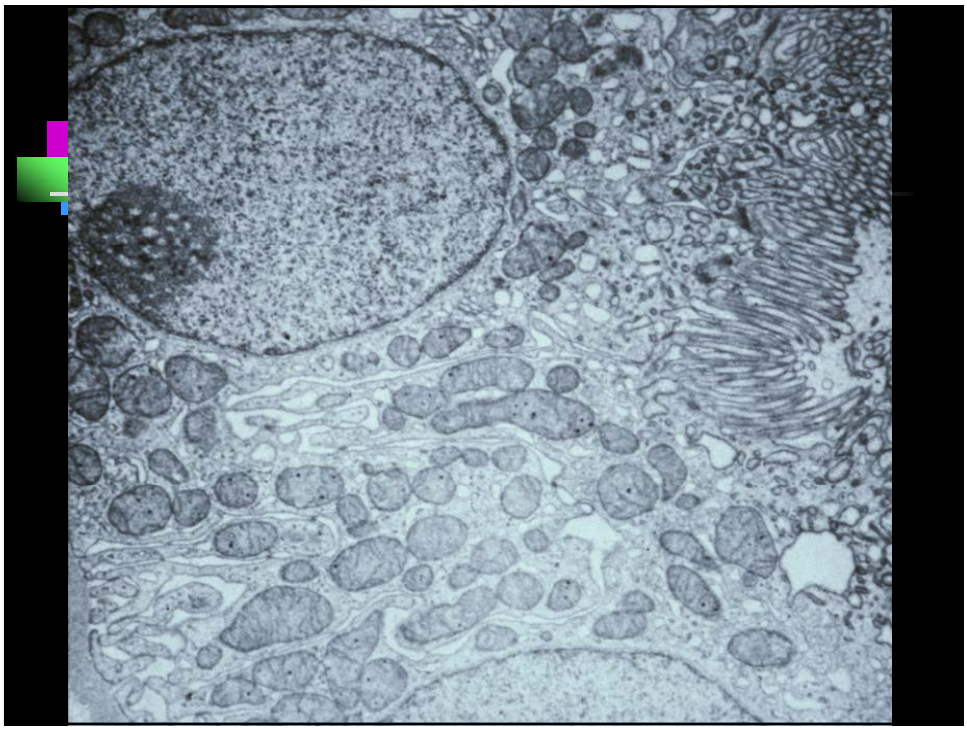
Mechanisms of Tubulointerstitial Disease

- 2 general categories:
  - Ischemic/toxic (non-inflammatory)
    - Acute tubular necrosis
  - Inflammatory
    - Tubulointerstitial nephritis
      - Infection, allergic/drug-induced, systemic disease (i.e. Sarcoid, Sjogren's), etc









Case 1

A 58 year old W M with a history of ETOH abuse , but normal renal function on ER visit 2 months ago, is admitted to the hospital in a stuporous condition having been found by his friend in his room to be unarousable. The friend states that they had been drinking 3 days ago and when he now called for his drinking buddy there was an empty bottle of Jack Daniels next to him.

Case 1

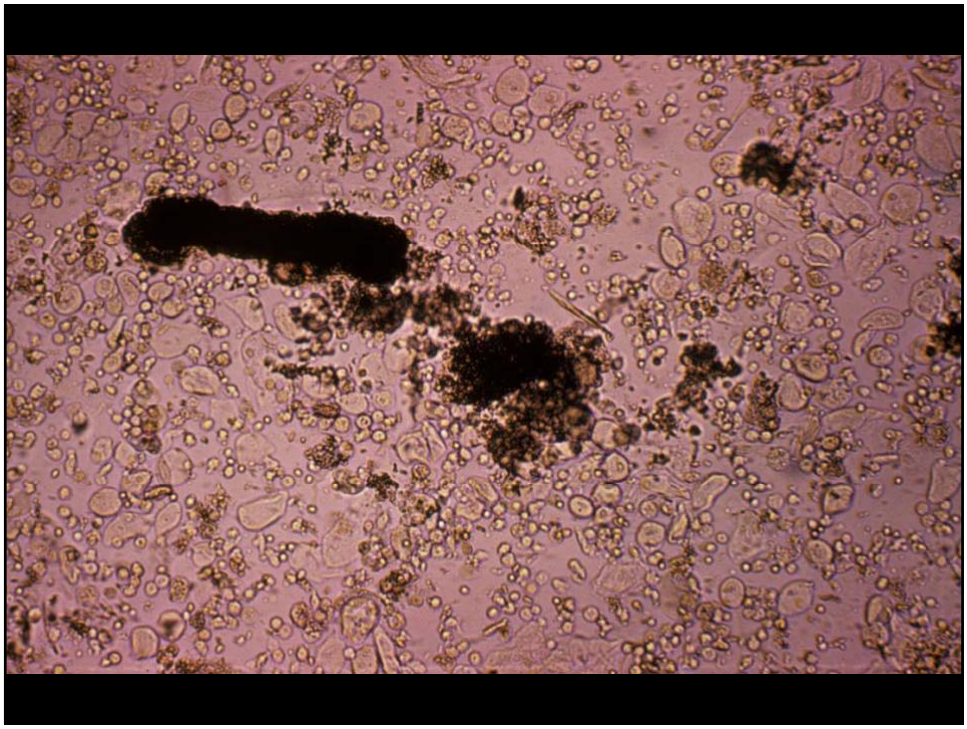
PE: BP 100/60 mm Hg, P 110, R12, Temp 101, Cor -, Chest rales at R base, Abd-, Ext swelling and tender R and L legs below the knee.

Lab: BUN 48 mg/dl, Creatinine 6.2 mg dl, CBC – wbc 15, 000, with increased polys, Cxray RLL infiltrate.

U/A tr prot, 4+ heme, no rbc or wbc.

Pt is hydrated with 1 L Saline and BP 135/82. Given 150 mg Gentamicin and 1g Ampicillin.

Over the next 2 days pt makes little urine and creatinine rises to 8.4 mg/dl.

