

Diagnostic Tests in Renal Disease

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Case One

- A 27 year old woman joins a group of friends to climb Mt. Washington 3 days after finishing her internship. On reaching the top she notes severe muscle pain and dark brown urine.
- The muscle pain grows worse and the brown urine continues. Three days after the climb, she goes to the emergency room. Urinalysis is dipstick positive for blood. There are no red cells on microscopic exam.
- What's going on here?

- When bubbles settle on the surface of the urine, they indicate disease of the kidney, and that complain will be protracted.
 - Hippocrates

Urinalysis

- Hippocrates (460-355 BC) bubbles in the urine indicate kidney disease
- The Sanskrit literature (100 BC) described sweet urine that attracted black ants
- Galen 129-200: urine is a filtrate of the blood. Fluid in = urine out
- 11th century: 1st 24 hr urine

Urine Color

- **Orange:** bilirubin, rifampin, pyridium
- **Brown:** myoglobin, porphersins, bilirubin
- **Pink/red:** blood, hemoglobin, porphersins
- **Blue:** methylene blue

Specific Gravity and Osmolality

- **Weight of dissolved particles in the urine compared with distilled water**
- **(1.001-1.035)**
- **Osmolality: number of particles dissolved in urine (40-1400)**

High Specific Gravity

- Concentrated urine
- Glucose
- Protein
- Dextrans
- Radiographic contrast

Glucose

- Replaced by finger stick glucose for monitoring diabetes
- Glucose in the urine indicates serum glucose > 170 mg/dl (Higher with age and decreased GFR, severe volume contraction)
- Renal Glycosuria

Ketones

- **Fasting (starvation ketosis)**
- **Ketoacidosis**

Occult Blood

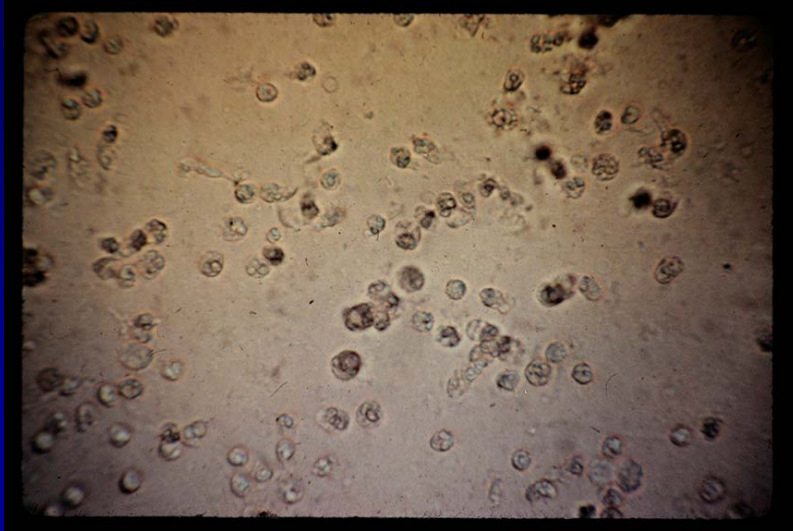
- **Red cells**
- **If dipstick is positive for blood and microscopic shows no RBCs**
 - **Hemoglobin**
 - **Myoglobin**
 - **Very dilute urine**

