Urine for a Treat: Become a Piss Prophet in One Easy Lesson on Urinalysis

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MAIN LEARNING OBJECTIVE

- Recognize the importance of urinalysis in the evaluation and management of acute and chronic kidney diseases.

URINALYSIS is awesome!

OUTLINE

- Brief historical perspective on urinalysis
- Discuss collection, preparation, and performance of the procedure
- Gross inspection and chemstrip (dipstick) interpretation
- Case-based examples of diagnostic usefullness of microscopic examination of urine

Why Do a Urinalysis?

"When the patient dies the kidneys may go to the pathologist, but while he lives the urine is ours. It can provide us day by day, month by month, and year by year with a serial story of the major events within the kidney."
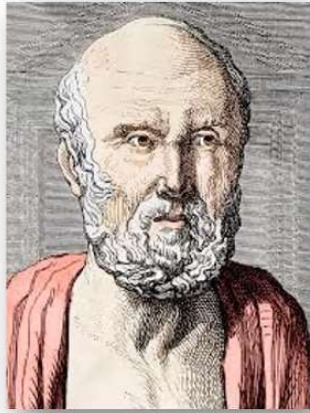Dr. Thomas Addis
(1881-1949)

- "Fluid Biopsy" of the Kidney "Biomarker" of kidney disease
- Economical and Quick
- Diagnose and Monitor Kidney and Urinary Tract Diseases
- Detect Systemic Disease

HISTORICAL PERSPECTIVE

In ancient times, a large part of medical practice began with an examination of the urine:
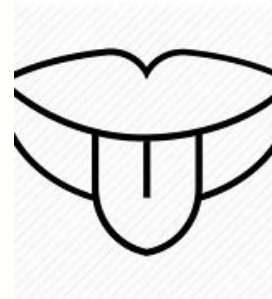
HISTORICAL PERSPECTIVE

Hippocrates
(460-375 BCE)

"….when bubbles settle on the surface of the urine, they indicate disease of the kidneys…"

Galen
(129-216)

"….kidneys play a role in the balance of body humors…"

Theophilus Protospatharius
(610-641)

Wrote *De Urinis* about macroscopic urine exam:
"…urine is a filtrate of the blood…"

HISTORICAL PERSPECTIVE

Jerusalem Code 1090:

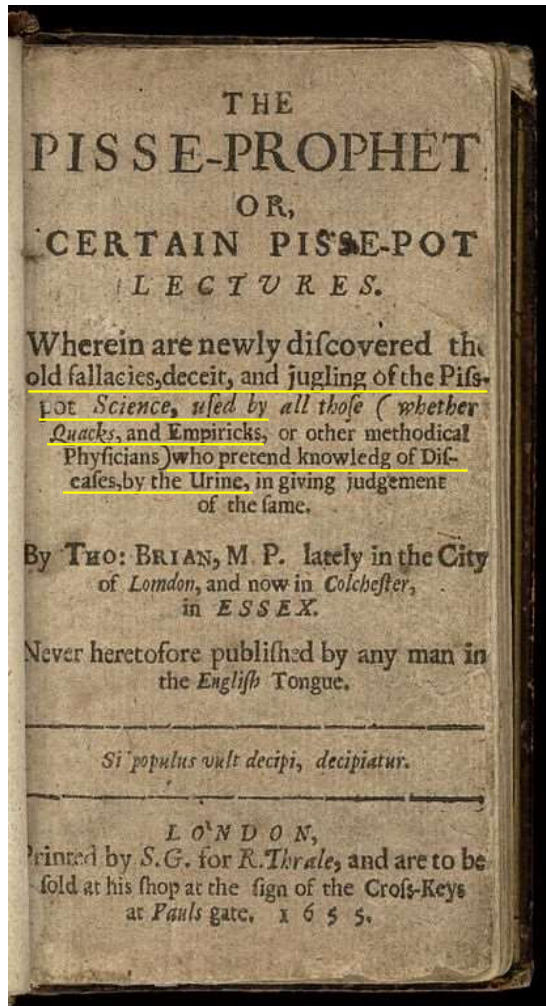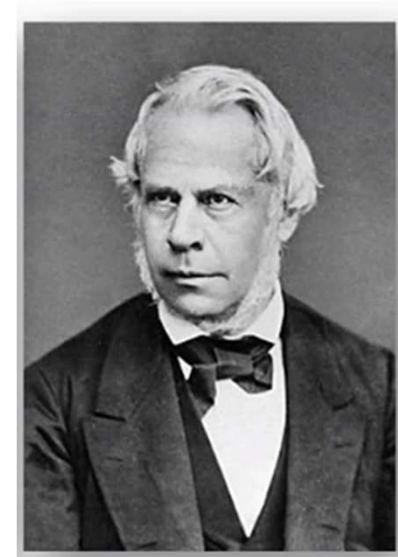"…Failure to examine the urine would expose the physician to public beatings…"

Pisse Prophets

Matula

HISTORICAL PERSPECTIVE

THE PISSE-PROPHET OR, CERTAIN PISSE-POT LECTURES.

Wherein are newly discovered the old fallacies, deceit, and jugling of the Piss-pot Science, used by all those (whether Quacks, and Empiricks, or other methodical Physicians) who pretend knowledg of Diseases, by the Urine, in giving judgement of the same.

By Tho: Brian, M. P. lately in the City of London, and now in Colchester, in ESSEX.

Never heretofore published by any man in the English Tongue.

Si populus vult decipi, decipiatur.

LONDON, Printed by S. G. for R. Thrale, and are to be sold at his shop at the sign of the Cross-Keys at Pauls gate. 1655.

Pierre Rayer
(1793-1867)

Established urine microscopy

Jakob Henle
(1809-1885)

Made connection between histology and urine tubular casts

PREPARATION, COLLECTION, AND PERFORMANCE OF A URINALYSIS

PREPARATION AND COLLECTION OF THE SPECIMEN

- First-voided morning specimen is best
  - Random specimens may be too dilute, yielding false negative results
- Midstream sample after cleansing the urethral meatus minimizes contaminating elements
- If specimen is kept at room temperature: examine within 2h; otherwise refrigerate specimen up to max. of 4 hours
  - Prolonged delay, esp. with alkaline pH or low osmolality, causes cell lysis and cast dissolution

Manoni F. Clin Chem Lab Med 2012;50(4):679-84
Fogazzi GB. Am J Kidney Dis 2008;51(6):1052-67

# PERFORMANCE OF A URINALYSIS

- Visual inspection
  - Color
  - Transparency
- Chemstrip (dipstick) evaluation
- Microscopic examination of urine sediment
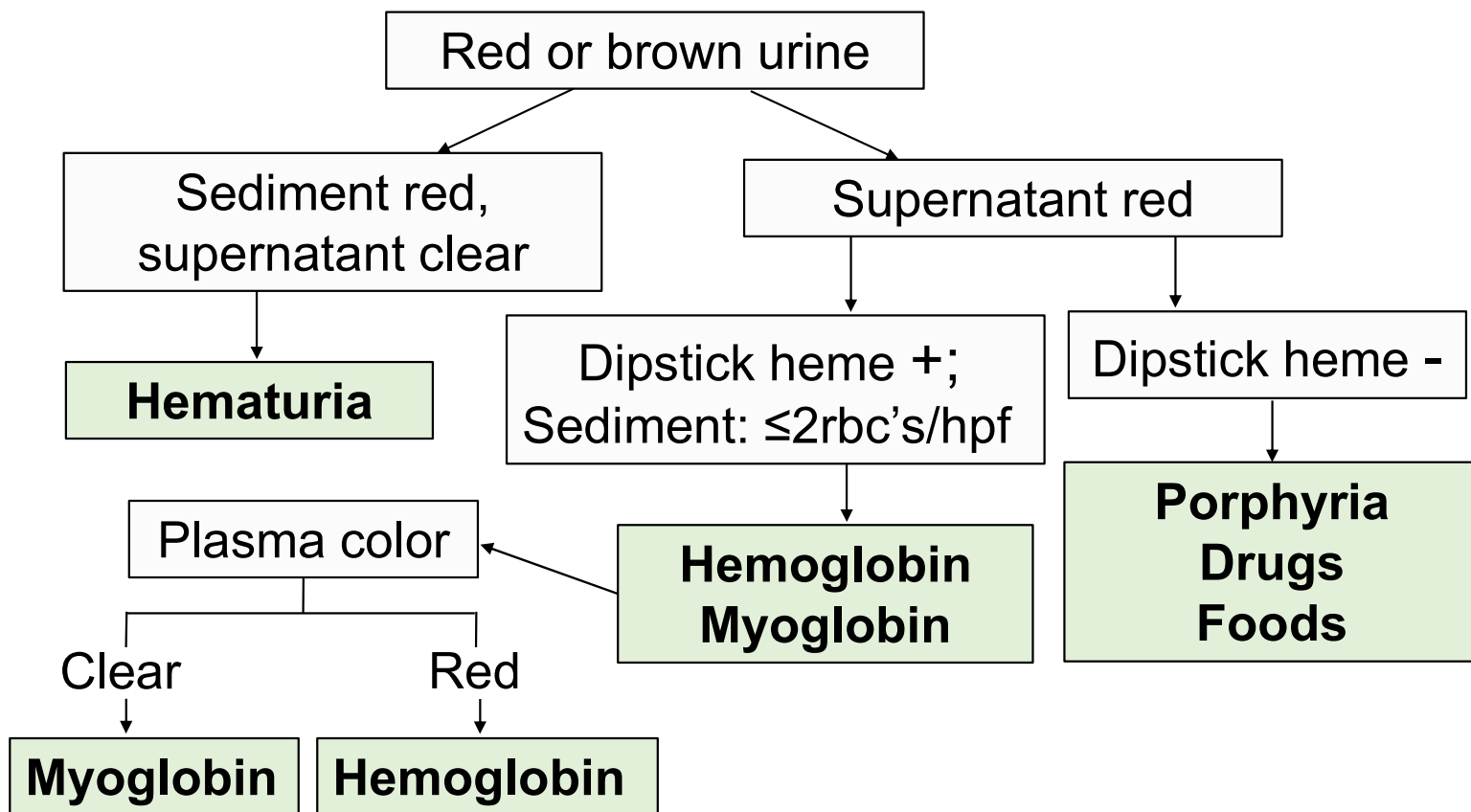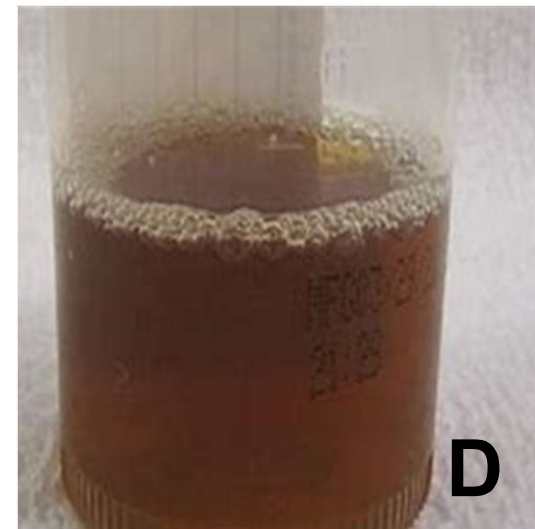
VISUAL INSPECTION

- Color
  - Normal: Yellow (pale straw to deep amber; reflects state of hydration)
  - Abnormal: Red, orange, brown-black, white, green, blue, purple
    - In 1487, Bartolomeo Montagnana (1380–1460) a professor at the University of Padua, published a treatise and a chart showing 21 shades of urine!
- Transparancy
  - Normal: Transparent (can read print through urine in a clear glass container)
  - Turbid or cloudy: RBCs, WBCs, squamous epithelial cells, bacteria, yeast, crystals, sperm, mucus
- Frothy: Proteinuria