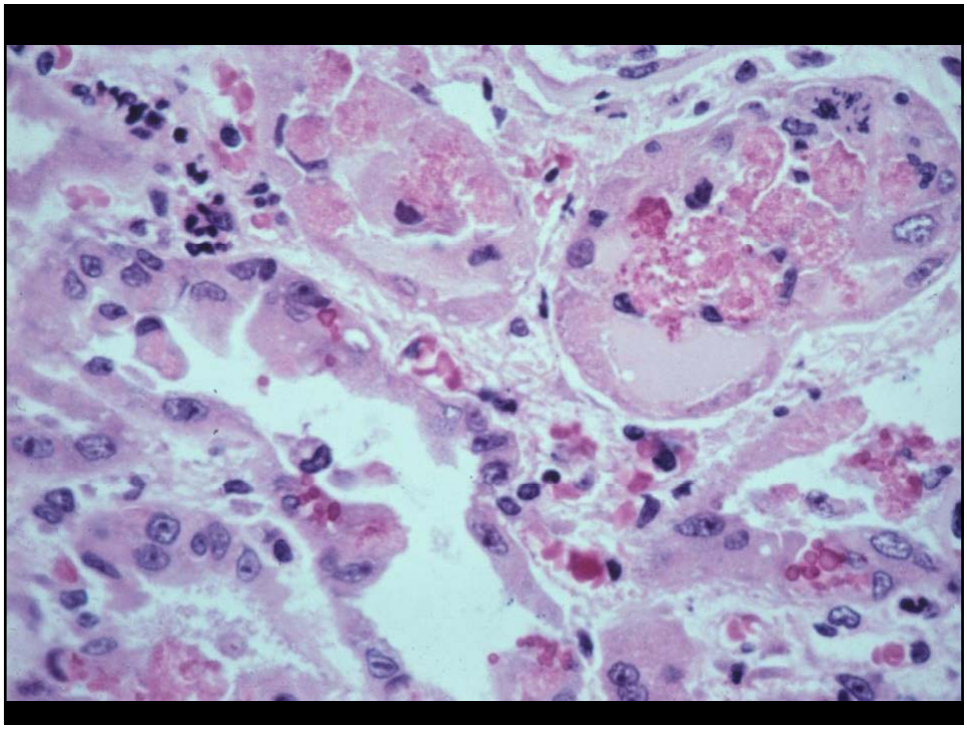


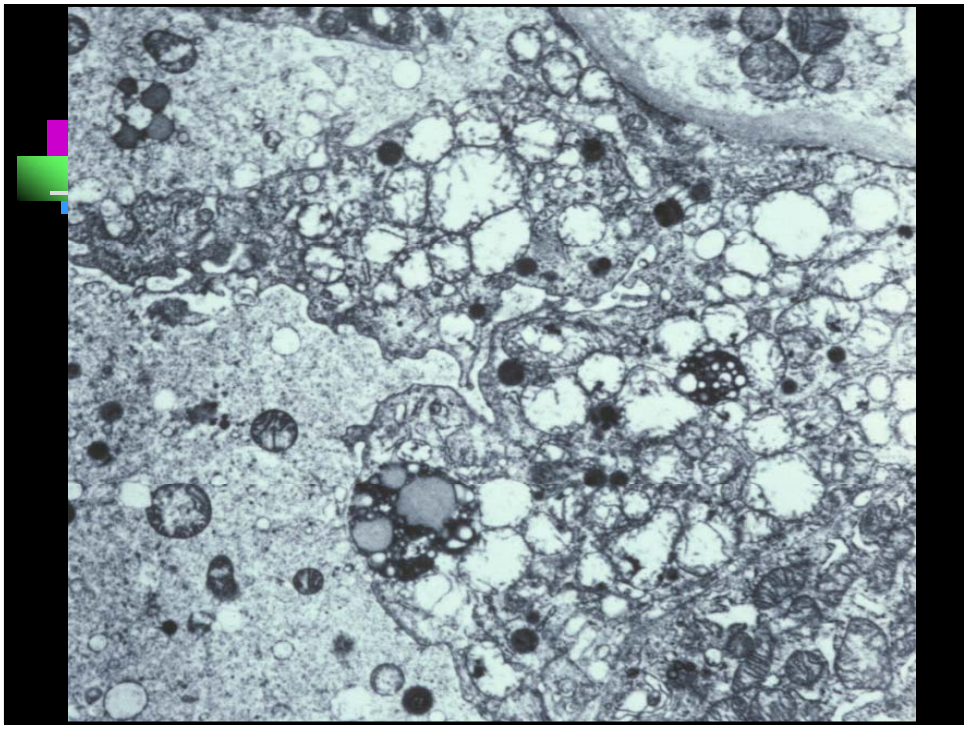
Case 1

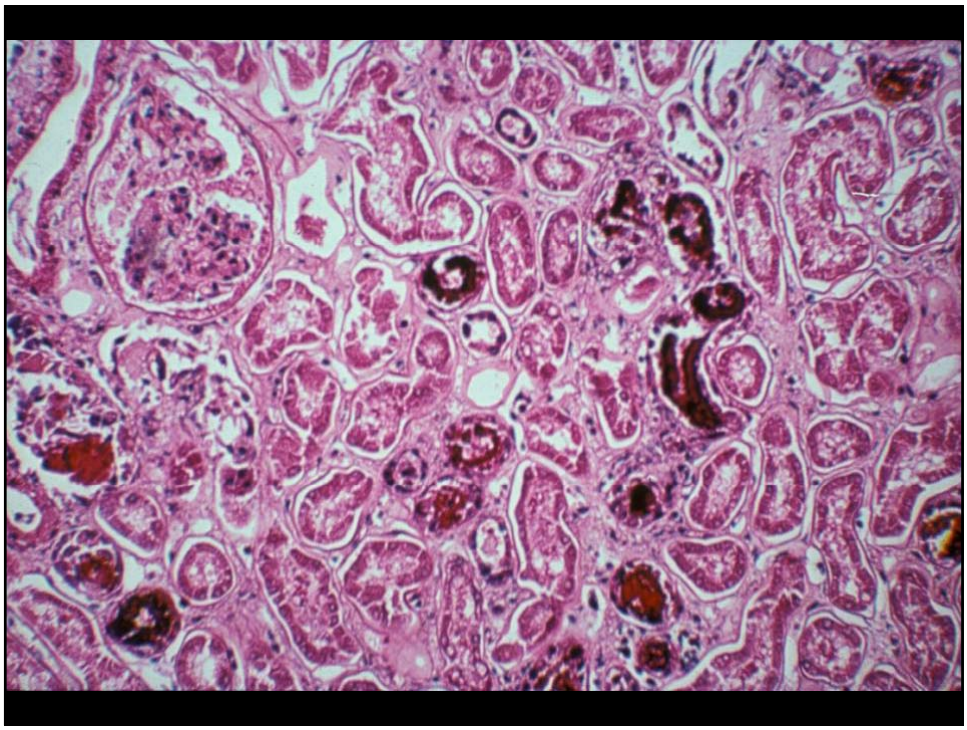
- Should a kidney biopsy be done?
- Is the renal failure acute or chronic? How do you know? How can you prove it?
- What is the likely etiology of the renal failure (hypotension, rhabdomyolysis, gentamicin, leptospirosis)
- What lab tests might confirm the diagnosis?

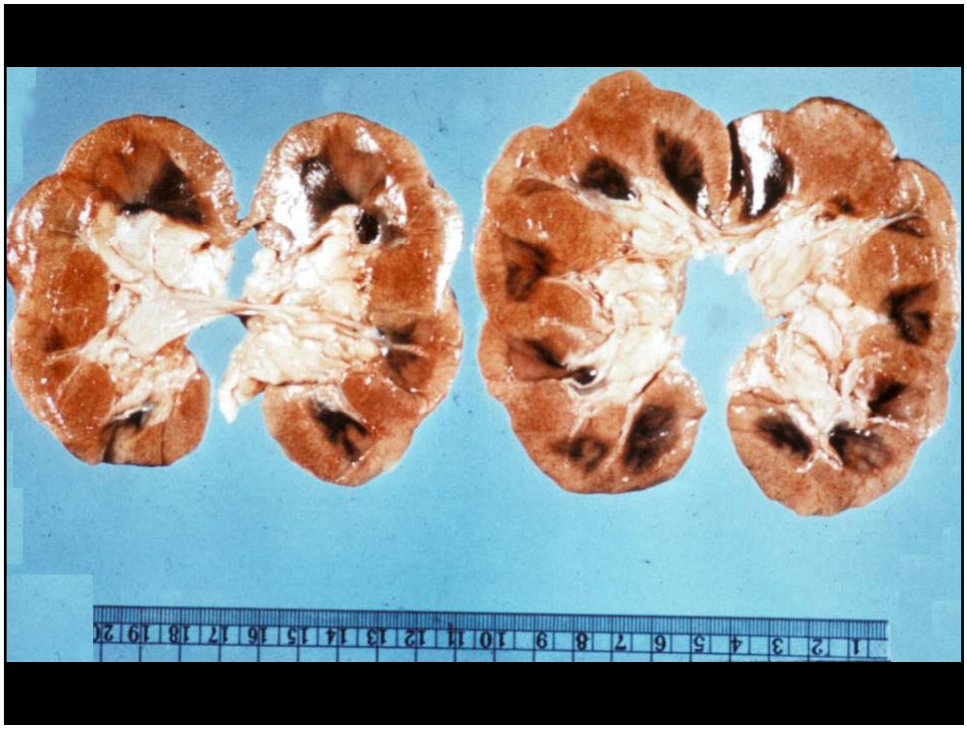
Acute renal Failure

- Prerenal azotemia
- Post-renal azotemia
- Acute tubular necrosis
- Acute interstitial nephritis
- Acute glomerulonephritis
- Vascular ARF









Acute Tubular Necrosis

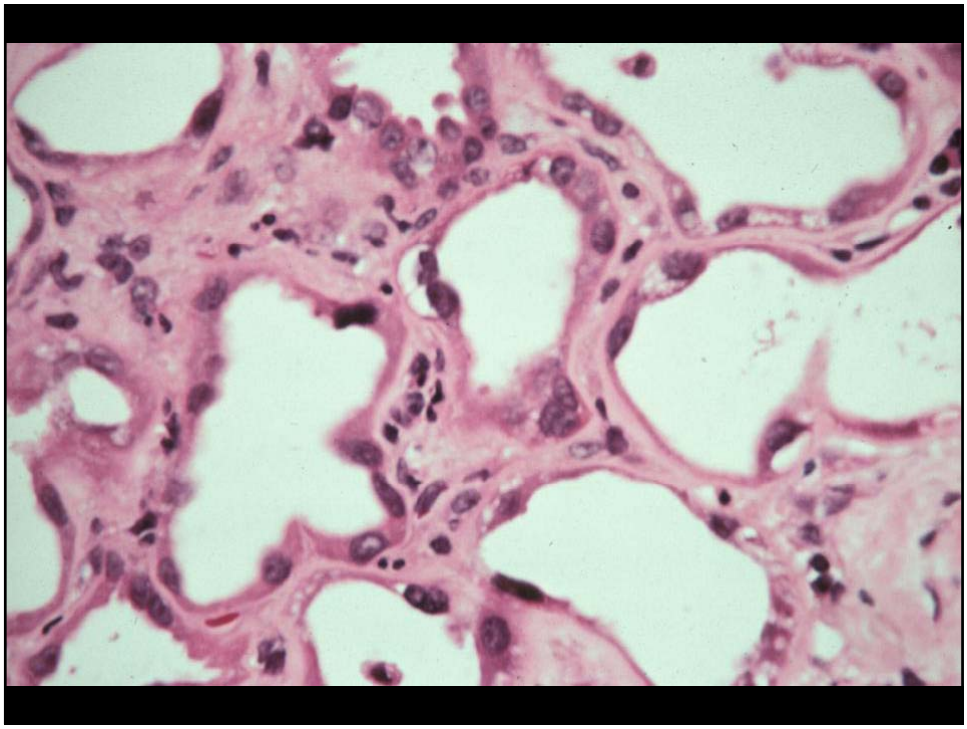
- Predisposition of tubular epithelial cell
  - High metabolic activity/02 requirements
    - Prone to ischemic/hypoxic injury
  - Role in concentrating/reabsorbing filtrate
    - Increased exposure to toxins
- Two subtypes of ATN
  - Ischemic ATN
  - Nephrotoxic ATN