Case 1

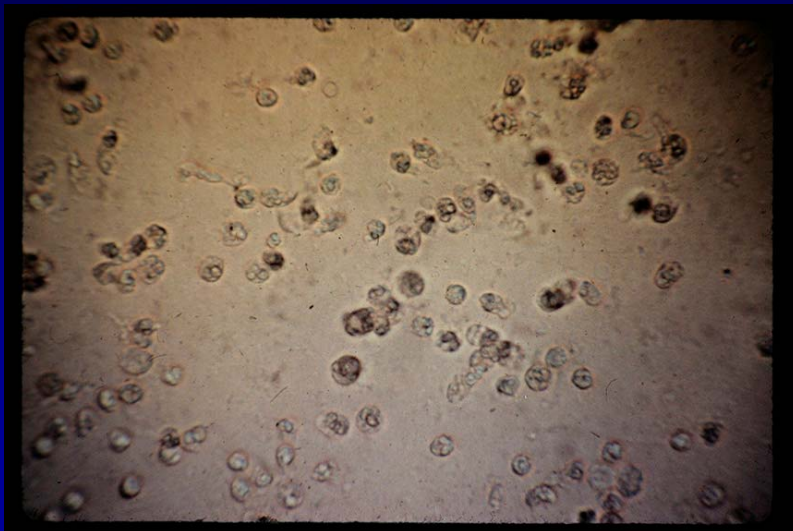
- The woman knew her diagnosis when she first saw brown urine.
- Brown urine after extreme exercise particularly in someone who is deconditioned is classic presentation of rhabdomyolysis.
- ER visit was delayed because doctors make bad decisions about their own care.