ABNORMAL COLOR

COLOR	CAUSES
Red (pink to reddish brown or cola-color)	Hematuria, hemoglobinuria, myoglobinuria, acute intermittent porphyria, rifampin, phenytoin, senna, beets, blackberries, rhubarb
Orange	Phenazopyridine (Pyridium™}, rifampin
Yellow-brown, brown, brown-black	Vitamin B complex, bilirubin, sulfasalazine (Azulfidine™), metronidazole, nitrofurantoin, chloroquine
Green to bluish-green	Phenols - propofol, promethazine (Phenergan™; indomethacin, methylene blue, amitriptyline, cimetidine, pseudomonas UTI
Purple	Bacteriuria in longstanding catheterized patients with alkaline urine: indoxyl → indigo (blue) + indirubin (red) → purple color
White (milky)	Pyuria, phosphate crystals, chyluria, propofol (milky pink due to uric acid crystals)
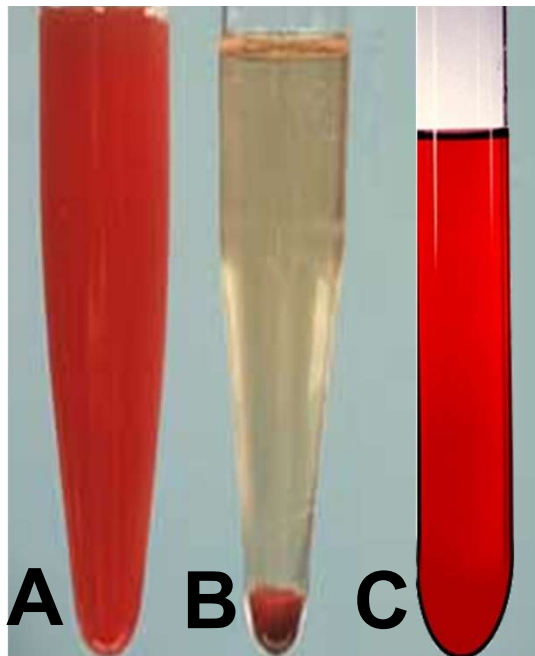
A. Uncentrifuged: ⎤
B. Centrifuged: ⎦ Lower tract hematuria
C. Hemoglobinuria, myoglobinuria, acute intermittent porphyria
D. Renal hematuria, hemoglobinuria or myoglobinuria

Red or brown urine

Sediment red, supernatant clear → **Hematuria**

Supernatant red

Dipstick heme +; Sediment: ≤2rbc's/hpf → **Hemoglobin Myoglobin**

Dipstick heme − → **Porphyria Drugs Foods**

Plasma color

Clear → **Myoglobin**

Red → **Hemoglobin**

TECHNICOLOR URINE

Propofol

Pyridium™

Pyuria

Bilirubin

Bacteriuria
+ alkaline pH

CHEMSTRIP (DIPSTICK)
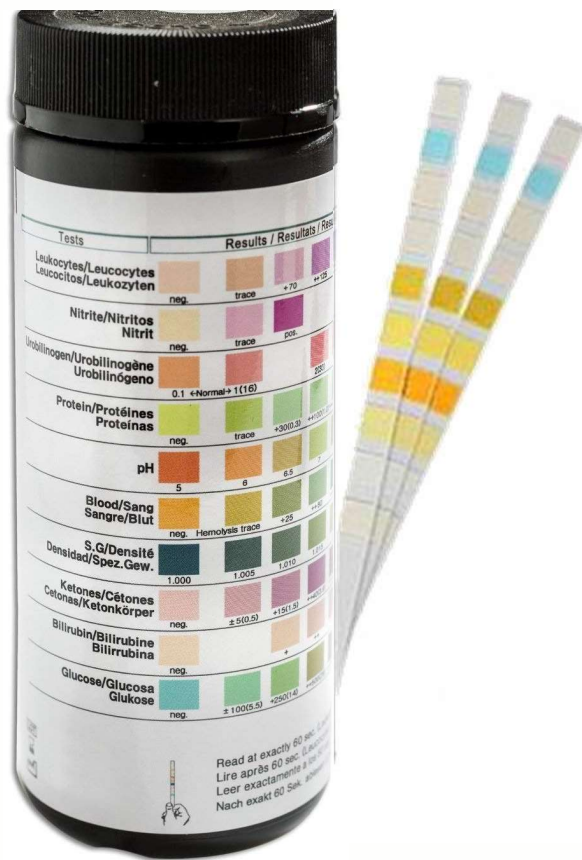
Specific Gravity

pH

Protein

Glucose

Ketones

Blood

Leukocyte Esterase

Nitrates

Bilirubin

SPECIFIC GRAVITY

Normal: 1.002-1.035: Reflects state of hydration

Impaired concentration

- Diabetes insipidus
  - Central or nephrogenic
- Chronic kidney disease
- Diuretics

Impaired dilution

- Dehydration
- Inappropriate ADH secretion (SIADH)

SPECIFIC GRAVITY – PITFALLS OF DIPSTICKS

- Insensitive to **nonionic** solutes
  - Underestimates high s.g. due to glycosuria and nonionic contrast agents
- Underestimates s.g. with urine pH >6.5
- Overestimates s.g. with protein concentration >7 g/L

∴ Use refractometer or osmometer for accuracy
  - These measure nonionic and ionic molecules

URINE pH

Normal: 4.5-8.0; usually 5-6.5

Persistently Low pH

- Metabolic acidosis
- Chronic ascorbic acid ingestion (vitamin C)
- Starvation or ketogenic diet
- Uric acid nephrolithiasis (low pH favors precipitation)

Persistently High pH

- Metabolic alkalosis
- Urea-splitting bacteria
  - True infection
  - Bacterial overgrowth in vitro due to delay in analysis
- Distal renal tubular acidosis (pH persistently >5.5)

GLUCOSE

- Normally absent
  - Renal threshold for glycosuria is blood glucose >180 mg/dL
- Present in:
  - Diabetes mellitus, uncontrolled
  - Renal glycosuria – blood glucose is normal
    - Genetic proximal tubular defect
    - Sodium-glucose cotransporter 2 inhibitors (SGLT2 inhibitors)
- False negative dipstick reaction
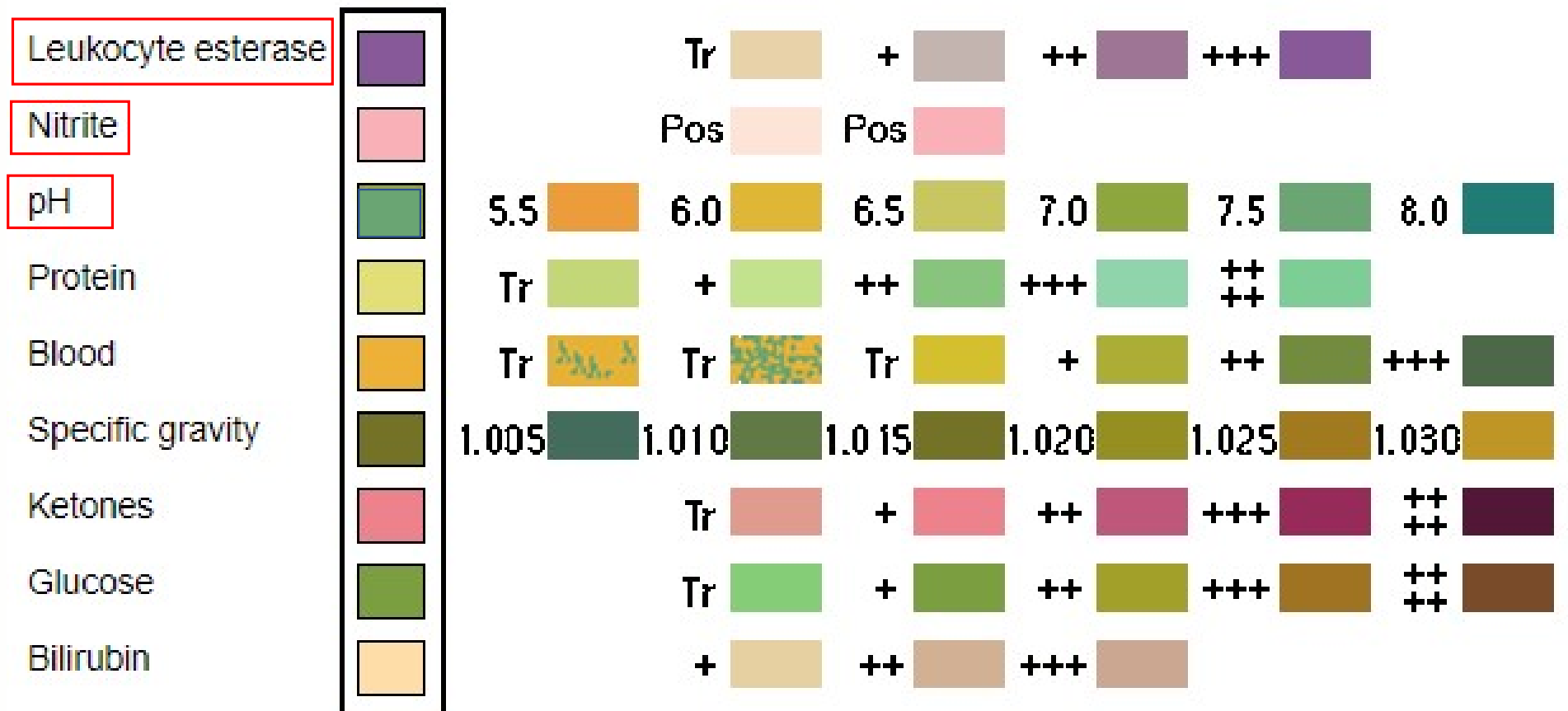 - Ascorbic acid in urine

LEUKOCYTE ESTERASE and NITRITE

Leukocyte esterase (LE)

- Detects neutrophils in urine

- Sensitivity 80-90% in diagnosis of UTI compared to urine culture

- Positive with sterile pyuria
  - Chlamydia urethritis
  - Nephrolithiasis
  - Glomerular and interstitial nephritis

- False positive: vaginal contamination

Nitrite

- Detects gram negative bacilli

- Sensitivity 50% for UTI compared to urine culture; increases with positive LE

CHEMSTRIP (DIPSTICK)

Leukocyte esterase		Tr		+		++		+++			
Nitrite		Pos		Pos							
pH		5.5		6.0		6.5		7.0		7.5	8.0
Protein		Tr		+		++		+++		++++	
Blood		Tr		Tr		Tr		+		++	+++
Specific gravity		1.005		1.010		1.015		1.020		1.025	1.030
Ketones		Tr		+		++		+++		++++	
Glucose		Tr		+		++		+++		++++	
Bilirubin		+		++		+++					

PROTEINURIA - DEFINITIONS

- Normal total protein excretion ≤150 mg/day (av. 40-80 mg/day)
- Normal albumin excretion <30 mg/day (av. ≤10-15 mg/day)
- Moderately increased albuminuria (formerly microalbuminuria)
  - 30 to 300 mg/day (30-300 mg/g creatinine on spot urine)
- Severely increased albuminuria (aka overt proteinuria and formerly macroalbuminuria)
  - >300 mg/day (>300 mg/g creatinine on spot urine)

PROTEINURIA

Normal constituents	Excretion rate mg/day	% of total
Filtered Plasma Proteins		
Albumin	12	15
IgG, IgA, IgM, light chains	8	10
Other plasma proteins	20	25
Subtotal of plasma proteins	**40**	**50**
Non-Plasma Proteins		
Tamm-Horsfall protein (uromodulin)	**40**	**50**
Total protein (nl. ≤150 mg/day)	**80 ± 24 (1 SD)**	**100**