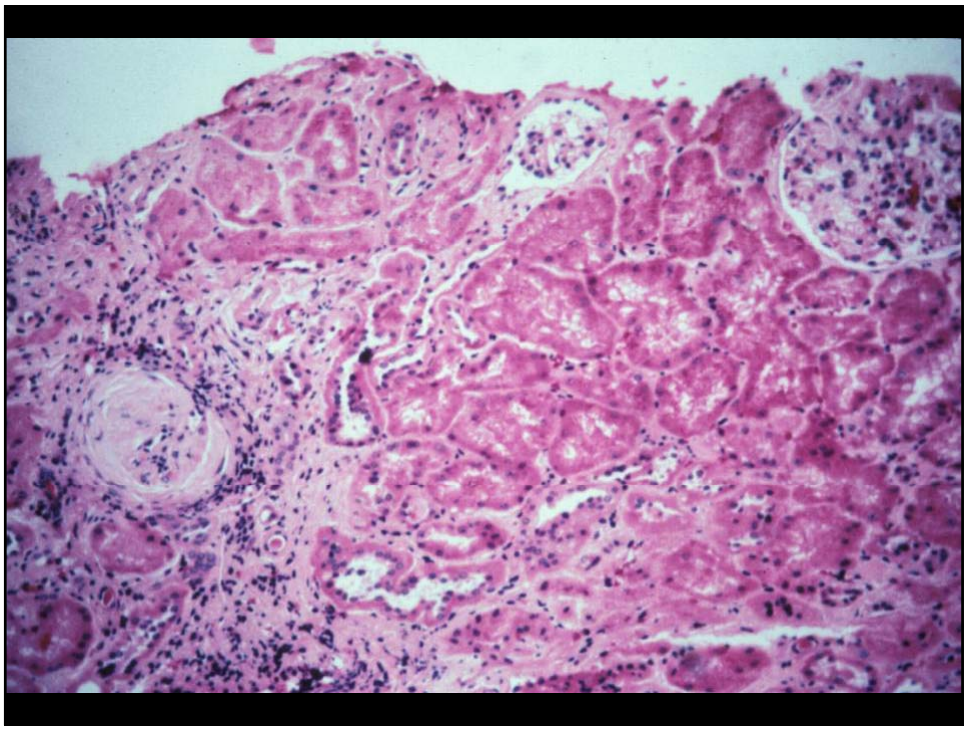
Ischemic ATN

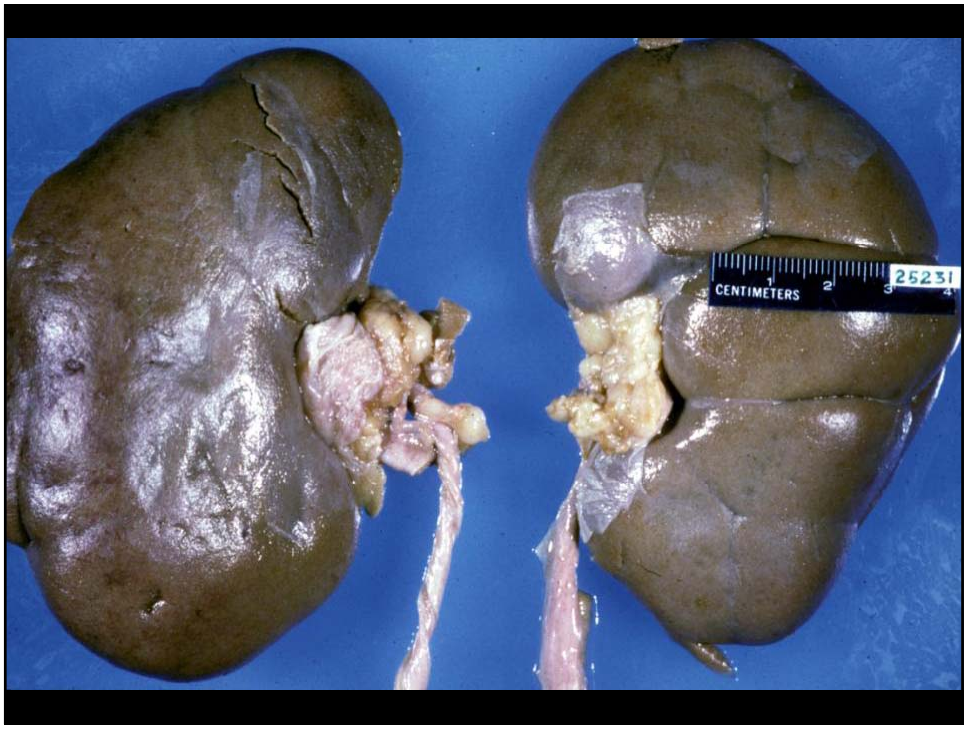
- Occurs in setting of decreased renal blood flow / hypotension, i.e. trauma/severe blood loss, CHF, septic shock
- Pathology
  - Gross: P & S
  - Degenerative changes
  - Subsequent regenerative changes
  - Most severe changes in proximal tub and mTAL

Clinical Phases of ATN

- Initiation
  - first 36 hours, dominated by initial event
- Maintenance
  - up to 3 weeks, oliguric, dialysis required
- Recovery ("diuretic phase")
  - increasing urine output – often substantial, electrolyte abnormalities
- Prognosis: > 90% recovery if survive initiating event





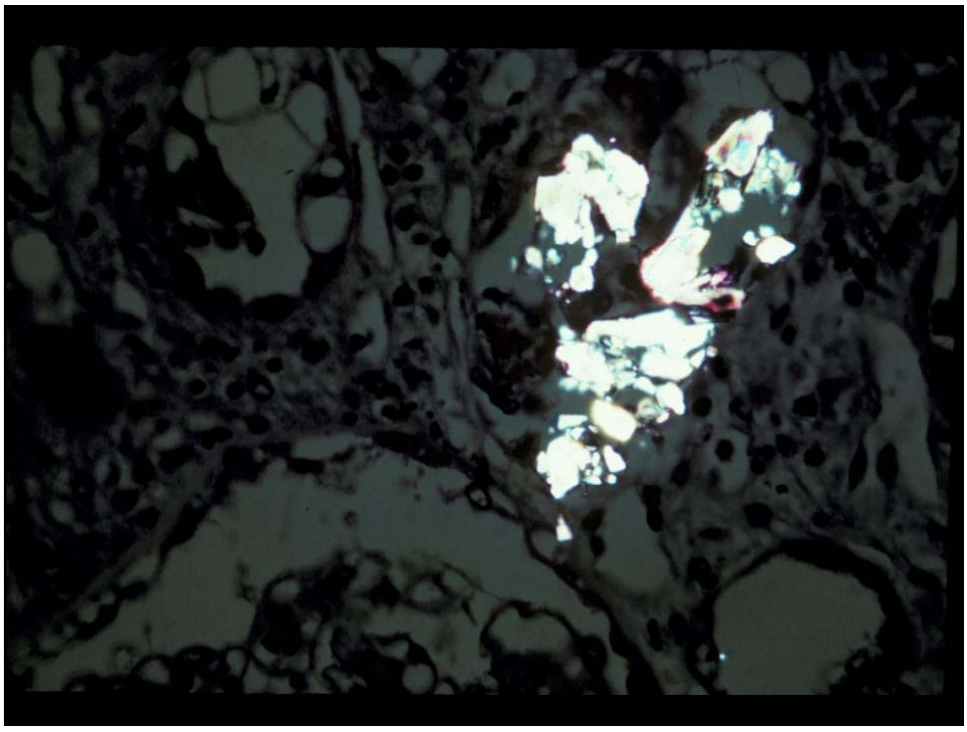


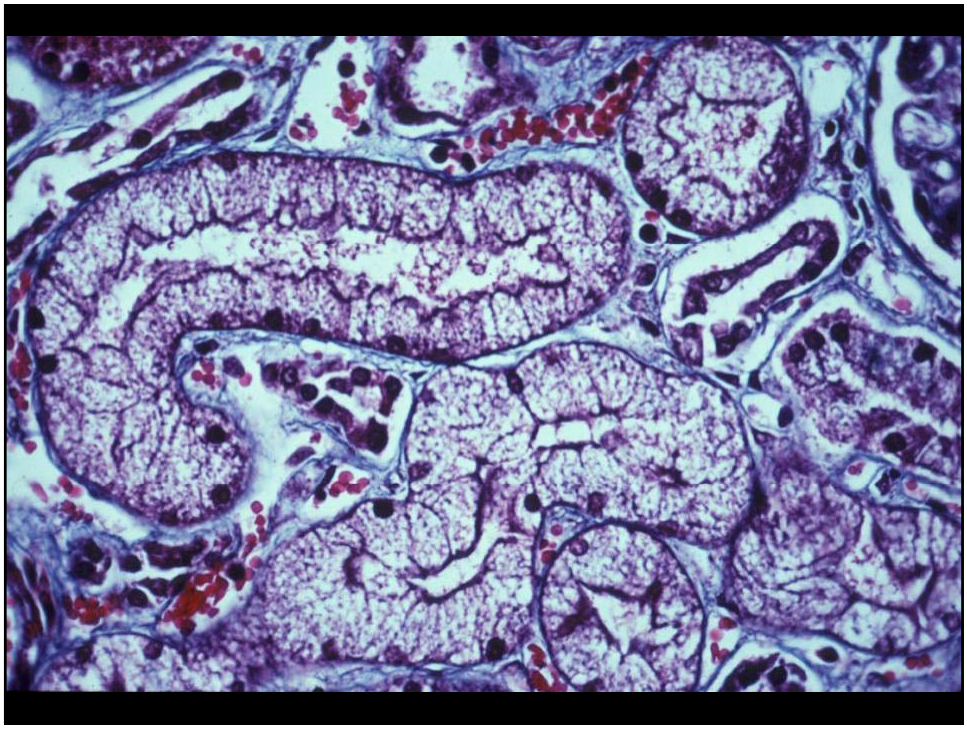
Nephrotoxic ATN

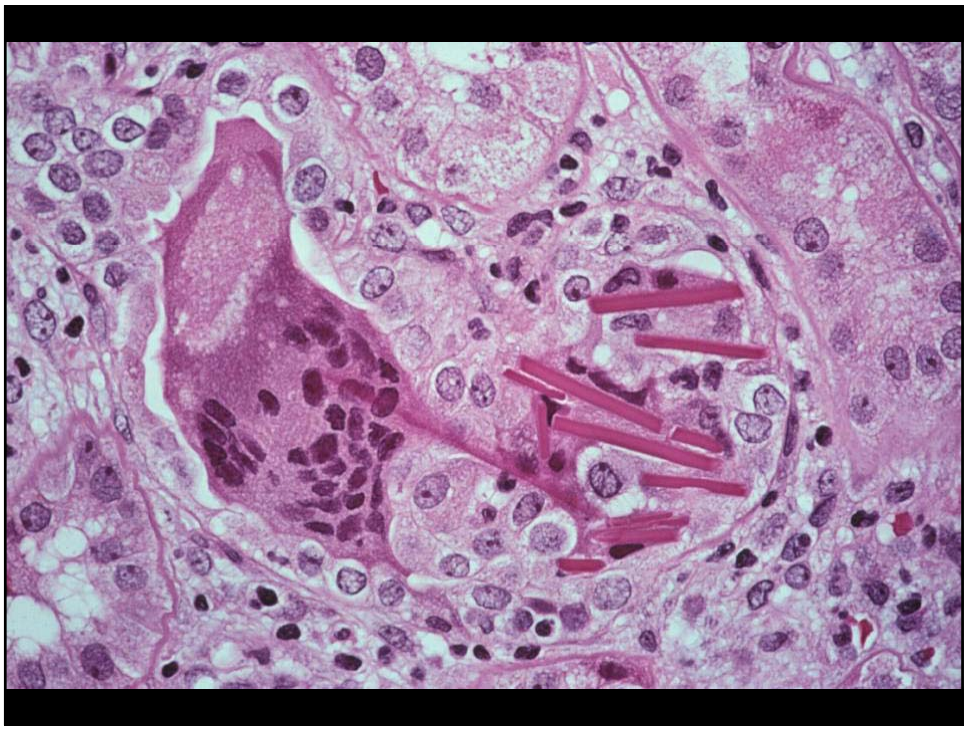
- Many toxins implicated
  - Heavy metals: Hg, Pb, gold, arsenic,…
  - Organic solvents: CCl_4, ethylene glycol
  - Therapeutics
    - antibiotics: gentamicin
    - antifungals: amphotericin B
    - chemotherapeutic agents: cisplatin
    - bisphosphonate: zoledronate
    - radiation & radiocontrast
    - pigments: Hgb, Mgb
    - abnormal levels of physiologic substances
    - osmotic agents: mannitol

Nephrotoxic ATN

- Similar pathology to ischemic ATN
- Additional, toxin-specific findings:
  - Ethylene glycol
  - Osomotic agents / radiocontrast
  - Light chains
  - Hemoglobin / Myoglobin