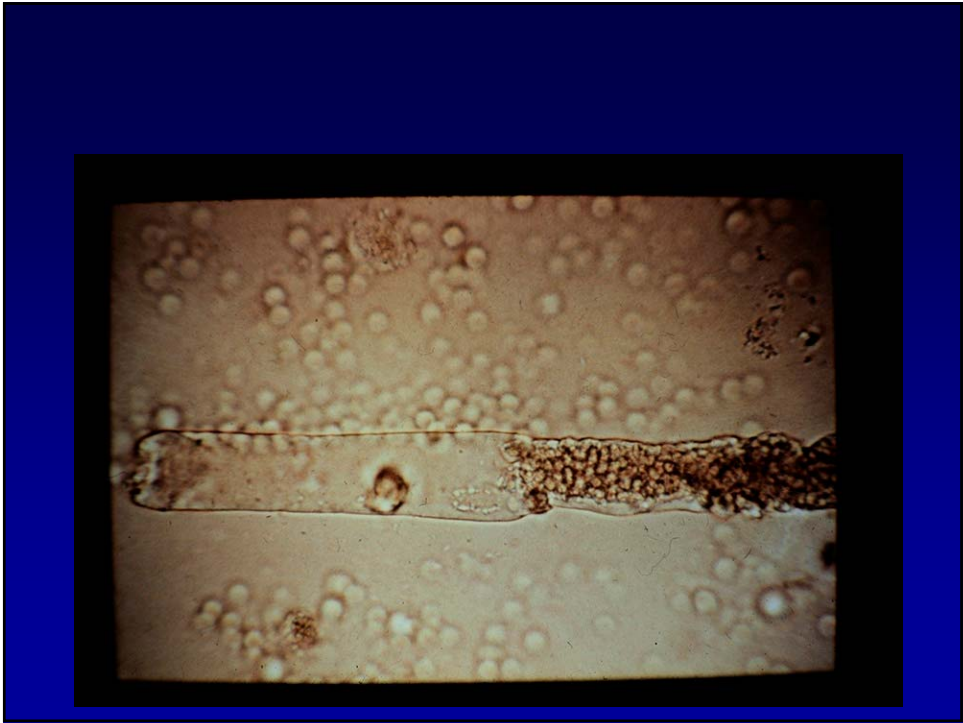
Microscopic Elements

- Cells
- Casts
- Crystals
- Bacteria
- Yeast

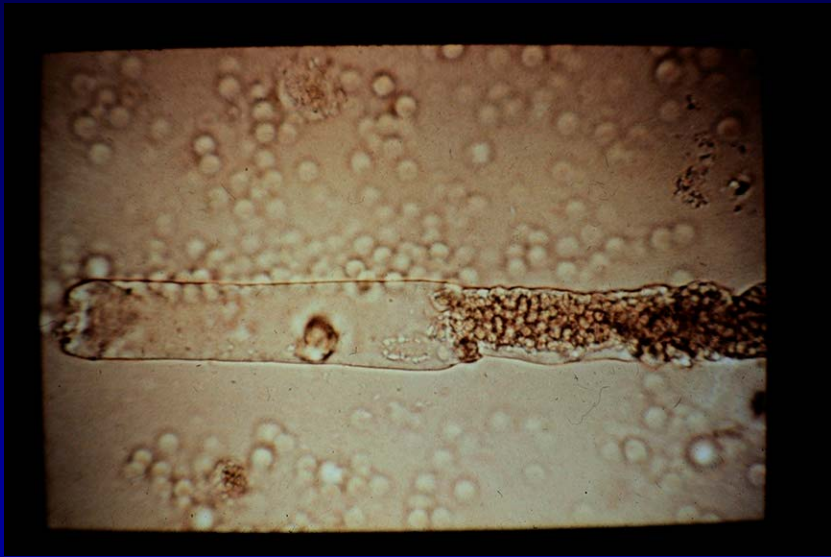


White Cells



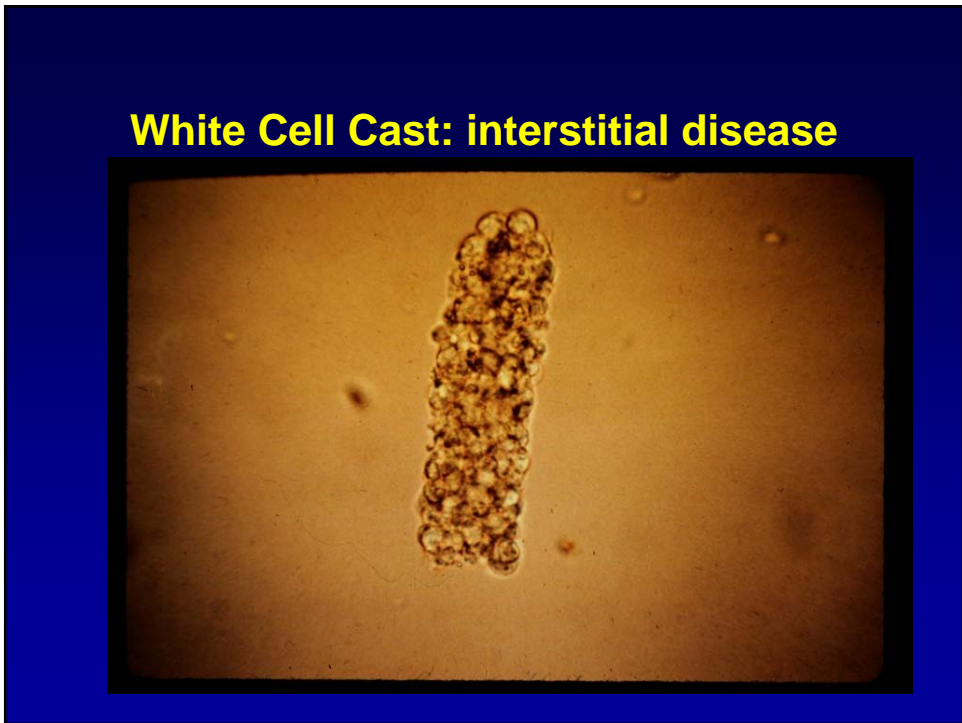


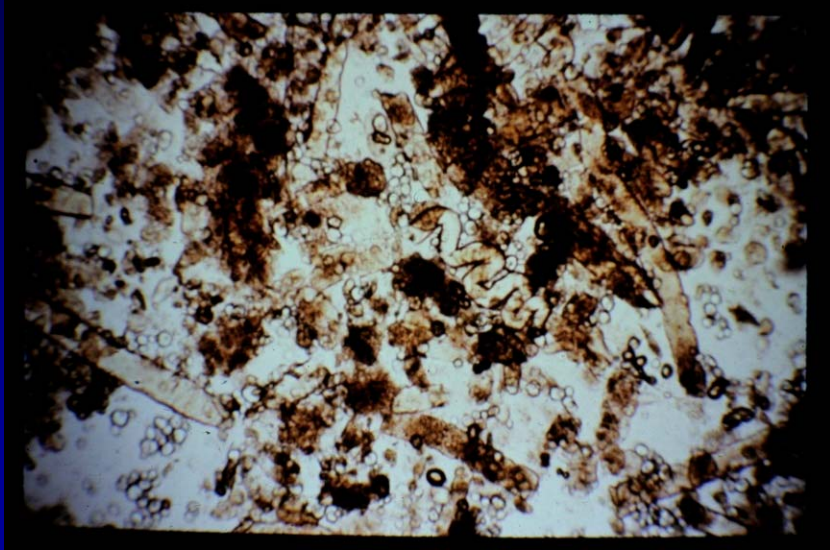
Red Cell Cast: Glomerular Disease



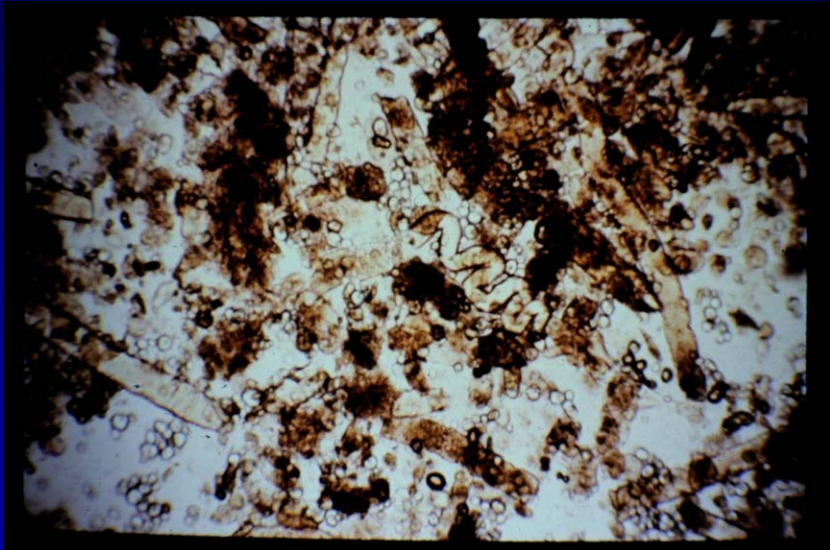


White Cell Cast: interstitial disease





Muddy Brown Casts: ATN



Urine Protein:Categories of persistent proteinuria

- **Overflow:** Capacity to reabsorb normally filtered protein in proximal tubules overwhelmed due to overproduction:e.g.light chains,hemoglobinuria and myoglobinuria
- **Tubular proteinuria:** Decreased reabsorption of filtered proteins by tubules due to tubulointerstitial damage ; usually <2 gm
- **Glomerular proteinuria:** Microalbuminuria to overt proteinuria usually>3.5 gm

Proteinuria

- **>150-300 mg/24 hrs indicates renal disease. Increase to 300 mg/dl in pregnancy**
- **> 3.5 grams: glomerular disease**
- **Tubular proteinuria**
- **Microalbuminuria: >30 mg of albumin in 24 hrs. Screening for diabetic nephropathy**

Dipstick for Protein

- **Proteinuria without renal disease: exercise, fever, high venous pressure**
- **Depends on Urine concentration**
- **Does not detect Bence-Jones proteins**

Protein: Creatinine Ratio

- **Protein : Creatinine ratio estimates 24 hr urine protein**
- **Useful for children**
- **Hard to collect 24 h urine even in adults**
- **Protein: creatinine ratio should be <0.15**
- **Microalbumin in mg : creatinine in grams ratio should be less than 30**

Case 2:

- A 35 year old primagravida develops acute renal failure after developing HELLP syndrome during her 1st pregnancy.
- After 3 months on dialysis, she begins to recover and over the next 7 years her serum creatinine comes down to 1.3 mg/dl

Case 2

- Her lawyer argues that she has a calculated GFR of 49 cc/min giving her stage 3 kidney disease. She therefore has a 90% chance of developing end stage renal disease and even if she doesn't, she has an increased risk of heart disease and should be compensated 3 million dollars.