PROTEINURIA - LIMITATIONS of DIPSTICKS

- Measures total protein <u>concentration</u>
- Very influenced by state of hydration
  - False underestimation with very dilute urine
  - False overestimation with concentrated urine
- Semiquantitative (trace to 4+)
- Insensitive – misses pathologic moderately increased proteinuria (microalbuminuria): under ~300 mg/day
- Mainly detects albumin: Misses light chains (multiple myeloma) and other low molecular weight proteins
- False positive: iodinated contrast, blood, urine pH >7.0

STANDARD DIPSTICK for PROTEIN

Dipstick reading	Approximate daily protein excretion
Negative	0
Trace	150 mg/day (ULN)
1+	200 to 500 mg/day
2+	500 to 1500 mg/day
3+	2000 to 5000 mg/day
4+	≥7000 mg/day

PROTEINURIA – BEYOND THE DIPSTICK

KDIGO Guidelines:

Positive dipstick ≥1+: Confirm with quantitative test in ≤3 months

Persistent proteinuria ≥3 months = chronic kidney disease

Quantitative tests for proteinuria

- 24-hour urine collection
  - Cumbersome, often not collected properly
- Spot urine for albumin:creatinine ratio (nl. <30 mg/g)
  - Accurate estimate of 24-hour urine albumin excretion
- Spot urine for protein:creatinine ratio (nl. <0.2 g/g)
  - Consider using it when albumin:creatinine ratio is high (>300 mg/g)

MICROSCOPIC EXAMINATION

Time-honored way
Manual inspection

Current way
Automated analysis

COMPARISONS OF AUTOMATED vs. MANUAL EXAMINATION of URINE

- **References:** Lab Med 2016;4792):124-133; Biochem Med 2016;26(3):365-375
  - Am J Kidney Dis 2016;67(6):954-964; Lab Med 2014;45(4):e152-e155; Am J Kidney Dis 2005;46(5):820-829
- **Bottom line on automated exams:**
  - Good for identifying RBCs, WBCs, squamous epithelial cells, bacteria, hyaline casts, common crystals
  - **Less reliable for identifying renal tubular cells, transitional cells, pathologic casts, less common crystals, lipids**

  ∴**Don't rely on lab reports for decision making in patients with or suspected of having acute or chronic kidney disease.**

NORMAL URINE CONSTITUENTS

- Red cells---normal 0-2 or 3/hpf

- White cells---normal 0-4/hpf

- Renal tubular and/or bladder epithelial cells (if few; 0-3/hpf)

- Hyaline casts (if few; 0-2/lpf)

- Granular casts (if few; 0-2/lpf)

- Squamous epithelial cells (from vagina, vulva, urethra)

- Crystals in small numbers (e.g., CaOx, uric acid)

ABNORMAL URINE CONSTITUENTS

- Red cell casts

- White cell casts

- Oval fat bodies

- Renal tubular and/or bladder epithelial cells
  (if in large numbers; >3/hpf)

- Hyaline and/or granular casts (if in large numbers; >3/lpf)

- Crystals – +/- depending on clinical context

APPLYING URINALYSIS TO DIAGNOSIS OF KIDNEY DISEASE

Clinical information + Labs

Dipstick data **+** **Urine sediment**

Diagnosis
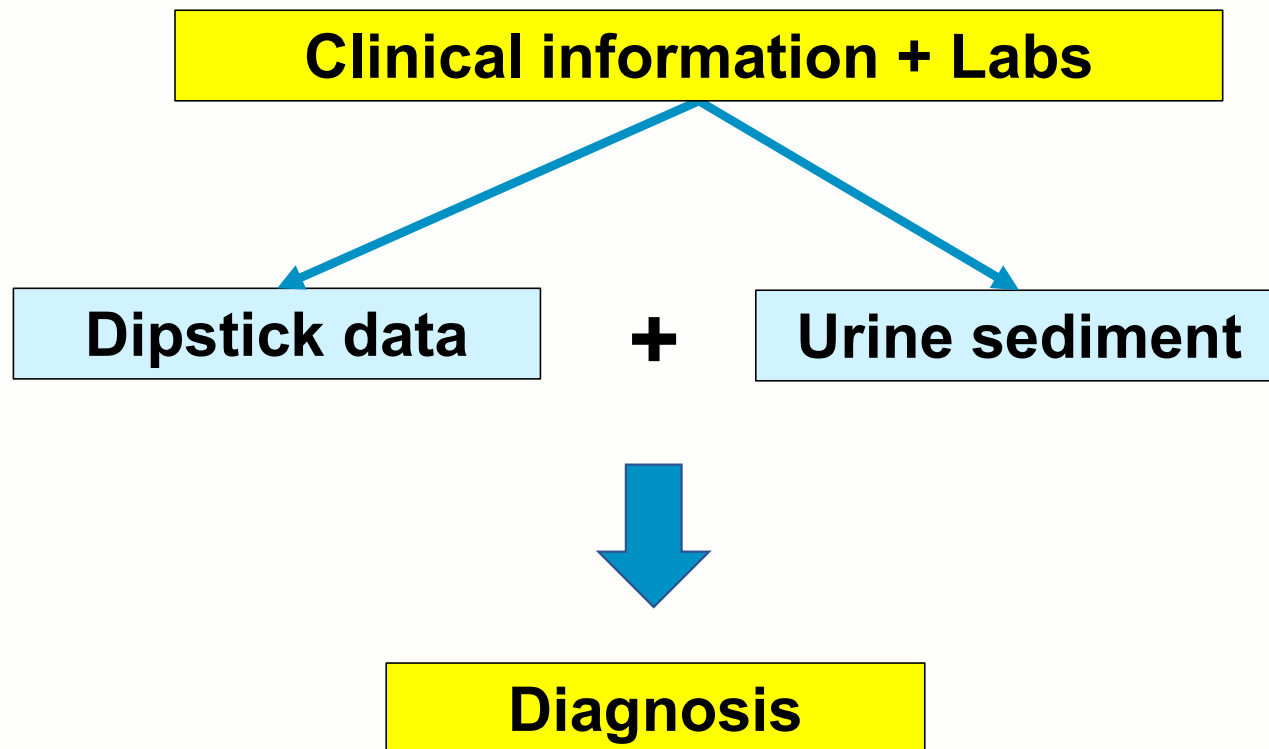
ACUTE KIDNEY INJURY

Prerenal
Glomerular
Tubular
Interstitial

Case 1

- **HPI:** A 70-year-old woman presents to the ED with intermittent vomiting, persistent diarrhea, fever, and abdominal pain that started 36 hours ago shortly after eating in a newly-opened neighborhood restaurant.

- **PMH:** Type 2 diabetes   **SH:** noncontributory

- **Meds:** Glyburide, acetaminophen prn arthralgias, vitamin D/calcium

- **Exam:** BP 100/60; P 104, T 100.5
  - Dry mucus membranes; skin warm and dry, no rashes
  - Neck veins flat
  - Lungs clear; cardiac exam normal except for tachycardia
  - Abdomen flat, hyperactive bowel sounds, mild diffuse tenderness, no rebound
  - Extremities – no edema, pulses 1+

- **Laboratory Findings:**
  - **Electrolytes:** Na+ 134, K+ 3.4, Cl 95, CO2 30

  - Glucose 100 mg/dL

  - BUN 40 mg/dL   Creat 2.0 mg/dL

  - **CBC:** Hb 13.5, WBC 11,500 with 80% neutrophils, 16% lymphs, 2% eos

  - **Urine Dipstick:** SG 1.025, pH 7.0, Protein trace, Blood neg., LE trace

Based on the clinical scenario and lab findings, what is the most likely diagnosis?

A. Acute tubular necrosis (ATN)

B. Acute interstitial nephritis

C. Acute membranoproliferative glomerulonephritis

D. Prerenal azotemia

E. Exacerbation of progressive chronic kidney disease

What would you expect to see in the urine sediment?

A. Renal tubular epithelial cells

B. Waxy casts

C. Fatty casts

D. Hyaline casts

E. White blood cells

Urine Sediment

What is the composition of hyaline casts and where are they formed?

Thick Ascending Limb of Loop of Henle

Site of secretion of Tamm-Horsfall mucoprotein (**uromodulin**)
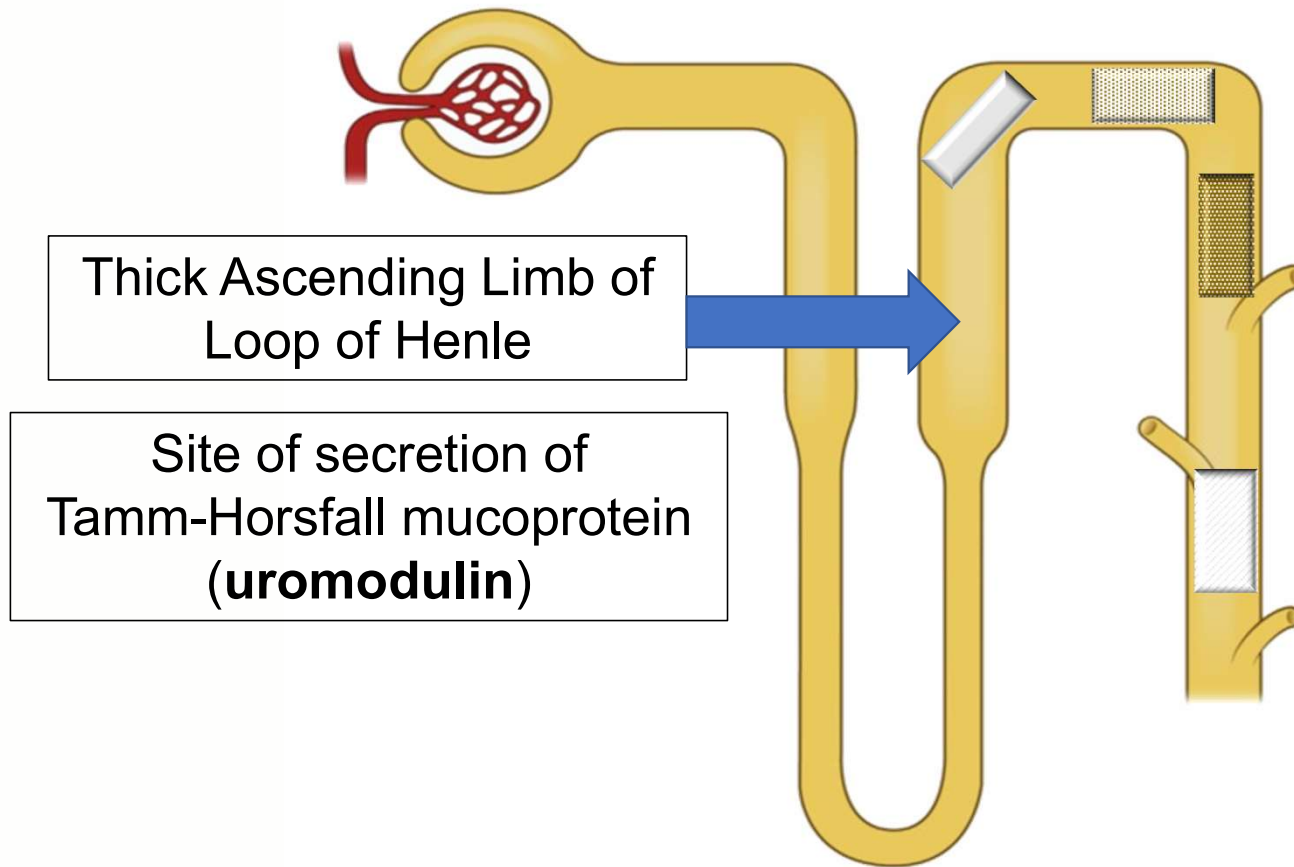
When can we see hyaline casts?