Case 2

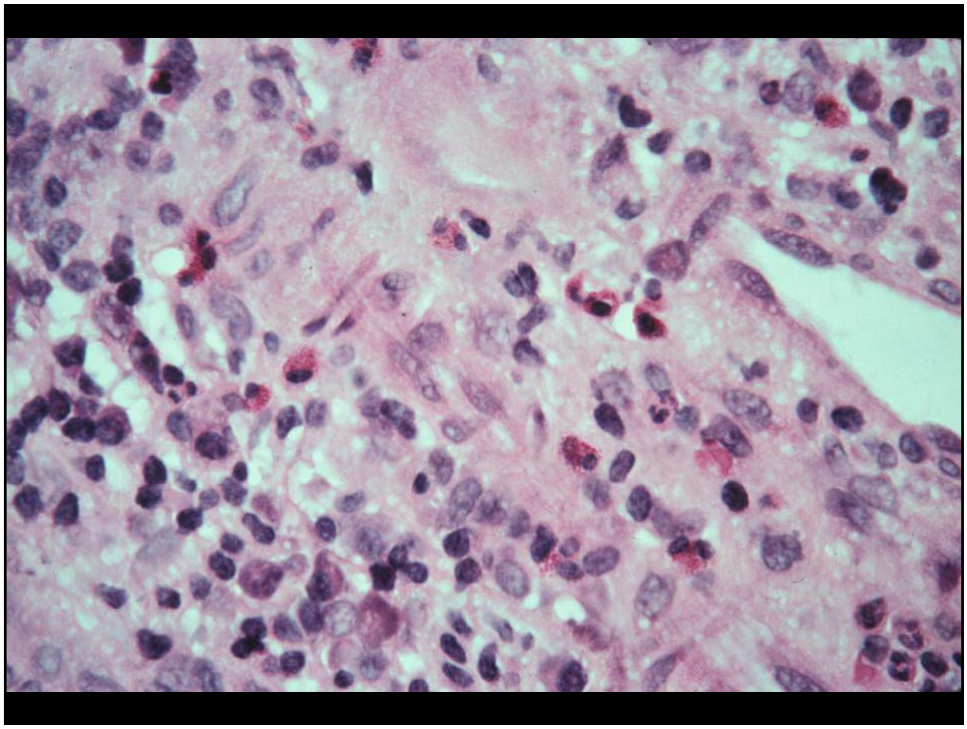
- 65 y o retired Ob-Gyn MD refer by NYC nephrologist for presumed RPGN
- Past Hx HBP x 40 yrs controlled on meds, arrhythmia →verapamil, hypothyroidism
- Some urinary urgency 1 wk PTA – Urologic check (U/A neg) ; Urticarial rash on legs several days PTA disappeared.
- 1 wk PTA gave blood and played golf.
- Not feeling well , thirsty. Check chem7

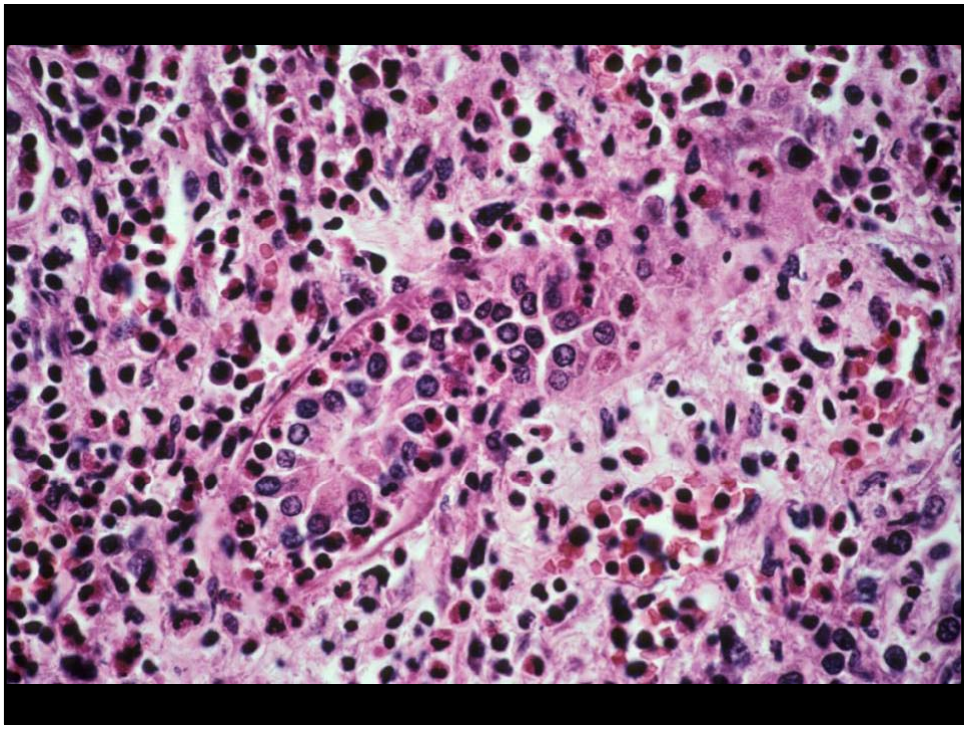
Case 2

- BUN 94, creat 4.4 mg/dl
- Friend nephrologist – BUN 91 creat. 4.9 mg/dl K+ 6.7 , alb 4.1 WBC 8.4, Hct 36, Plts 441, U/A some rbc , no casts, ANA- , ASLO 33, UIF normal pattern, Ccr 32 cc/min
- Meds calan SR, PPI, zoloft, synthroid, cozaar – given Kayexolate →CPMC ? BX
- Px BP 170/90, P82, Cor-Chest-Abd- neg, no edema , fine maculo-papular rash on chest and upper arms.
- BUN 96 creat 5.1 U/A tr prot, 2+ heme, no casts

Case 2

- What is the differential Dx of the acute renal failure?
- What labs help or hurt each diagnosis?
- Would you biopsy now? Wait and then consider biopsy if no recovery? Treat and then biopsy if no recovery? (What therapy if treating?)





Drug-Induced Interstitial Nephritis

- Pathogenesis: cell-mediated hypersensitivity reaction (T's)
- Pathology
  - interstitial inflammation & edema
  - EOSINOPHLS
  - Tubulitis
  - + / - granulomas

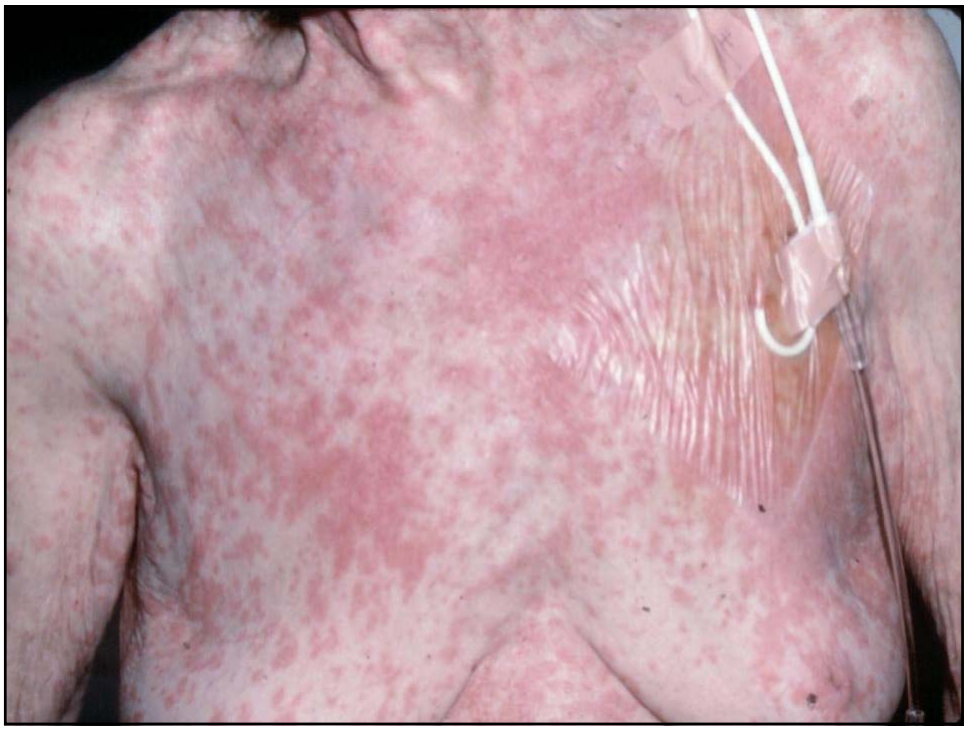
Clinical Features Penicillin-Related AIN

Rash = > 40%

Fever = > 75%

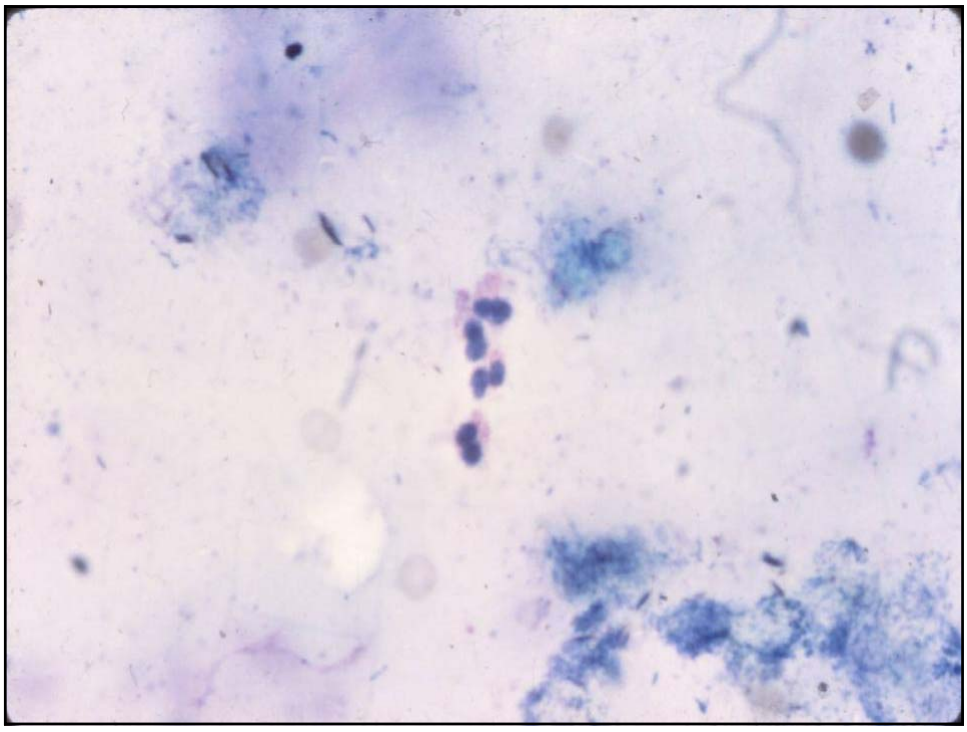
Eosinophilia = > 80%

Hypersensitivity Triad = 30%
(R + F + E)



Urinary Findings in Penicillin-Related AIN

- Mild proteinuria
- Hematuria in over 90% (Gross hematuria in over 30%)
- Sterile pyuria
- Eosinophiluria