Creatinine

- **1926: Creatinine used as a marker of filtration**
- **Assumptions**
 - Creatinine production is constant
 - Creatinine is removed only by the kidney
 - Creatinine is filtered but not secreted or reabsorbed

Creatinine Production

- **Meat contains 3.5 to 5 mg/g of creatine (68-98 mg/ounce)**
- **65% converted to creatinine during cooking**
- **A quarter pounder can generate 350 mg of creatinine.**
- **Serum creatinine may rise by 0.5 mg/dl 2 hrs after eating a meat meal.**
- **Levey, KI 38: 167-184, 1990**

Factors affecting Endogenous Creatinine Production

- **Age**
- **Sex**
- **Race**
- **Muscle Mass**
- **Renal disease**

Extra Renal Creatinine Removal

- **Removal of creatinine in feces increases with decreasing renal function**
- **Extrarenal Cr loss: 776-1752 mg/day**
- **16-66% loss**
- **Levey, KI 38: 167-184, 1990**

Tubular Secretion of Creatinine creatinine clearance/GFR

- GFR.80cc/min 1.16
- GFR 40-80 cc/min 1.57
- GFR , 40 cc/min 1.92
- Levey, KI 38: 167-184, 1990

Formulas for Estimate GFR MDRD Equation

- $GFR = 175 \times (Scr)^{-1.154} \times (age)^{-0.203}$
- X .742 for women
- X 1.212 for blacks

Cockcroft-Gault

- $(140 - \text{age}) \times \text{weight} / \text{serum creatinine} \times 72$
- For women multiple $\times .85$

Limitations of Formulas

- Not useful in a non steady state
- Don't use in hospitalized patients
- May not be accurate in people with normal renal function

Precise Measurement of GFR

- Inulin Clearance: gold standard but cumbersome
- Renal Scan with Tc-DTPA is not accurate
- Radioisotope clearance
 - Iothalamate
 - EDTA
 - Tc-DTPA

Blood Urea Nitrogen

- Other countries use blood urea which is about 2x BUN
- Predicts when a person will feel sick
- Affected by variable production and reabsorption

Causes of disproportionate Increase in BUN

- **Increased production**
 - High protein intake: diet or TPN
 - Corticosteroids
 - Tetracycline
 - Blood: especially GI
- **Decreased Excretion**
 - Obstruction
 - Prerenal states

Landmark BUNs

- 100 mg/dl: most people have some symptoms
- 150 mg/dl: 95% of people can no longer deny symptoms
- 330 mg/dl: highest I've seen
- 595 mg/dl: highest I've heard of

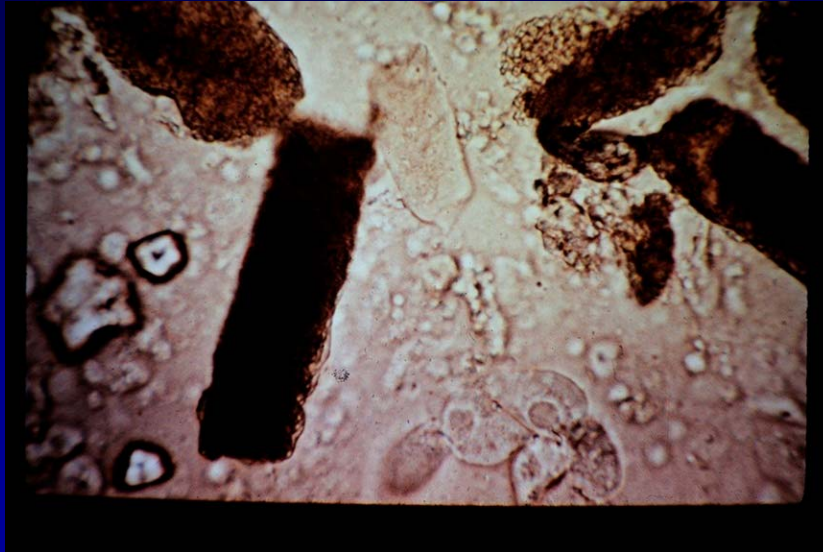
Stages of Kidney Disease

- Stage 1: Normal GFR with proteinuria or urine sediment changes
- Stage 2: GFR 60-90 cc/min
- Stage 3: GFR 30-59 cc/min
- Stage 4: GFR 15-29 cc/min
- Stage 5: GFR < 15 cc/min