- Healthy people (in small numbers)
  - After strenuous exercise
  - In concentrated urine

- Diuretic therapy

- Many varieties of acute and chronic kidney disease (in larger numbers, in company of other abnormalities)

- Prerenal azotemia

Case 1

Clinical information/labs

- Vomiting and diarrhea x 3 days
- Abdominal pain, low grade fever
- ↑ BUN >> ↑ creatinine; leukocytosis
- Low BP, increased pulse rate

Dipstick data   **+**   **Urine sediment**

- SG 1.020
- Trace protein
- Hyaline casts

Diagnosis

Prerenal azotemia

Case 2

- **HPI:** 30-year-old woman presents with pain in her knees and hands, fatigue, mild intermittent febrile episodes, anorexia and weight loss over the past month. No prior h/o hypertension or kidney disease.

- **PMH:** Three miscarriages, DVT in left leg   SH: Noncontributory

- **Exam:** BP 150/100. Malar rash, tender fusiform swelling of finger joints, tender knees with mild effusion, and 1+ pedal edema.

- **Laboratory findings:**
  - CBC: Hb 10.0, WBC 11,000
  - BUN 35 mg/dL, creatinine 2.4 mg/dL
  - Anti-dsDNA +++
  - Anti-phospholipid Abs +++

  Urine dipstick:
  - SG 1.010
  - protein 2+
  - blood 3+
  - LE 2+

What do you see in this patient's urine sediment?

A. Budding yeast cells
B. Renal tubular epithelial cells
C. White blood cells
D. Dysmorphic red blood cells
E. Isomorphic red blood cells
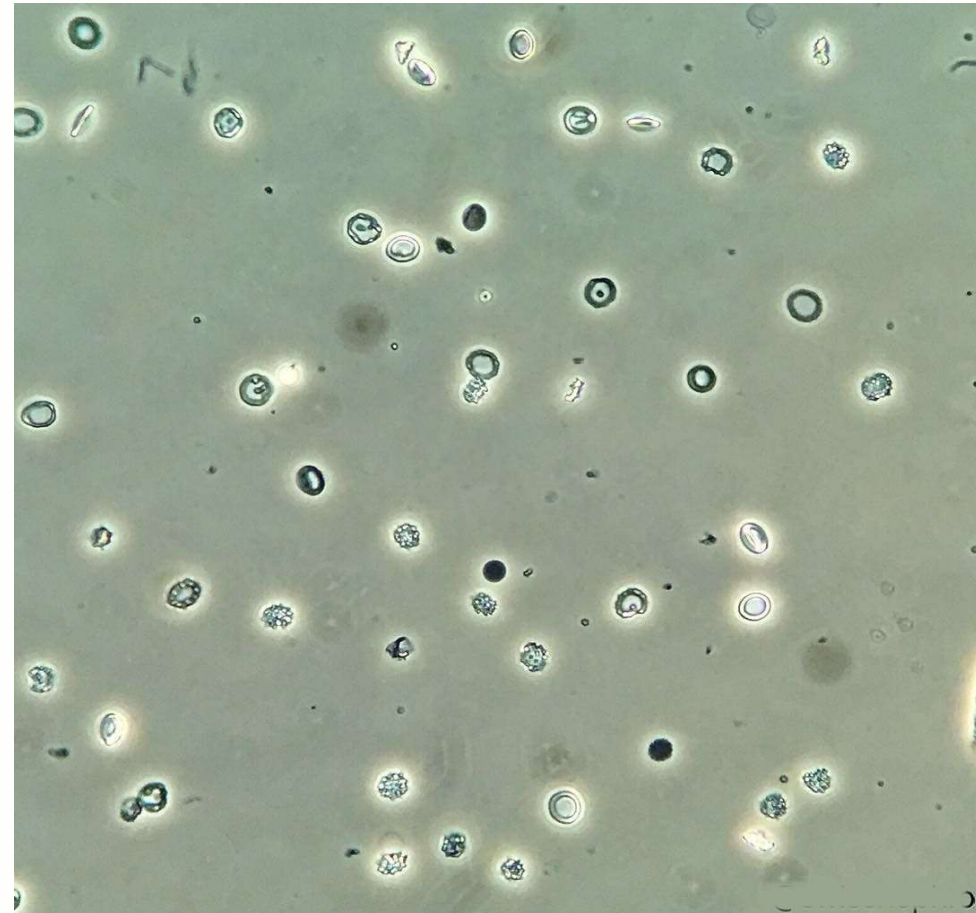
Dysmorphic RBCs and Acanthocytes
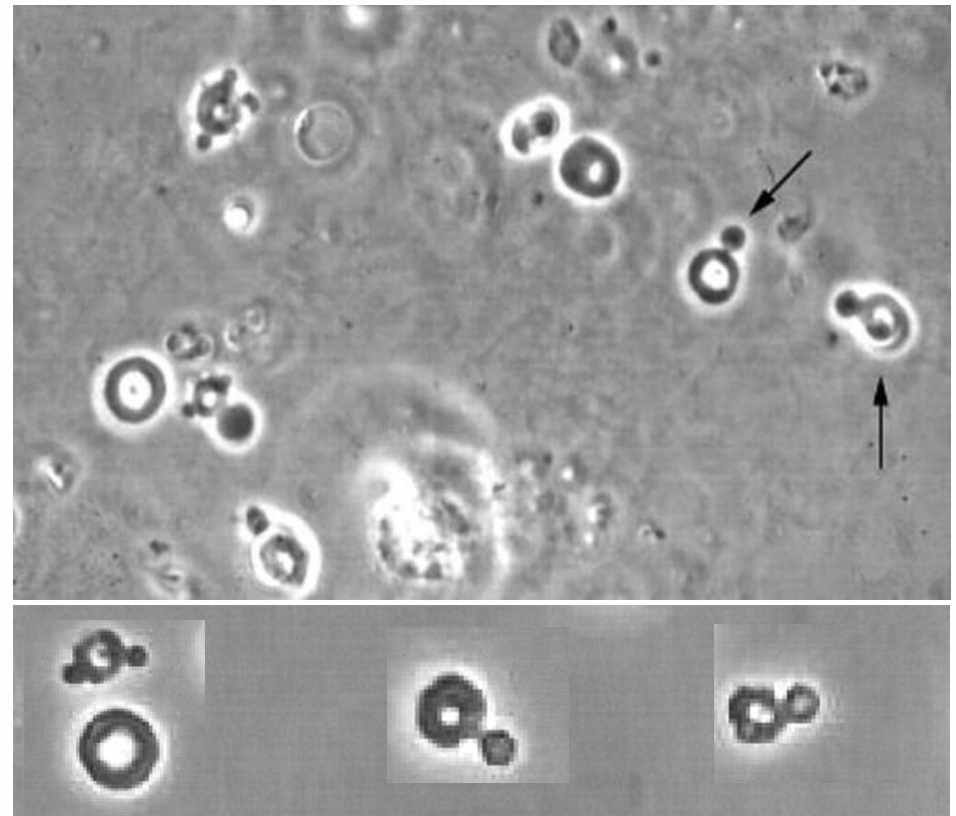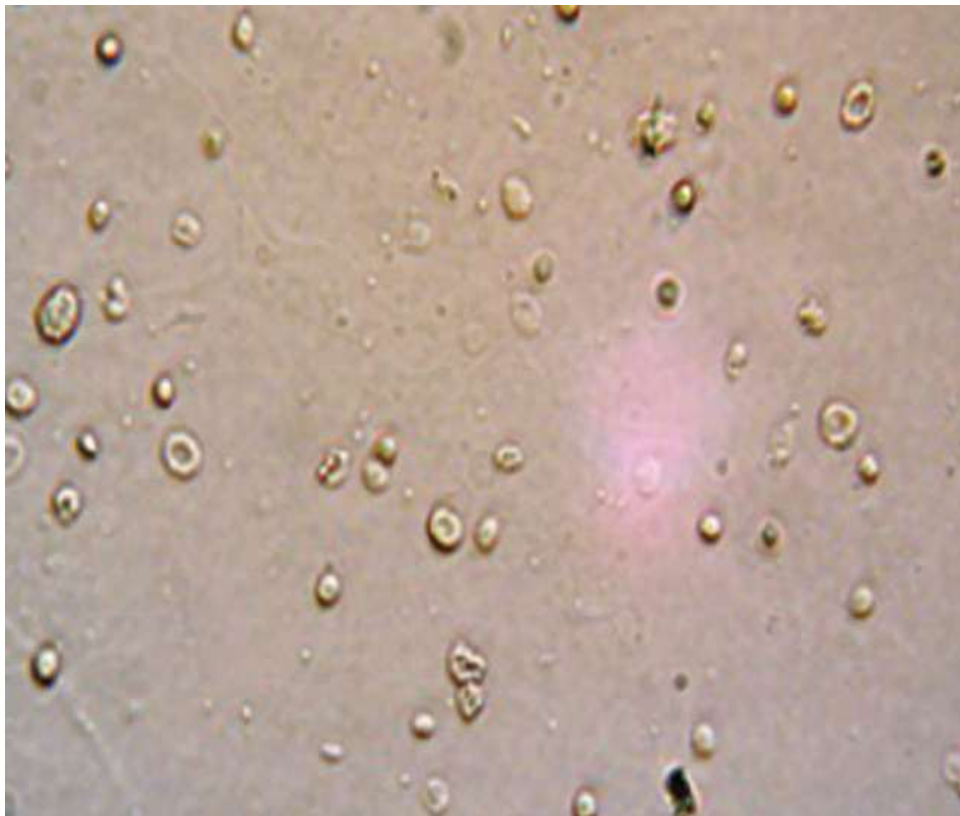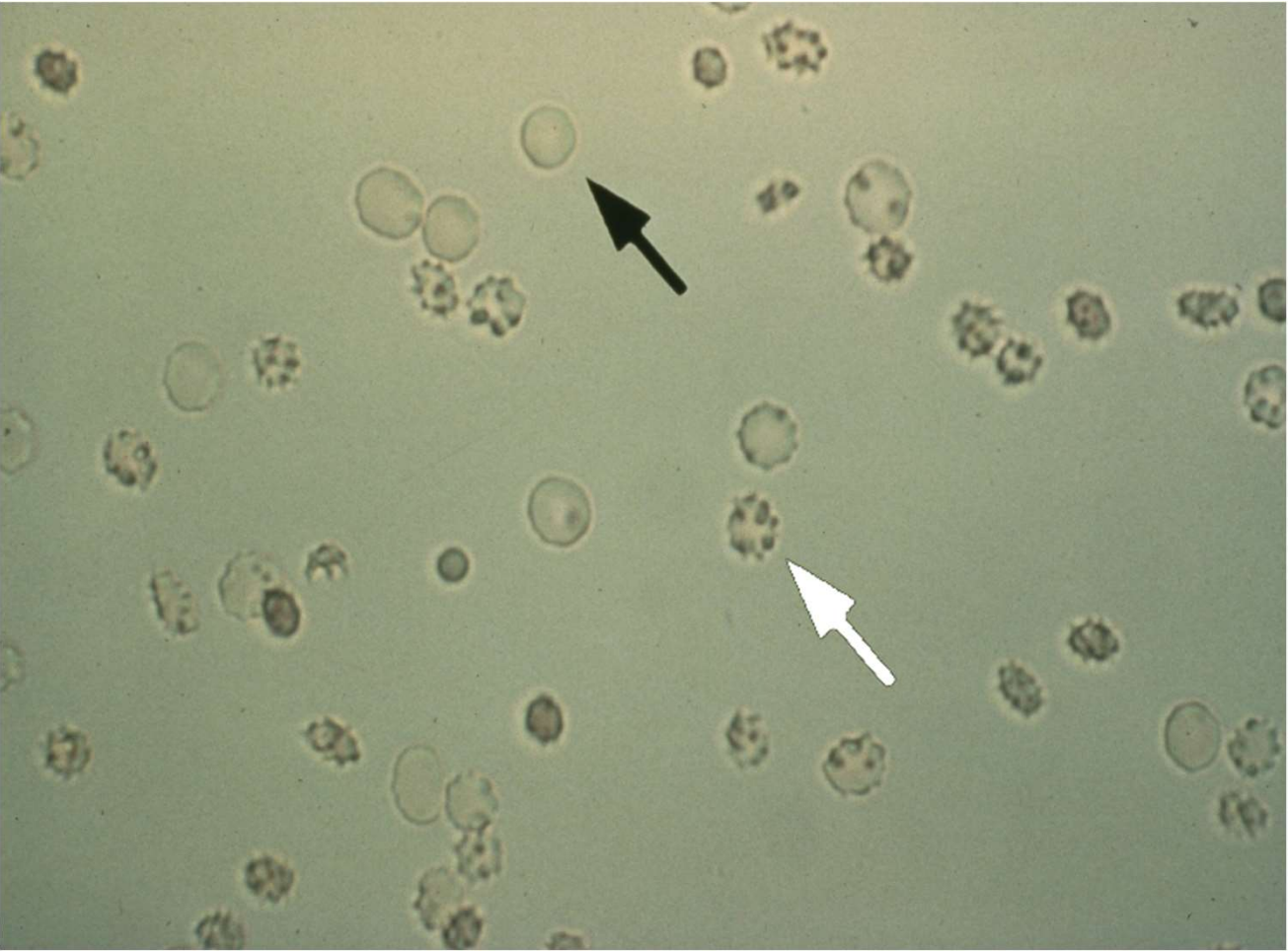
Isomorphic (normal) RBCs
(black arrow)