Medication Associated AIN

Beta-Lactam Antibiotics
Other Antibiotics- Sulfonamides
TM-SMX
Rifampin
Quinolones
Diuretics
NSAIDS
Other Drugs – Cimetidine, Dilantin, Sulfinpyrazone, Allopurinal
Proton Pump Inhibitors

Course Patient 2

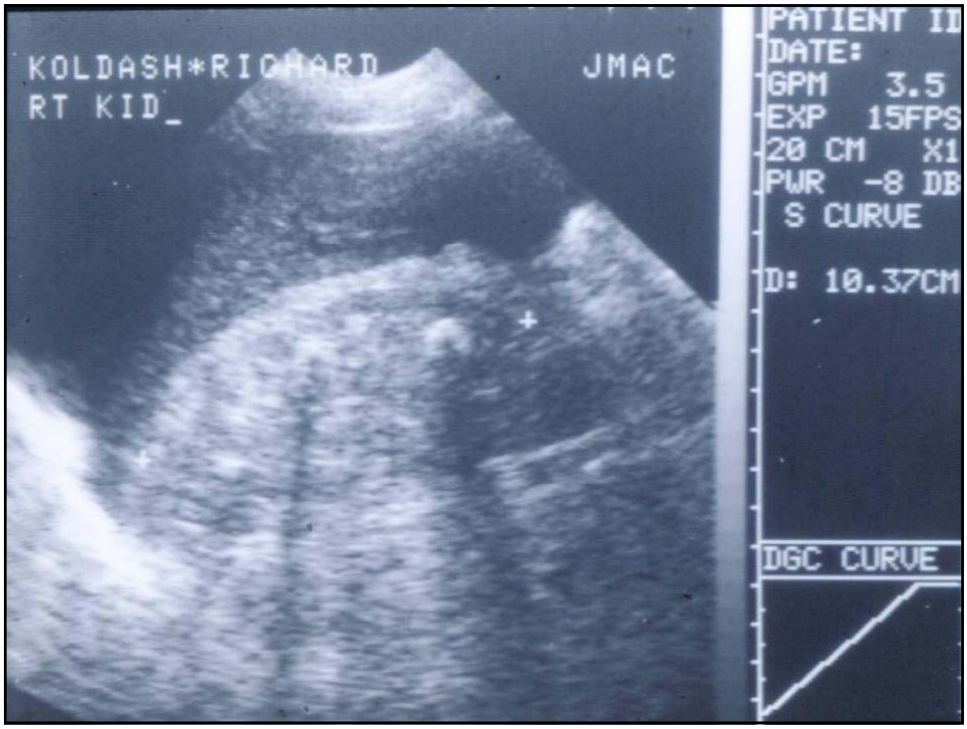
- D/C all meds – use alts for HBP and ulcer disease
- Prednisone 120 mg QOD x 6 wks
- Plasma creatinine decreased from 5.1 to 1.8 mg/dl
- Stable RFTs 4 yr later

Case 3

- A 64 yo BF has had diabetes and mild HBP for 6 yrs. Her BS has recently been poorly controlled and and she has had polyuria and nocturia. Recently she noticed dysuria and frequency as well.
- She develops fever, chills , and left flank pain which increases over 24 hrs. She calls her MD who send her to the ER immediately.

Case 3

- In the ER her BP is 110/72 , P 100, Temp102, R14. She has marked L CVA tenderess.
- BUN 35 mg/dl, Creatinine 1.4 mg/dl
- WBC – 16,500, Hct 39%, platelets nl.
- U/A shows 3+gluc, 2+ heme, tr alb, 10-15 rbc, wbc –TNTC, and wbc casts.
- Urinary Na+ is 42 mEq/L. FENa+ is 1.8.
- USG shows no hydronephrosis (obstruction) but a stone in L kidney.
- She is treated with hydration, amp, gent.
- Over the next 24 hours her BP incr to 145/82, temp 100, and urine output remains copious.
- BUN decrease to 14 mg/dl and creatinine to 0.7 mgl/dl.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RT KID_
JMAC
PATIENT II
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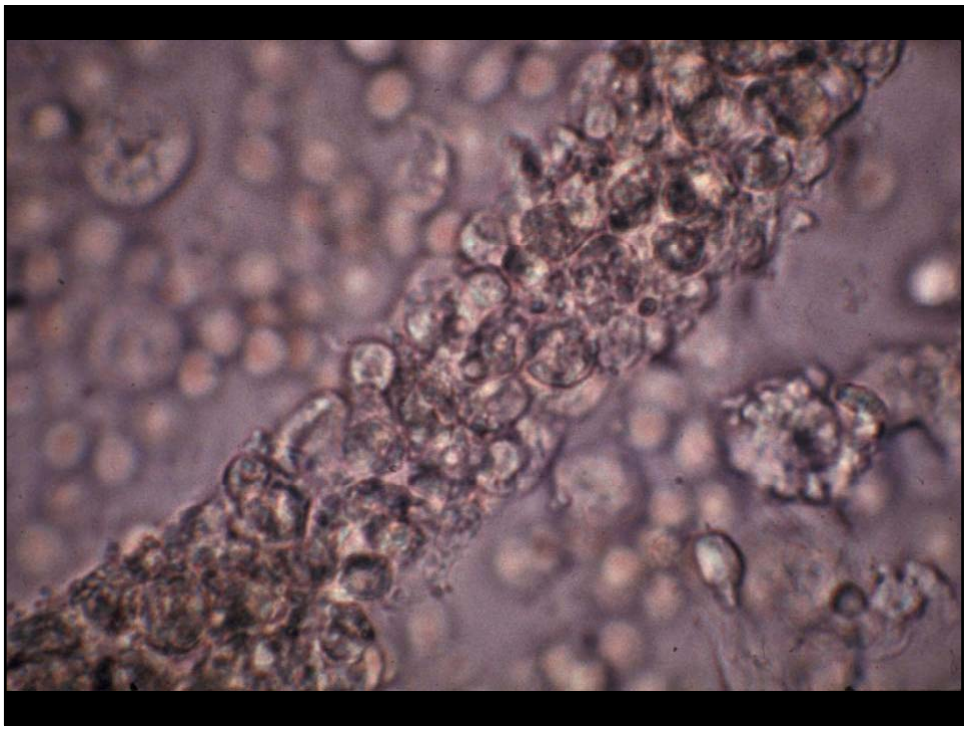
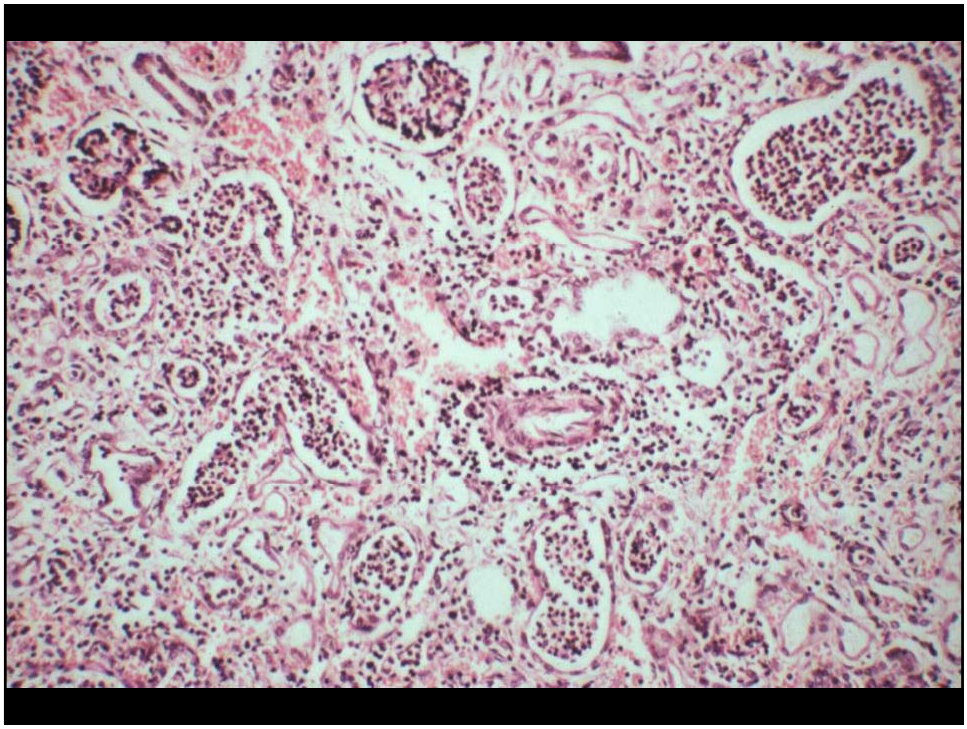
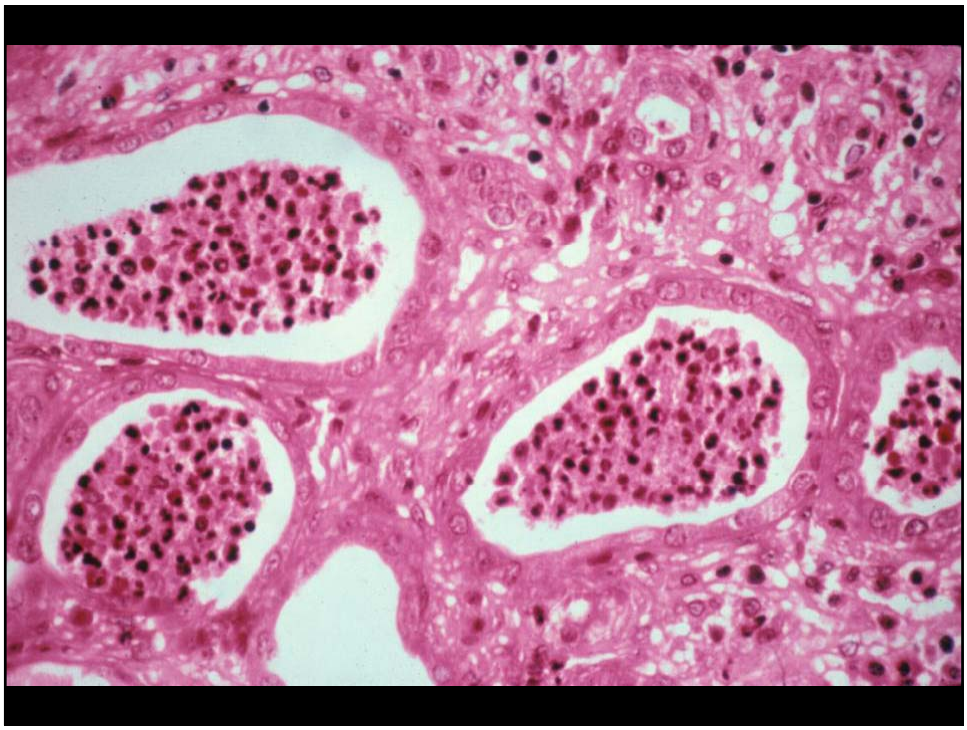
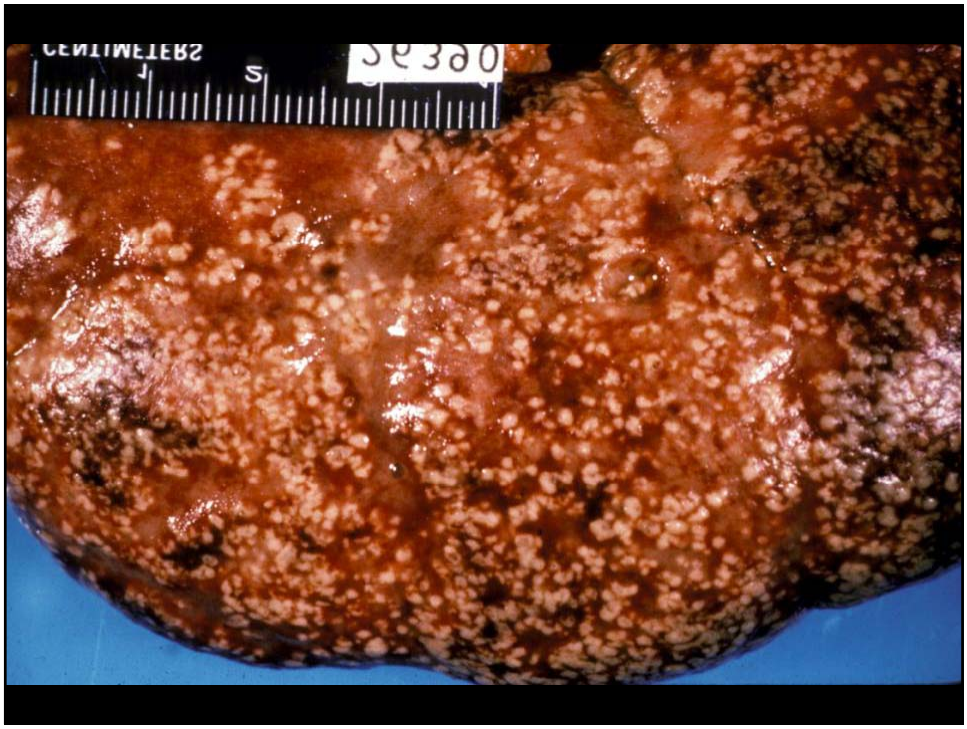
GPM 3.5
EXP 15FPS
20 CM X1
PWR -8 DB
S CURVE
D: 10.37CM
DGC CURVE