Pre Renal Azotemia vs ATN

- | | |
|---------------------------------|------------------------------------|
| • Pre Renal | • ATN |
| • Urine Osm:> 500 | • Urine Osm < 350 |
| • Urine Na < 20 | • Urine Na > 40 |
| • Urine:plasma urea nitrogen >8 | • Urine: plasma urea nitrogen: < 3 |
| • Urine:plasma creatinine > 40 | • Urine:plasma creatinine < 20 |
| • FENa < 1% | • Fe Na > 1% |

Muddy Brown Casts



Fractional Excretion of Sodium

- The fraction of filtered sodium which ends up in the final urine

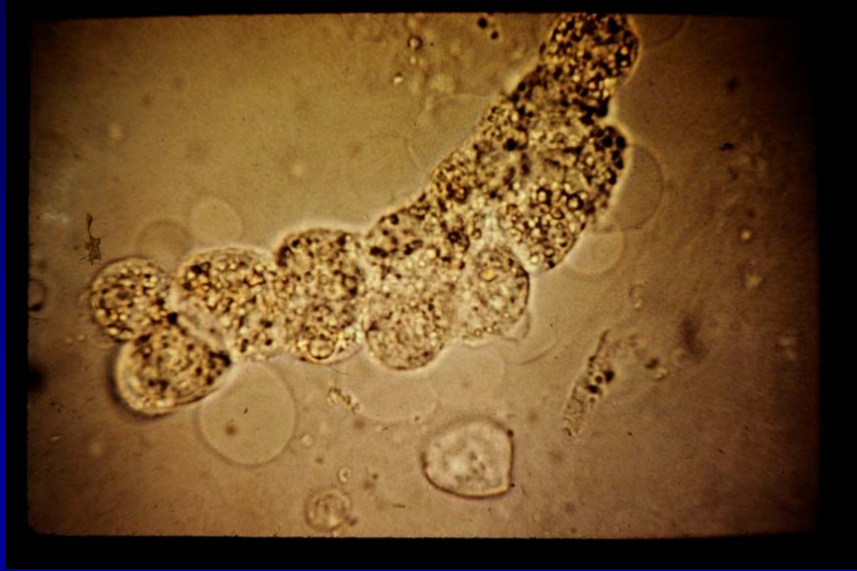
$$\frac{\text{Urine [Na]} \times \text{Plasma [Creatinine]}}{\text{Plasma [Na]} \times \text{Urine [Creatinine]}} \times 100$$

Fractional Excretion of Sodium

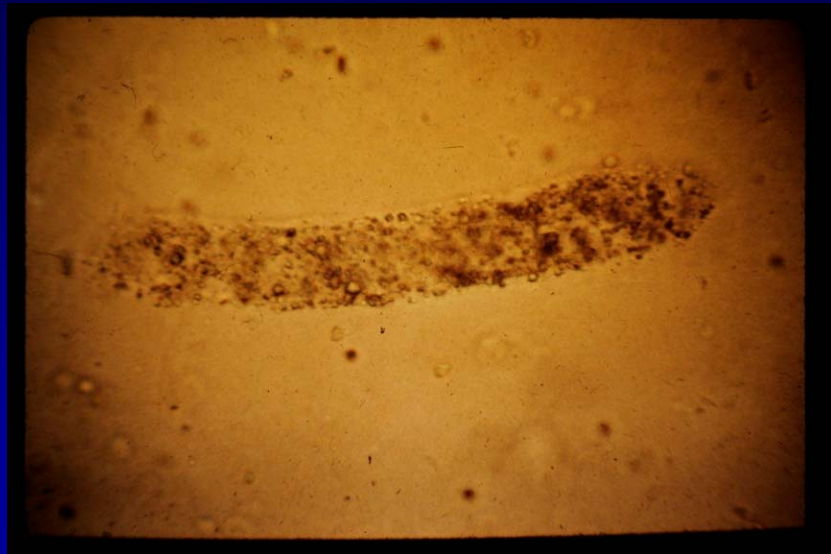
- Pre Renal azotemia vs ATN not other intra renal diseases
- In the setting of oliguria. Normal person can have FeNa >1%
- Higher in chronic renal disease