Crenated RBCs
(white arrow)
Seen in hypertonic urine

What additional finding are you likely to see in the urine sediment that will localize the renal lesion present in this patient?

A. White cell casts

B. Red cell casts

C. Renal tubular epithelial cells

D. Granular casts

E. Transitional epithelial cells

RED BLOOD CELL CASTS

Intact RBC cast

Intact RBC cast)

Degenerated RBC cast (heme pigment cast)

- RBC casts are almost pathognomic for glomerulonephritis or small vessel vasculitis. They are rarely seen in acute interstitial nephritis.
- RBC casts appear in a background of hematuria with dysmorphic RBCs, WBCs, granular casts, and proteinuria (i.e., a <u>nephritic</u> sediment)

Based on the clinical scenario, lab findings, and urinalysis, what is the most likely diagnosis?

A. Microscopic polyarteritis
B. Post-infectious glomerulonephritis
C. Henoch-Schonlein glomerulonephritis
D. Thrombotic microangiopathy
E. Proliferative lupus glomerulonephritis

Case 2

Clinical information/labs
- Arthralgias, malar rash, fevers, ↑BP
- Joint swelling with effusion, pedal edema
- Hypercoagulable state, miscarriages + DVT
- Anemia, ↑ BUN and creatinine, anti-dsDNA
- Antiphospholipid antibodies

Dipstick data   +   **Urine sediment**
- SG 1.010
- Protein 2+
- Blood 3+
- LE 2+

- Dysmorphic RBCs
- RBC casts
- WBCs

Diagnosis
Proliferative glomerulonephritis due to SLE

Nephritic syndrome
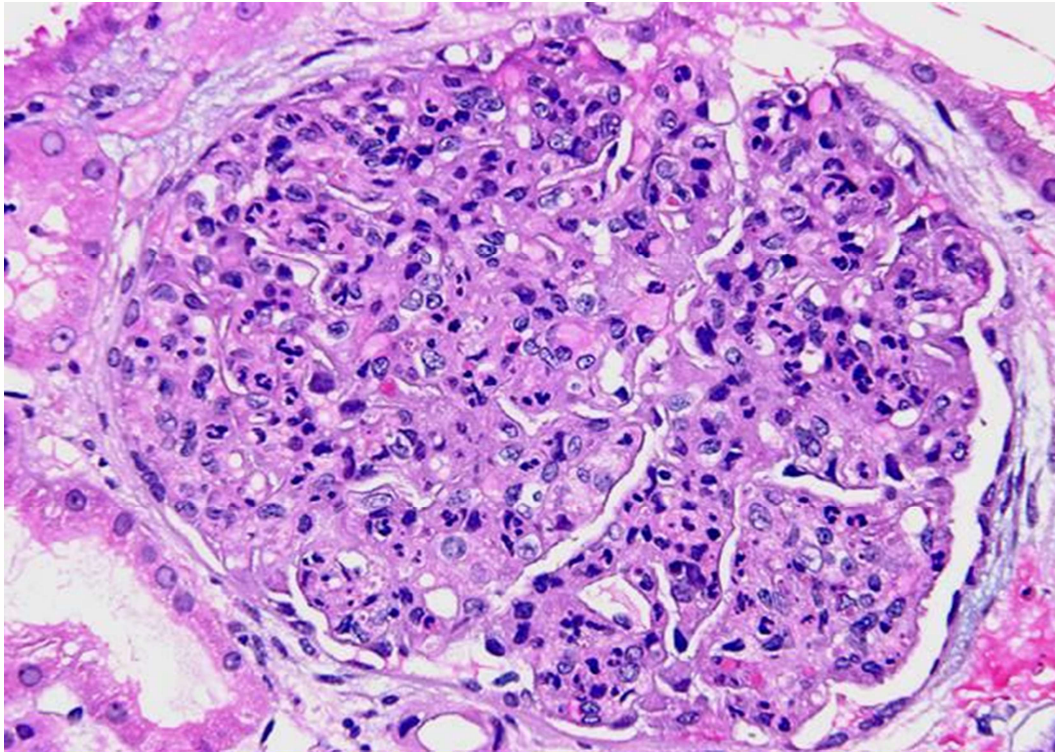
Proliferative Glomerulonephritis

Clinical features

- Hypertension
- Hematuria
- Edema
- Renal failure
  acute or subacute
  (days to a few months)
- Oliguria (<400 ml/day)

Pathologies*

- Proliferative GN
- Crescentic GN (RPGN)
- Membranoproliferative GN

*Usually immunologically
  mediated

*May be primary or due to a
  secondary disease

Case 3

- **HPI:** A 60-year-old man with chronic kidney disease (serum creatinine 1.9 mg/dL) is hospitalized with lobar pneumonia due to MRSA and has been treated with vancomycin for 10 days. His creatinine is now 3.8 mg/dL and he is oliguric despite receiving IV fluids at 100 cc/hr.

- **PMH:** HTN, T2DM, hyperlipidemia

  Meds: lisinopril, linagliptin, atorvastatin

- **PE:** BP 150/80, P 85, R 20, T 100.0
    - Increased JVP
    - Decreased fremitus, crackles, and bronchophony over RLL
    - Trace ankle edema bilaterally

- **Laboratory findings:**
  - Electrolytes: Na+ 133, K+ 5.3, Cl 101, CO2 20
  - BUN 45 mg/dL, creat 3.8 mg/dL, glucose 200 mg/dL
  - Hb 11.5, WBC 14,000

  Urine dipstick:
  - SG 1.010
  - Protein 1+
  - Glucose 1+

What cell type would you expect to predominate on microscopic exam of the urine?

A. White blood cells

B. Red blood cells

C. Transitional epithelial cells

D. Lipid-ladened macrophages

E. Renal tubular epithelial cells

What types of casts would you expect to predominate on microscopic exam of the urine?

A. Granular casts

B. White blood cell casts

C. Waxy casts

D. Red blood cell casts

E. Hyaline casts

Renal tubular epithelial cells and RTEC casts
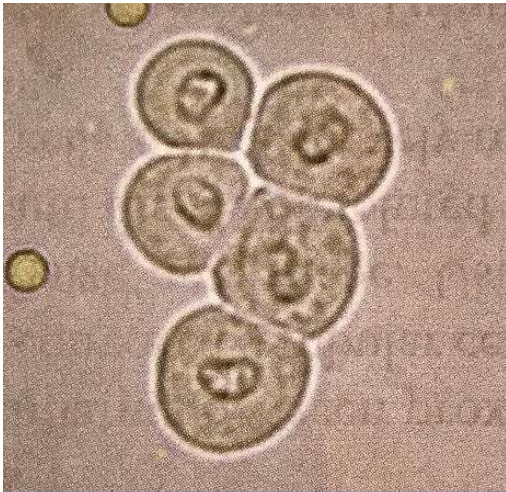
RTECs
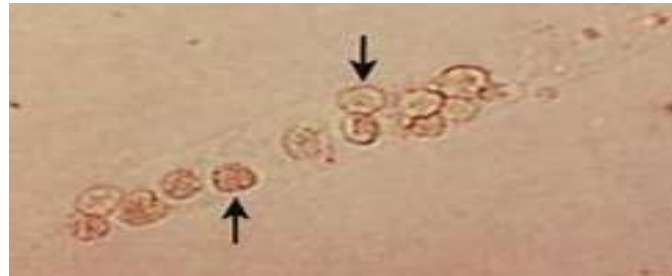
RTEC casts

RTEC 15-30 μm
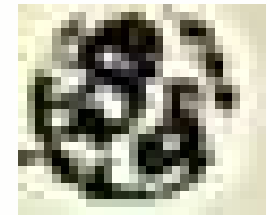
WBC 10-15 μm

Granular casts and muddy brown granular casts

Granular cast
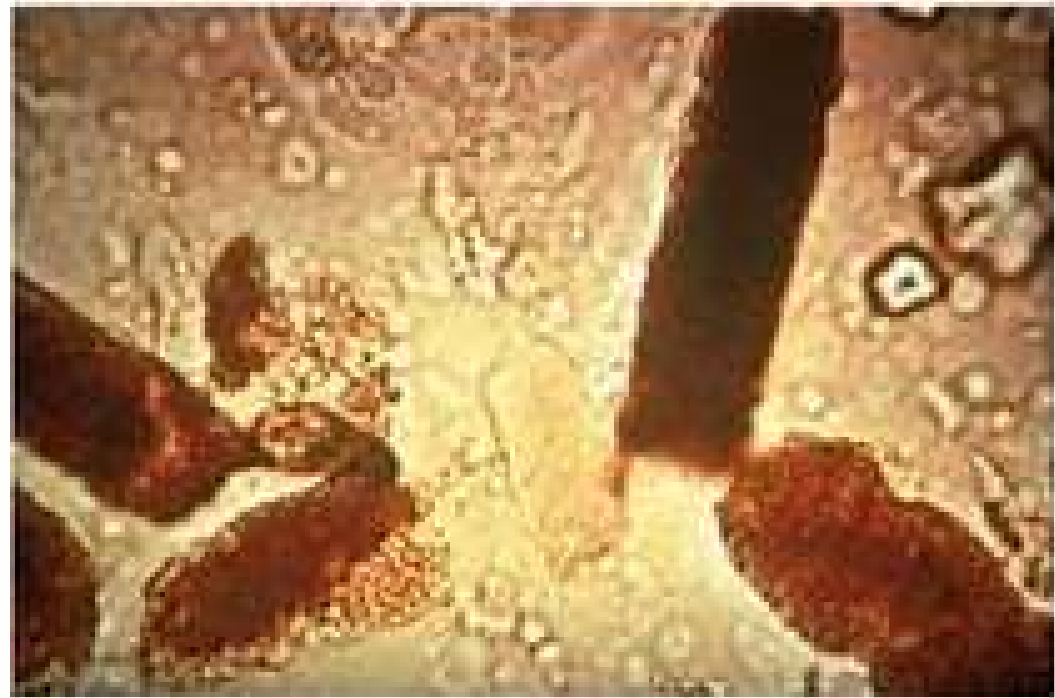
Muddy brown granular cast

Based on the clinical scenario and urinalysis, what is the cause of this patient's acute kidney injury?