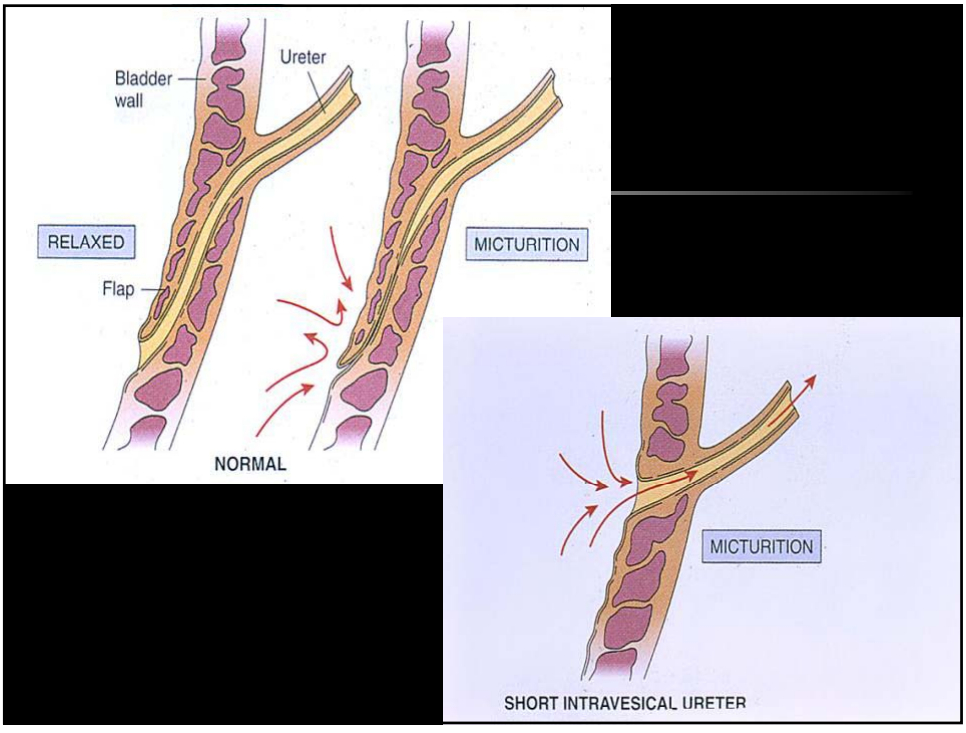


Acute Pyelonephritis

- Acute suppurative infection of kidney
- Clinical: back pain, fever, pyuria, +/- RI
  - Urine cultures: confirmation / Ab sensitivity
- Route of infection
  - ascending > hematogenous
  - ascending starts in bladder as UTI (F>M)
  - hematog: septic emboli, bacteremia (F=M)
- Organisms
  - 85% gram negative bacilli (#1 E. coli)
  - fecal flora

Acute Pyelonephritis

- Increased risk of ascending infection in three clinical settings
  - Obstruction: BPH, tumors, pregnancy, neurogenic bladder (DM)
  - Instrumentation
  - Vesicoureteral reflux
    - 50% UTI's in 1st year of life
    - congenital anomaly: intravesical portion of ureter lacks normal oblique course that prevents reflux

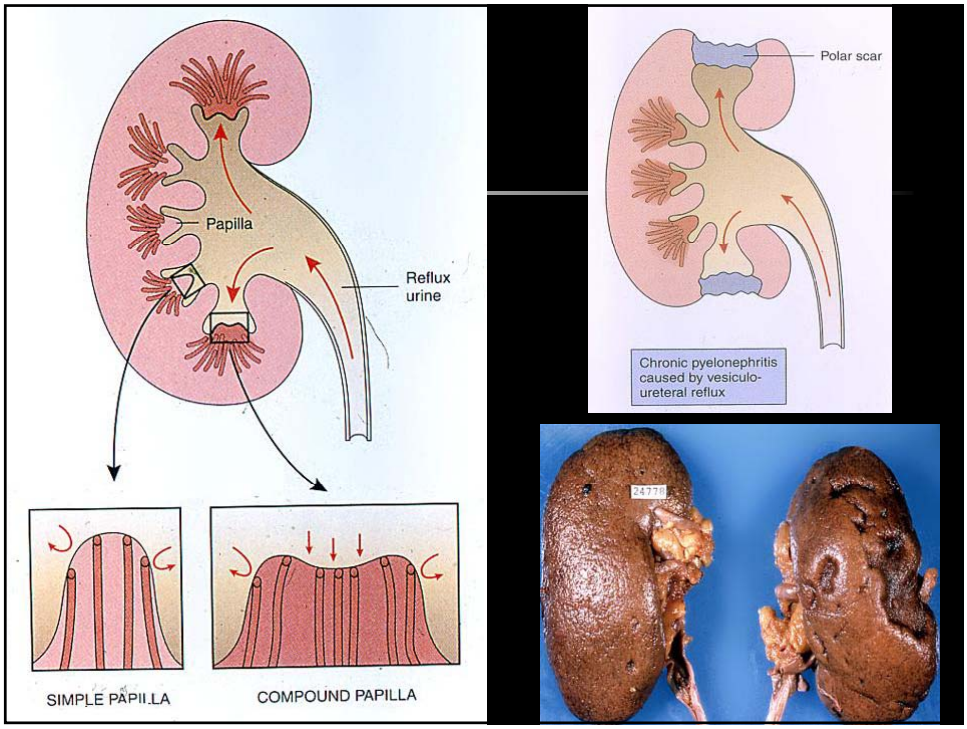


Acute Pyelonephritis

- Gross: normal size, +/- coalescent abscesses
- Micro: severe inflammation, PMN's
  - Microabscesses
  - PMN casts & tubulitis
  - Distribution:
    - Ascending: originates near medulla
    - Hematogenous: cortical

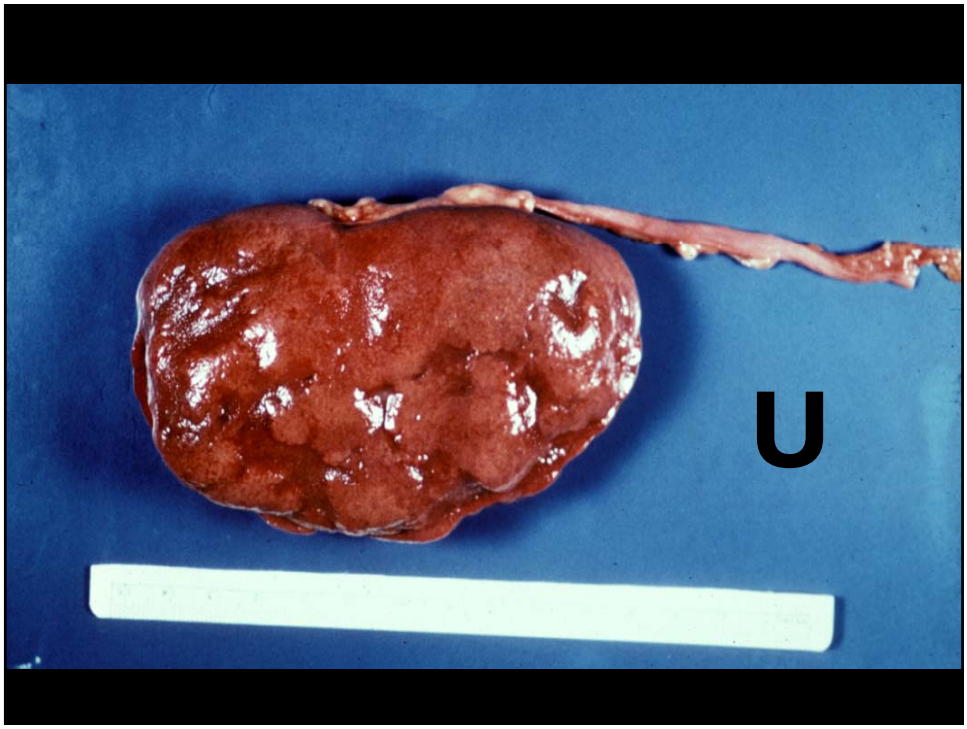
Chronic Pyelonephritis

- Definition: chronic renal disorder with scarring, inflammation, and deformity of calyces/pelvis (ascending*)
- Gross: shrunken
  - Irregular, asymmetric broad/flat scars (U*)
  - Papillary blunting and calyceal deformity
- Micro:
  - Disproportionate tubulointerstitial scarring
  - Atrophic tubules with colloid casts ("thyroidization")
  - Chronic inflammation (not PMN's)