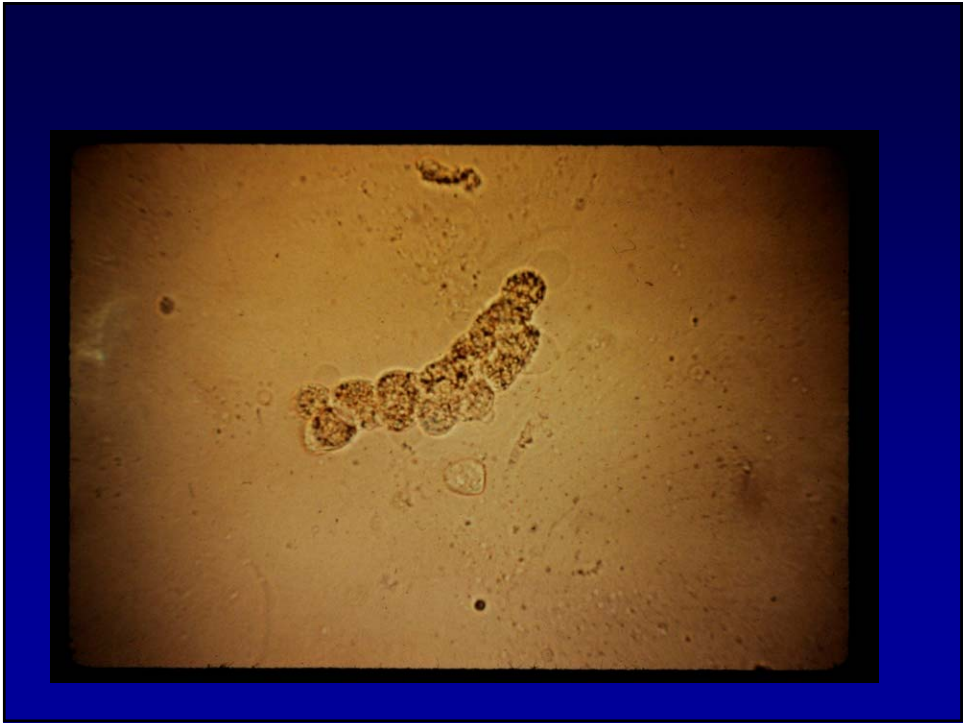


Oval Fat Body Cast



**Oval Fat Body Cast
Polarized Light**

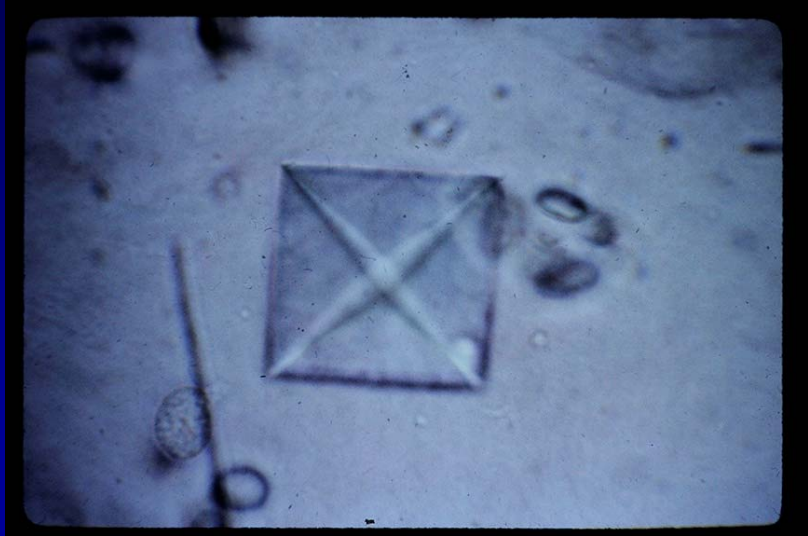






Red Cell Cast: Glomerulonephritis





Amorphous Phosphate