A. Prerenal azotemia

B. Acute tubular necrosis

C. Acute interstitial nephritis

D. Acute pyelonephritis

Case 3

Clinical information/labs

- MRSA lobar pneumonia, on vancomycin
- Chronic kidney disease, creat 1.9, HTN, T2DM
- Acute ↑ BUN and creatinine: 45/3.8

Dipstick data   **+**   **Urine sediment**

- SG 1.010
- Protein 1+
- Glucose 1+

- RTECs
- RTEC casts
- Granular (muddy brown) casts

Diagnosis
Drug-induced acute tubular necrosis (ATN)

Quantitative Urine Microscopy Improves Diagnosis and Prognosis of ATN

Scoring system for ATN based on number of RTE cells and granular casts			
RTE cells per HPF	**Granular casts per LPF**		
	0 (0 points)	1-5 (1 point)	≥6 (2 points)
0 (0 points)	0	1	2
1-5 (1 point)	1	2	3
≥6 (2 points)	2	3	4

Perazella MA et al. CJASN 2008;3(6):1615-19
Perazella MA et al. CJASN 2010;5(3):402-08

Microscopy Improves Diagnosis of ATN vs. Prerenal AKI

Odds Ratio of ATN vs. Prerenal AKI
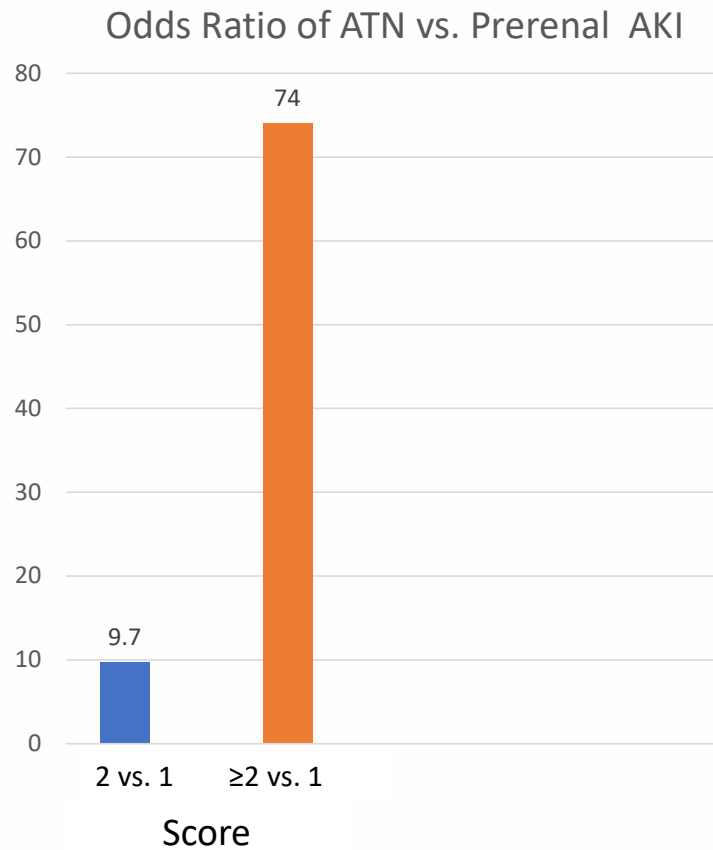
Microscopy Predicts Worsening of ATN

Relation of Microscopy Score to Worsening Severity of ATN
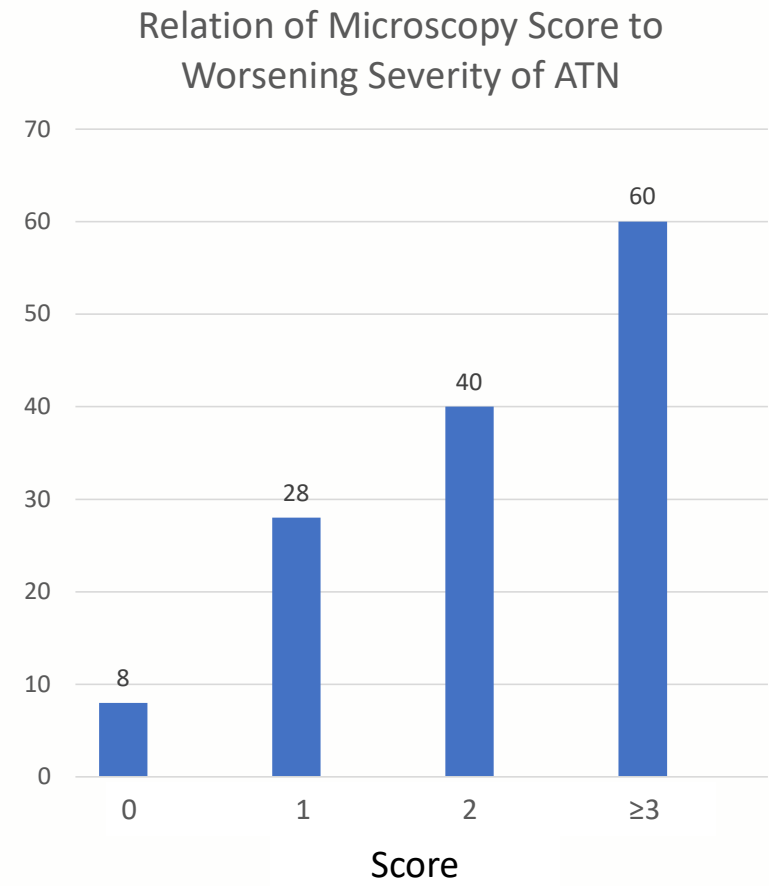
Case 4

- HPI: 35-year-old African American man presents with gradually worsening lower extremity edema, fatigue, and anorexia over the past 3 months.

- PMH: Hypertension x 5 years, prediabetes x2 years

- Meds: Amlodipine

- PE: BP 146/85, P 80, R 14, T 98.6

  - HEENT: Periorbital puffiness, slightly pale conjunctiva
  - Neck: No JVD
  - Lungs: Clear except for dullness at the right base posteriorly with e→a change
  - Heart: NSR, no murmurs or gallops
  - Abdomen: No tenderness, masses or organomegaly
  - Extremities: 3+ edema in lower extremities extending to just below the knees

Case 4

- Laboratory findings:
  - Hb 10.5, WBC 8,000, platelets 240,000
  - BUN 30 mg/dL, creatinine 2.5 mg/dL
  - LDL cholesterol 200 mg/dL, Triglycerides 170 mg/dL
  - Serum albumin 2.5 g/dL

  Urine dipstick
  - SG 1.014
  - Protein 4+
  - LE neg
  - Blood neg

What cell type would you expect to predominate on microscopic exam of the urine?

A. White blood cells

B. Red blood cells

C. Transitional epithelial cells

D. Lipid-laden macrophages

E. Renal tubular epithelial cells

What types of casts would you expect to predominate on microscopic exam of the urine?

A. Granular casts

B. Fatty casts

C. Waxy casts

D. Red blood cell casts

E. Hyaline casts

Oval fat bodies (lipid-ladened macrophages or RTECs) and fatty cast
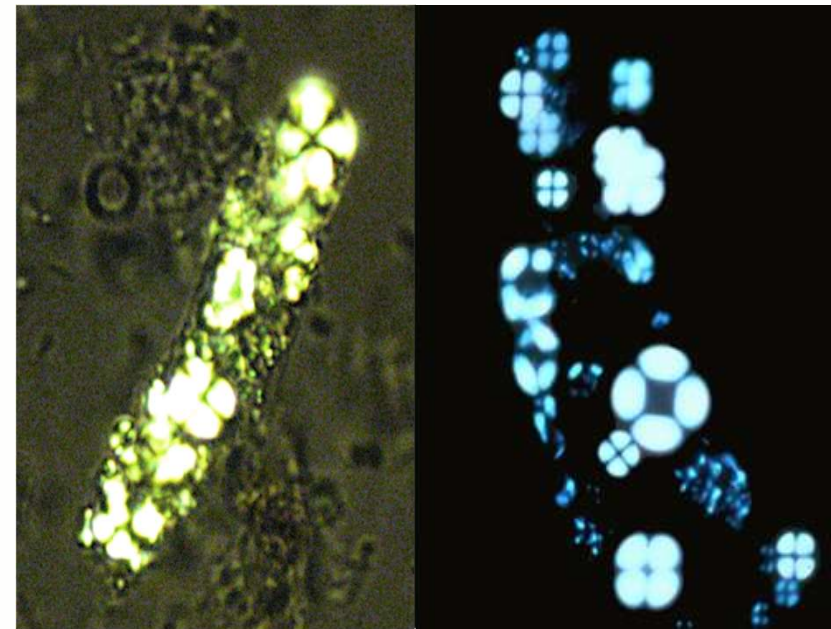
Case 4

Clinical information/labs

- African American male
- Progressive edema, fatigue, anorexia
- Kidney disease, HTN
- Anemia, hyperlipidemia, hypoalbuminemia

Dipstick data   **+**   **Urine sediment**

- Protein 4+

- Oval fat bodies
- Fatty casts

Diagnosis
Nephrotic syndrome
(most likely due to focal segmental glomerulosclerosis)

Nephrotic syndrome
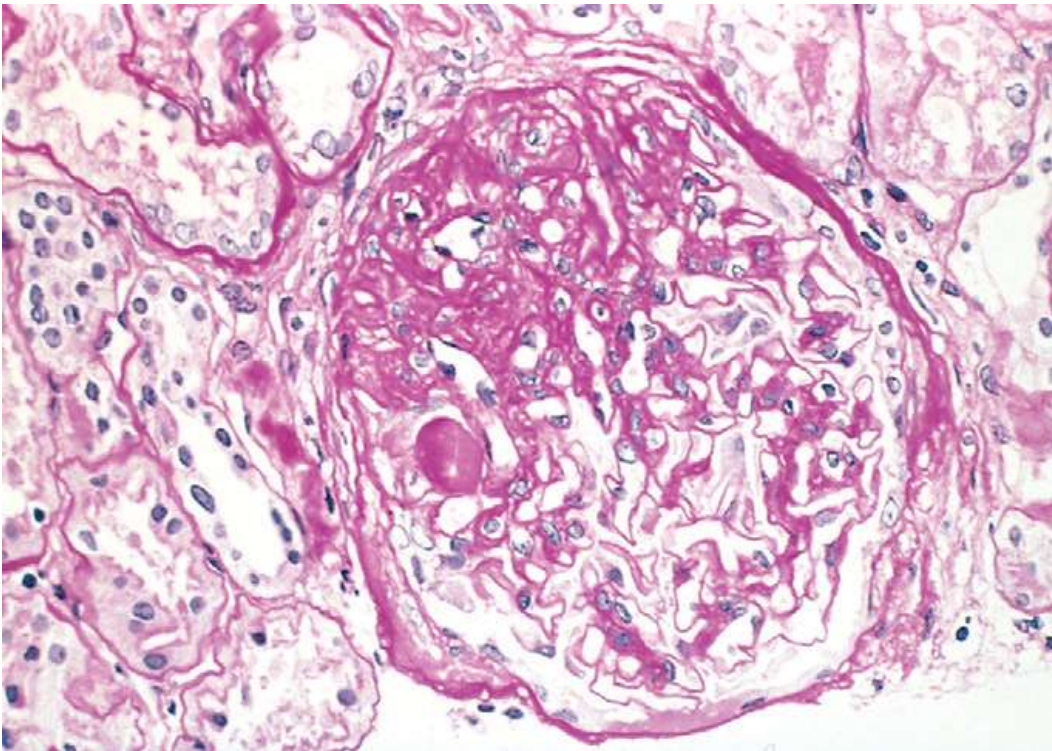
Focal segmental glomerulosclerosis

Clinical features

- Hypoalbuminemia
  - Edema
  - Hypovolemia
- Hyperlipidemia
- Lipiduria

Pathologies*

- Minimal change disease
- Focal segmental glomerulosclerosis
- Membranous glomerulopathy

*Usually immunologically mediated

*May be primary or secondary

Case 5

- **HPI:** 65-year-old female presents to her PCP with new inset low grade fever, malaise, joint pains, and a rash on her chest and upper extremities.
  She has just completed a two-week course of Bactrim therapy for a severe UTI. Her baseline serum creatinine is 1.2, but now is 1.7 mg/dL.