Chronic Pyelonephritis

- Clinical
  - insidious onset of RI
  - + / - HTN, mild proteinuria, decreased urinary concentration, culture neg
  - Rarely follows “usual” acute pyelo
  - More common with persistent obstruction or VUR
  - + / - awareness of acute episodes
  - Rx: relieve obstruction / correct VUR, antibiotics as indicated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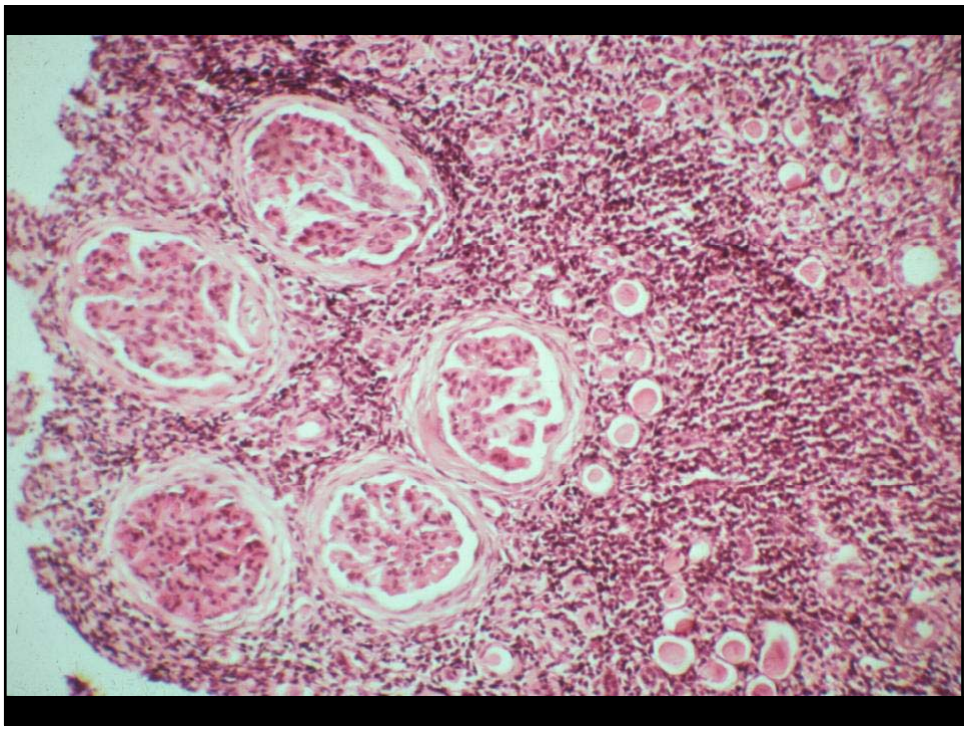
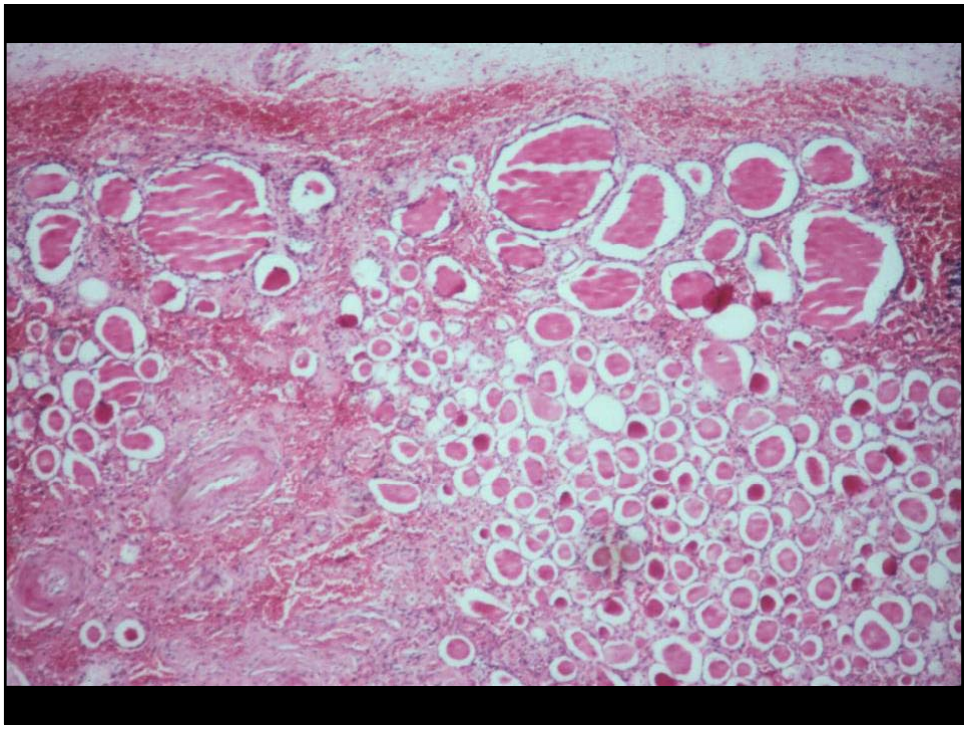
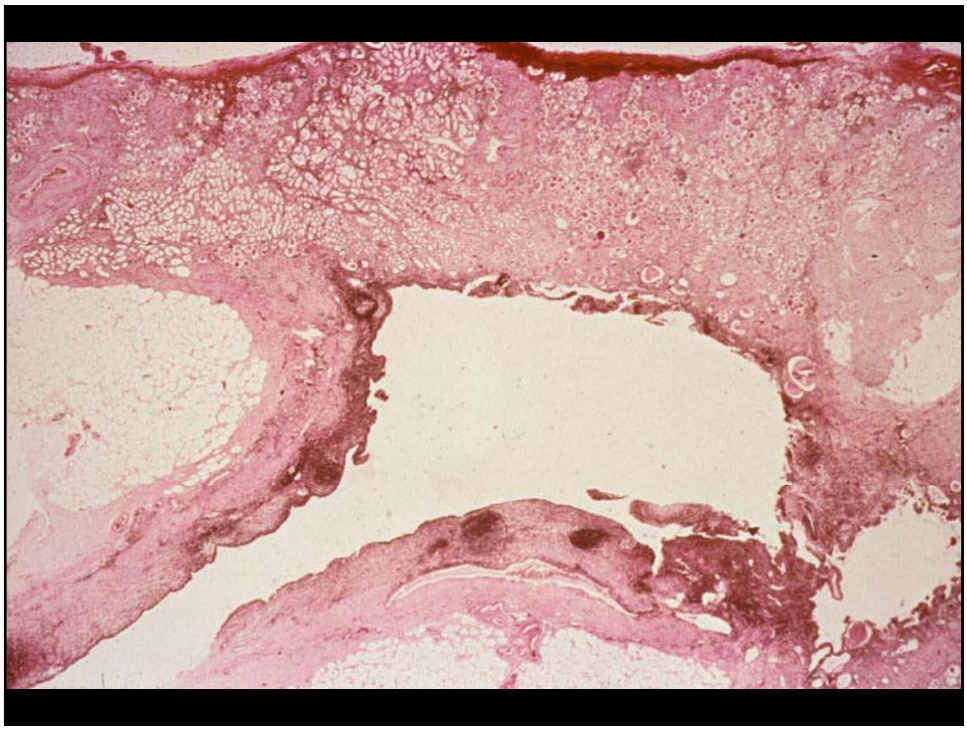
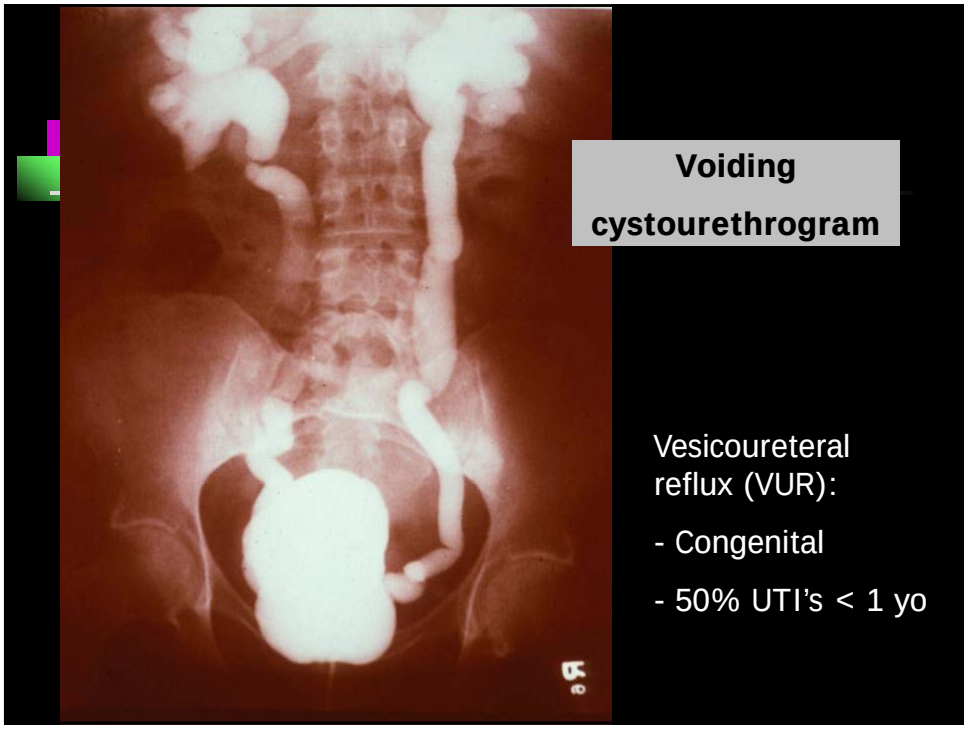