- **PMH:** Hypertension, osteoarthritis, GERD

- **Meds:** HCTZ, naproxen, omeprazole

- **Laboratory Findings:**
  – Electrolytes: Na+ 138, K+ 5.5, Cl 104, CO_2 24
  – Hb 11.0, WBC 11,000; 72% neut, 22% lymph, 5% eos, 1% baso
  – BUN 25, creatinine 1.7

- **Urine dipstick:** SG 1.015, pH 5.5, protein 1+, blood 1+, LE 2+
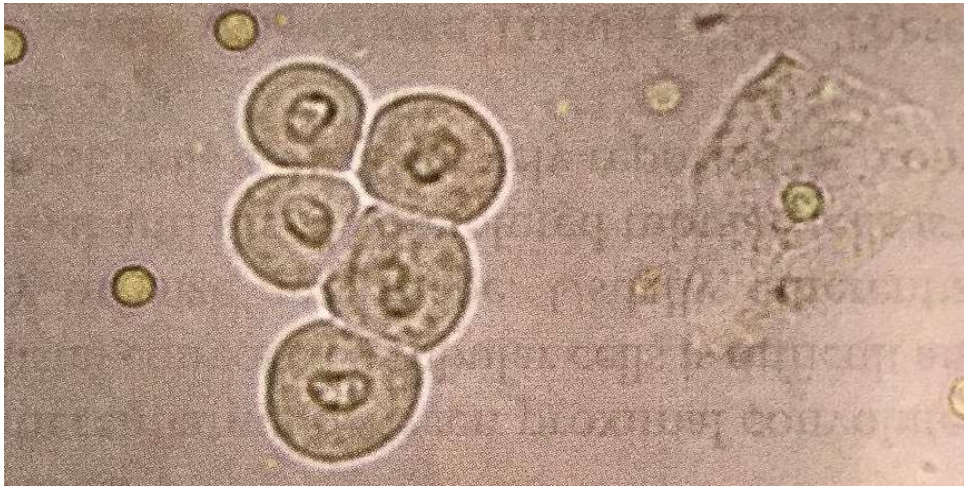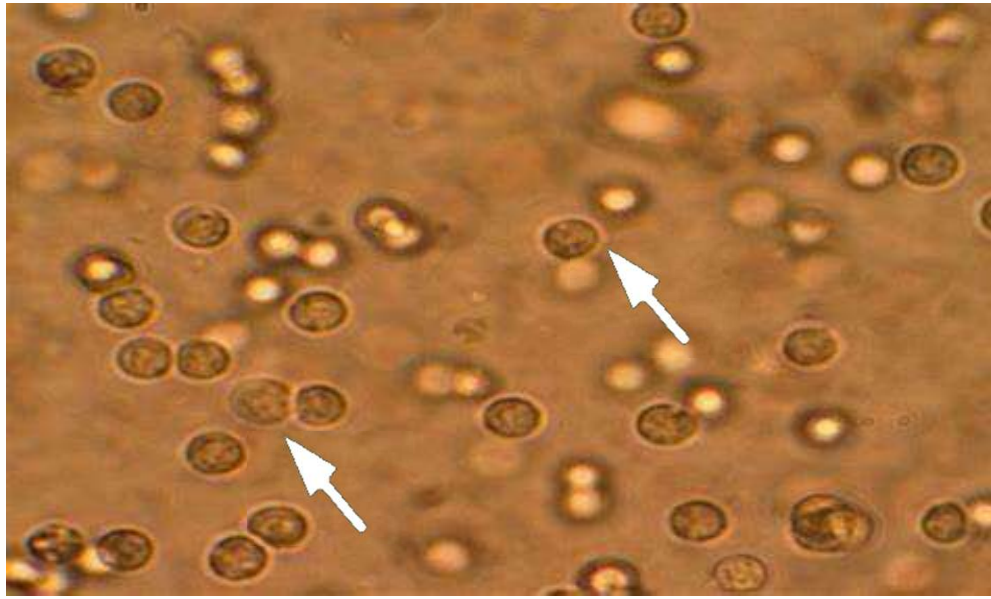
Based on the clinical scenario and urinalysis, what is the cause of this patient's acute kidney injury?

A. Prerenal azotemia

B. Acute tubular necrosis

C. Acute interstitial nephritis

D. Acute pyelonephritis

Case 5

Clinical information/labs

- Elderly female with recent UTI, on Bactrim
- Fatigue, fever, rash, arthralgias
- Acute kidney injury
- Mild anemia, leukocytosis, mild ↑eosinophils

• Dipstick data   +   Urine sediment

- Protein 1+
- Blood 1+
- LE 2+

- WBCs, WBC casts
- RBCs (isomorphic)
- RTECs, RTEC casts

Diagnosis
Drug-induced Acute Interstitial Nephritis (AIN)

Lack of specific clinical or laboratory features for diagnosing AIN

133 patients with biopsy-proven AIN studied at Mayo Clinic

Muriithi AK et al. AJKD 2014; 64(4):558-66

Renal biopsy is necessary to make the Dx of AIN

Feature	Drug-induced (%)	Other causes (%)
Fever	20	8
Rash	22	3
Eosinophilia	23	6
Triad of fever, rash, eosinophilia	10	0
Eosinophiluria	38	15
Hematuria	34	21
Proteinuria	91	95
WBCs in urine	47	45
WBC casts	4	0

Leading Causes of Acute Interstitial Nephritis

- Drugs (71%)
  - Antibiotics (35%)
    - Penicillins, fluoroquinolones, cephalosporins, sulfonamides
  - Proton pump inhibitors (10%)
  - NSAIDs (7%)
- Autoimmune (20%)
  - Sarcoidosis, Sjogren syndrome
- Infections (4)
  - Bacterial, viral, fungal
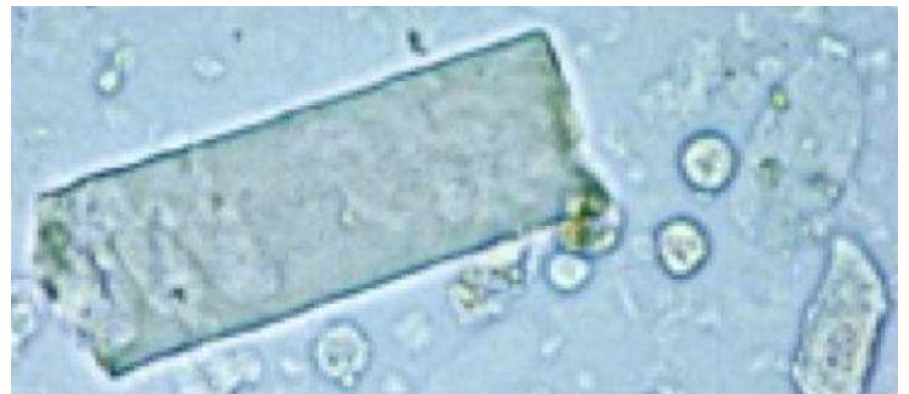
Other cellular elements

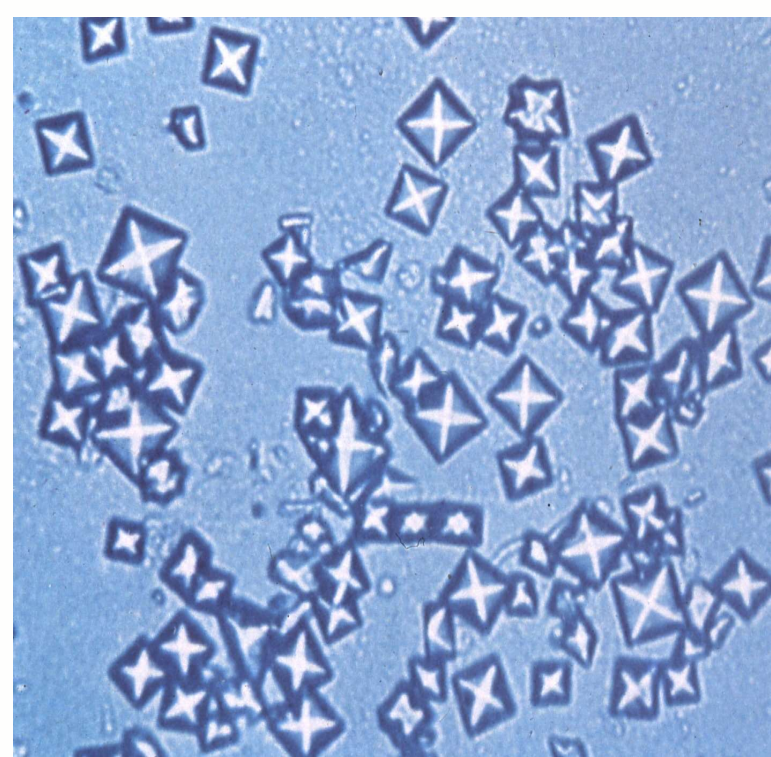Squamous epithelial cells
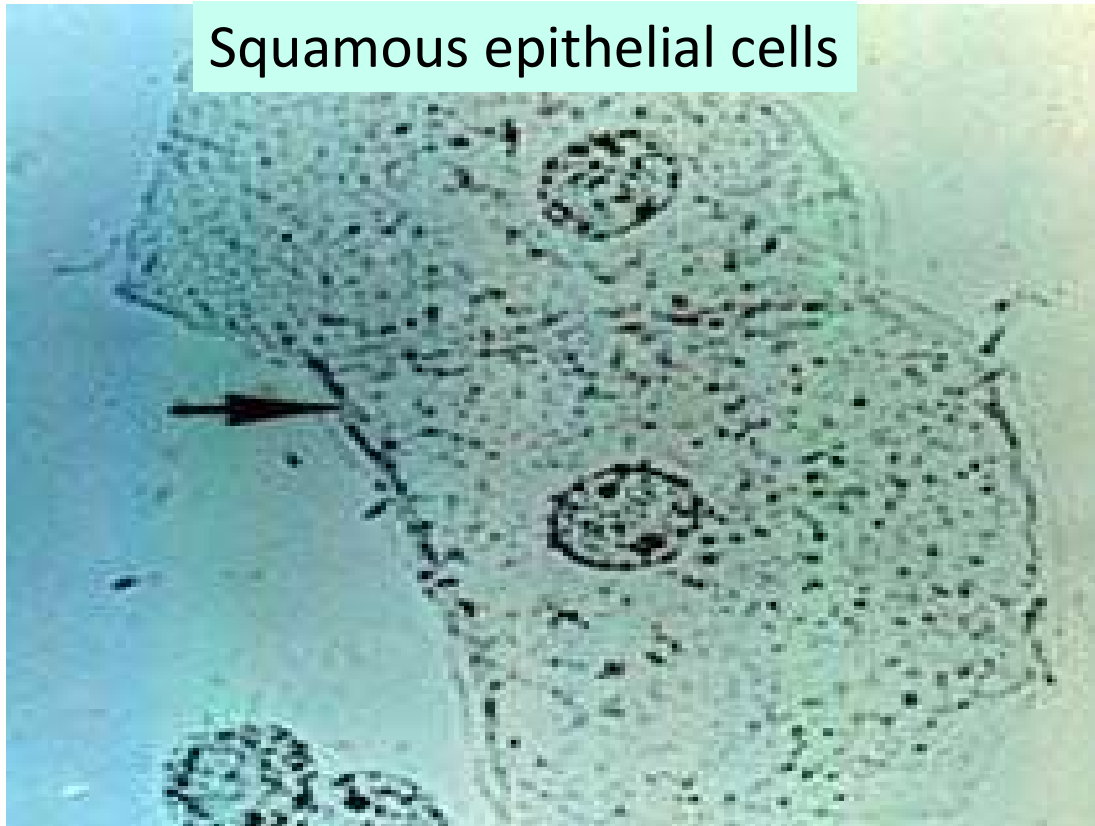
Transitional epithelial cells

Waxy casts (Renal failure casts)
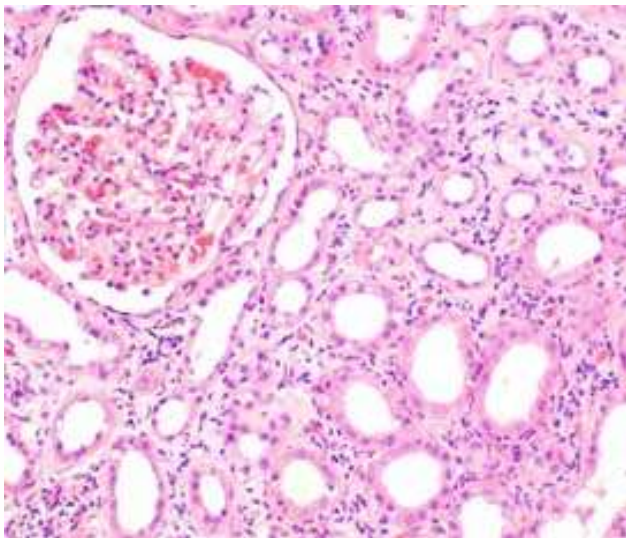
End-stage kidney disease biopsy

Endogenous Crystals
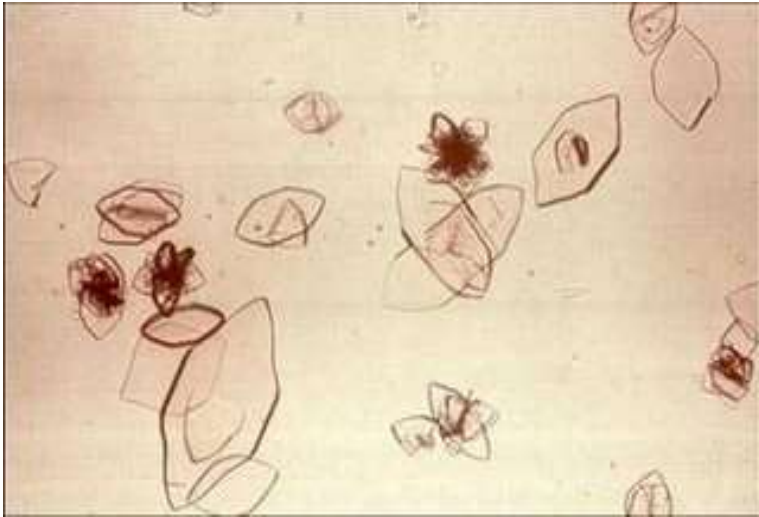

CALCIUM OXALATE
dihydrated (U-pH < 5.4 -6.7)
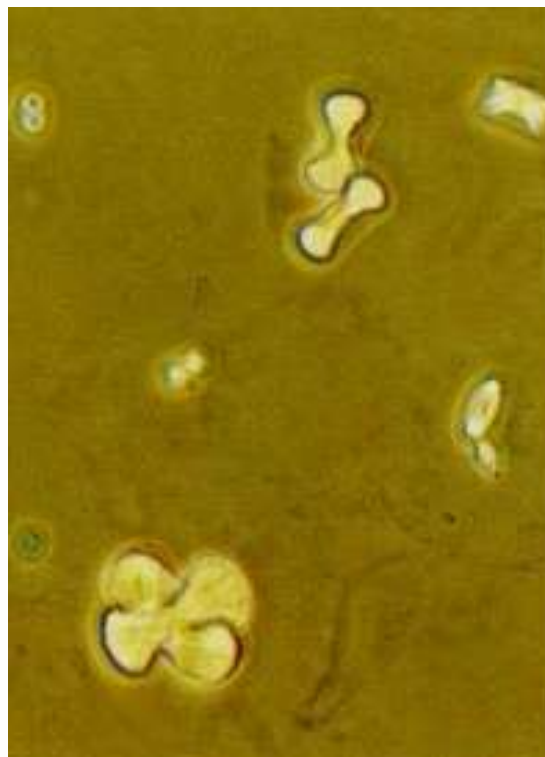
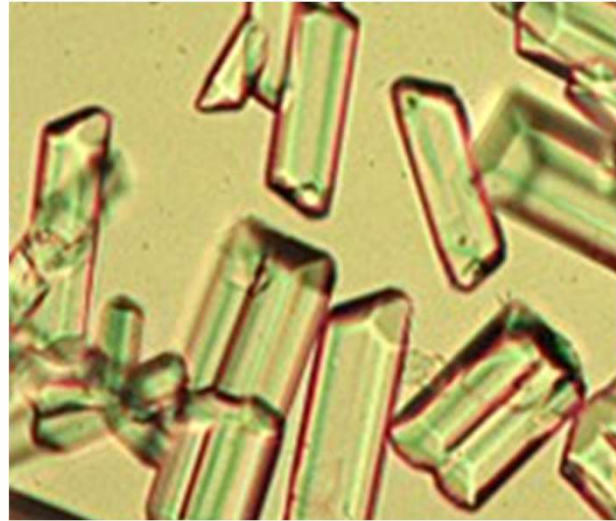**CALCIUM OXALATE**
monohydrated (U-pH < 5.4 -6.7)

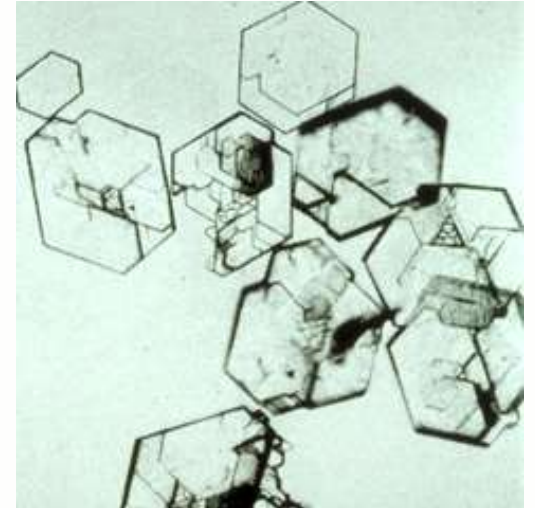**CALCIUM PHOSPHATE**
rosettes and pointed fingers (U-pH ≥7.0)

Endogenous Crystals

URIC ACID (U-pH ≤5.4)

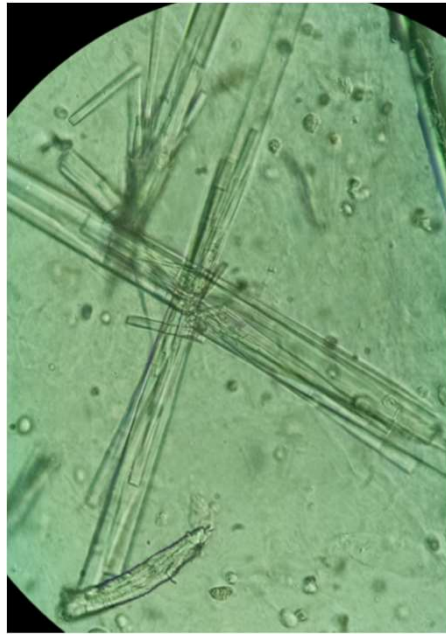**TRIPLE PHOSPHATE (U-pH ≥7.0)**

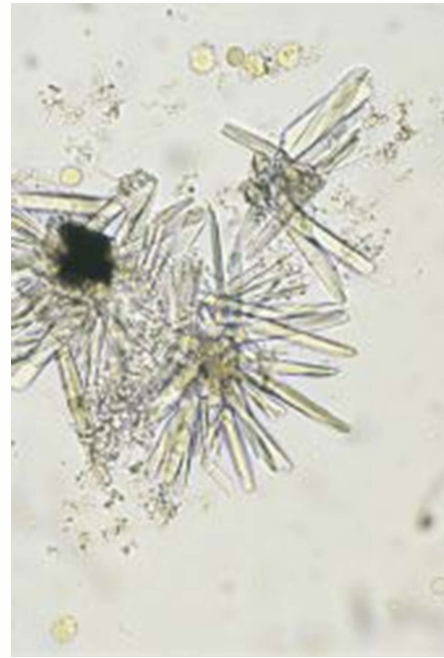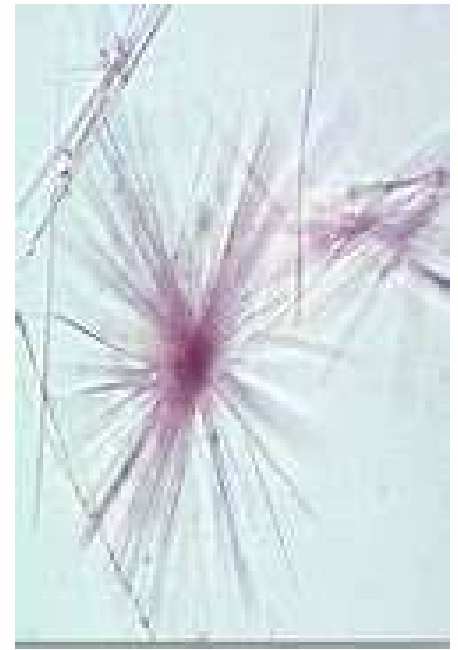**Cystine (U-pH < 5.4 -6.0)**

Drug Crystals

Sulfonamide

Acyclovir

Ciprofloxacin

Amoxicillin

Summary of Urinalysis Abnormalities

Kidney Disorder	Urine Dipstick	Urine Sediment
Prerenal azotemia	–/+ protein	Hyaline casts, few granular casts, occasional RTECs
Acute tubular necrosis	–/+ protein	RTECs, RTEC casts, granular +/- muddy brown granular casts
Acute interstitial nephritis	–/+ protein, +/++ LE, +/++ blood	WBCs, WBC casts, RTECs, RTEC casts, RBCs
Nephritic syndrome	+/++ protein, +/++ LE, ++/+++ blood	Dysmorphic RBCs, acanthocytes, RBC casts, WBCs, WBC casts
Nephrotic syndrome	+++/++++ protein	Oval fat bodies, lipid droplets, lipid-laden casts
End-stage CKD	–/+ protein, –/+ LE	Waxy casts, hyaline/granular casts

Take home points

- Despite modern diagnostic technologies, urinalysis remains a very useful tool to diagnose a wide variety of acute and chronic kidney diseases.

- The urine sediment compares favorably with other biomarkers that can distinguish between prerenal and intrinsic renal causes of acute kidney injury.

- Hallmarks of glomerular injury are dysmorphic RBCs and RBC casts (nephritic syndrome) and oval fat bodies (nephrotic syndrome).

- Hallmarks of tubular injury are renal tubular epithelial cells, renal tubular epithelial cell casts and granular casts.

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Questions…..

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