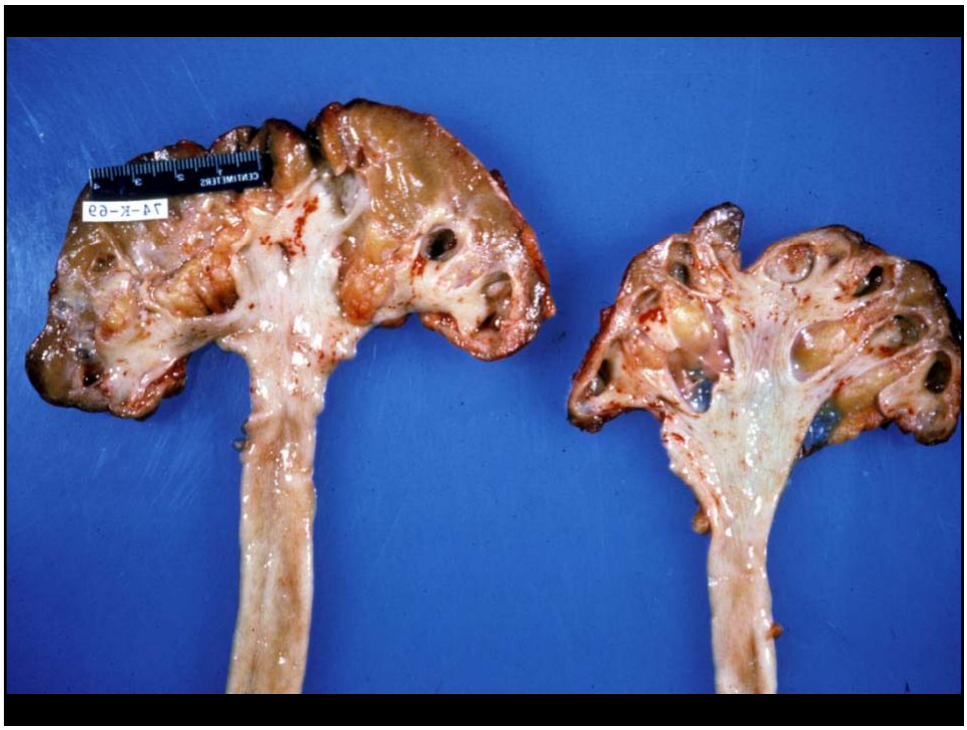




Voiding cystourethrogram

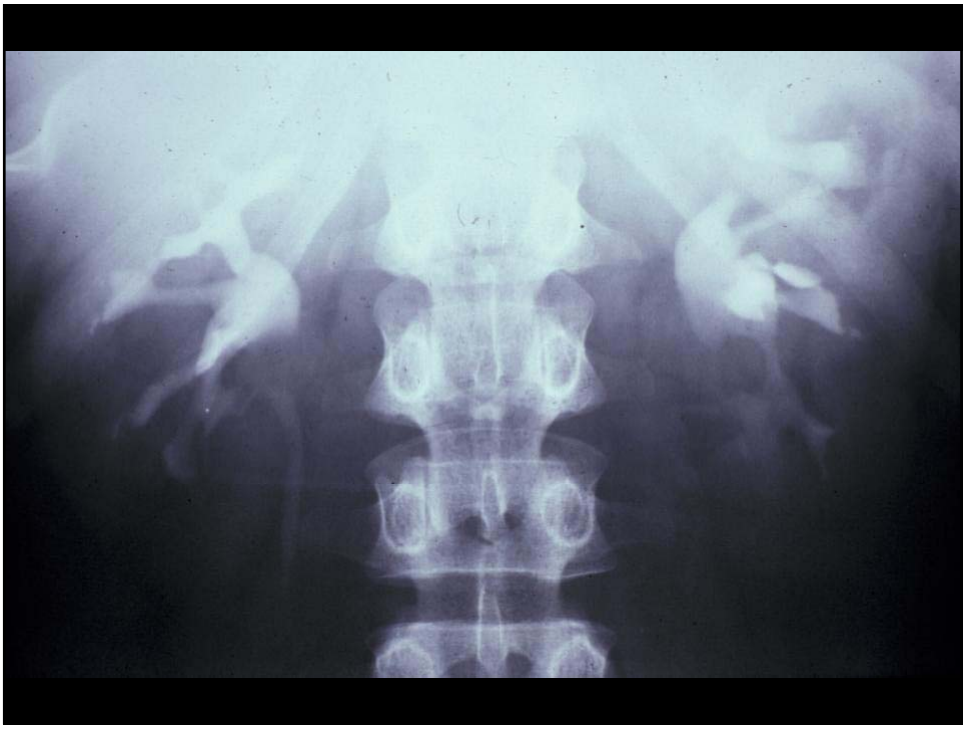
Vesicoureteral reflux (VUR):

- Congenital
- 50% UTI's < 1 yo



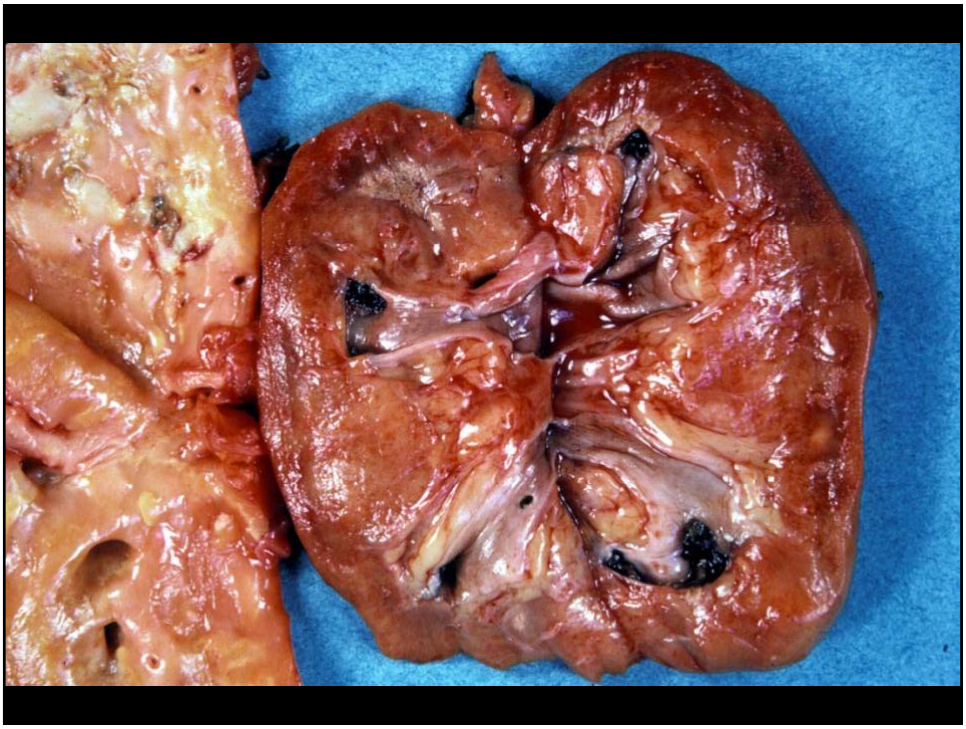
Case 4

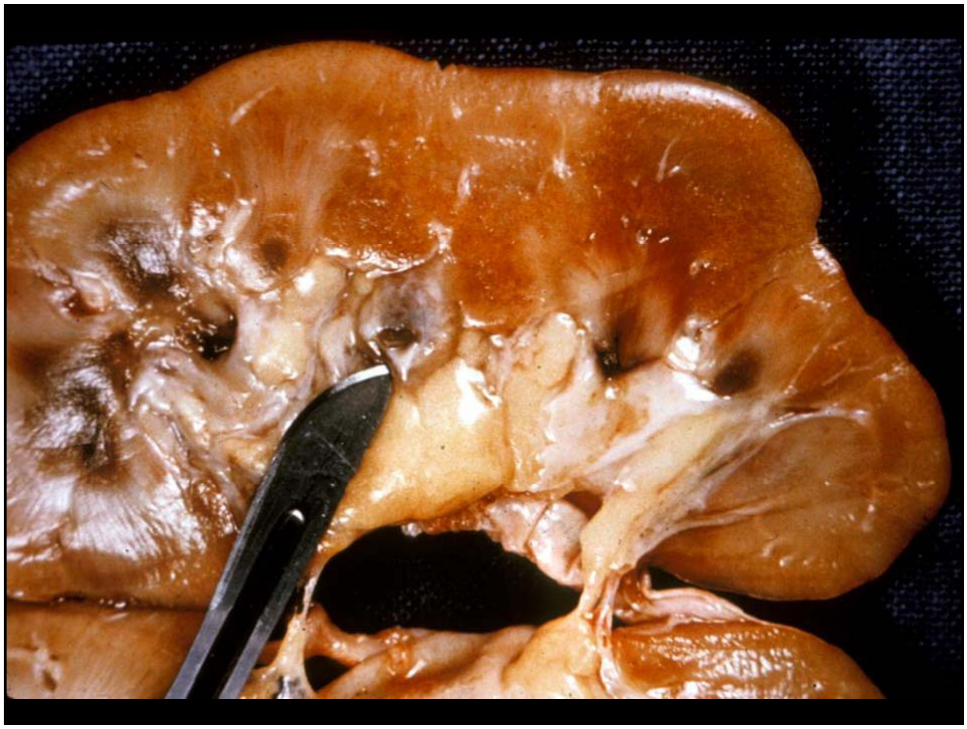
- A 52 yo F has had rheumatoid arthritis for 20 yrs and has been taking aspirin, tylenol, and NSAID's daily but no other medications for her disease. She develops R flank pain, but no fever , chills, or dysuria. Physical examination shows marked deformities of her joints but no edema.
- Labs: U/A tr protein, few rbc and many wbc. BUN 32 mg/dl, Pcreatinine 2.4 mg/dl, 24 hr prtoein 0.4 g/d, and negative or normal tests for complement, anti-DNAantibody, HBV, BS, HCV, etc. Urine culture is "no growth" after 2 days.
- An Intravenus Urogram is performed.



Case 4

- Is bacterial pyelonephritis the cause of this patients back pain?
- What are other possible causes?
- What other diseases could cause this picture?





Analgesic Nephropathy

An international disease (Australia, Switzerland, Scandinavia, USA)

Abusers and Users – Headaches and Arthritis

Female:Male 6:1

Large amounts over prolonged time periods

Renal abnormalities

- sterile pyuria
- only mild proteinuria and hypertension
- Decreased concentration ability
- Decreased net acid excretion
- Salt wasting
- Papillary necrosis

Patients can recover function if they stop analgesic use

Causes of Papillary Necrosis

- **Obstructive pyelonephritis**
- **Sickle Cell Anemia**
  - **medulla leads to sickling**
  - **sickling leads to medullary ischemia**
- **Analgesic abuse (phenacetin*)**
  - **increased risk with combinations**
  - **direct toxicity and ASA-induced PG deficiency**
- **Diabetes Mellitus**

NSAIDs

- Multiple patterns of renal disease
  - Acute interstitial nephritis
  - Acute tubular necrosis
    - Loss of PG vasodilation / precip ATN in the setting of volume depletion
  - Minimal change disease (rarely MG)
  - Papillary necrosis
- Same nephrotoxicity for COX-2 inhibitors