Urinalysis Conundrums

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Disclosures

I have no relevant relationships with ineligible companies to disclose within the past 24 months.
(Note: Ineligible companies as those whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.)

Objectives

- At the conclusion of this session, participants should be able to:

1. Correlate urine dipstick results to provider-performed urine microscopy findings to assist in making a clinical diagnosis
2. Analyze the urine dipstick and microscopic findings of common renal disorders noted in primary care
3. Utilize urinalysis dipstick and microscopic findings to separate unusual disorders from more commonly encountered disorders

Question #1

In which of the following conditions are white blood cell casts commonly noted in the microscopic analysis of the urine?

A. Urethral syndrome
B. Chronic cystitis
C. Renal tuberculosis
D. Acute pyelonephritis

Question #2

Which of the following urine microscopic findings are indicative of glomerulonephritis?

A. Waxy casts
B. Dysmorphic RBCs
C. Calcium oxalate crystals
D. Renal tubular epithelial cells

Question #3

In which of the following conditions would a patient present with decreased glomerular filtration rate, the presence of protein in the urine, and a urine microscopic that notes the presence of broad waxy casts?

A. Tubular necrosis
B. Urinary tract infection
C. Advanced renal failure
D. Acute glomerulonephritis

Why Order a Urinalysis?

Because it is:

- A quick test to assist in diagnosis
- Relatively inexpensive
- Painless and non-invasive
- Reliable, reduce follow-up tests

Case 1

- 23 year-old female presents with fever and left flank pain.
  - She also notes some dysuria about 4 weeks ago.
- Her past medical history is remarkable for recurrent urinary tract infections.
- She denies vaginal discharge.

Case 1

- T 38.7°C; P 110/min; RR 20/min; BP 114/72 mmHg
- Pulmonary and cardiac examination are normal
- No hepatosplenomegaly is noted
- Moderate left costovertebral angle tenderness is noted
- Pelvic exam is normal

Case 1

CBC

- WBC 10,200/µL
- Hgb 12.0 g/dl
- Hct 36%
- MCV 86 fL
- PLT 290,000/µL

- BUN 3 mg/dl
- Creatinine 0.4 mg/dl

Urinalysis

- Color – yellow
- Appearance - cloudy
- Specific gravity - 1.010
- pH - 5.0
- Ketones - Negative
- Protein – 2+
- Glucose - Negative
- Bilirubin - Negative
- Blood – 1+
- Nitrite - Positive
- Leukocyte esterase – 3+

Case #1, Question #1

Which of the following conditions are associated with a urinalysis report that is positive for protein, nitrites and leukocyte esterase?

A. Exercise induced proteinuria
B. Leukemia
C. Renal tubular damage
D. Urinary tract infection

Case #1, Question #1 Rationale

- Exercise induced proteinuria
  - Positive for protein, but negative for nitrites and leukocyte esterase
- Leukemia
  - Negative for all three, unless there is renal involvement
- Renal tubular damage
  - Positive for protein and possibly WBCs, but not positive for bacteria
- Urinary tract infection
  - Positive for all three,
    especially if infection is in the kidneys

Case # 1, Question # 2

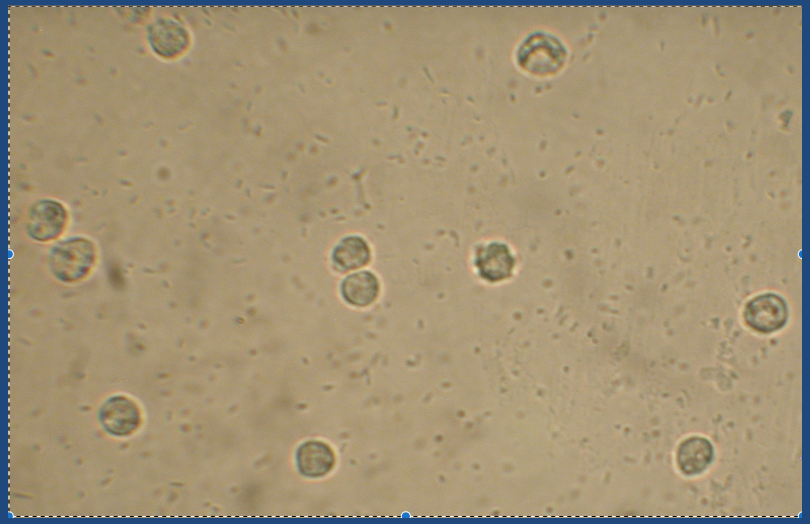
Given this patient's HPI and urinalysis report, what type of casts would you expect to see on the microscopic analysis of the urine sediment?

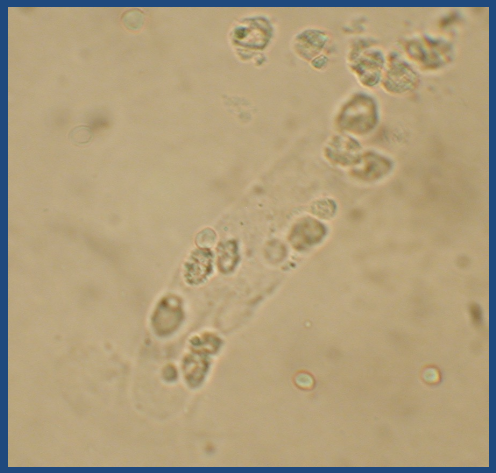
A. Hyaline
B. Red blood cell
C. White blood cell
D. Waxy

Case 1 – Urine Microscopic

Microscopic:

- WBCs:
  - 20-30 / hpf
- RBCs:
  - 5-10 / hpf
- Epithelial Cells:
  - Few squamous
  - Few transitional
  - Few renal tubular
- Bacteria:
  - 3+
- Casts:
  - 0-2 WBC casts/hpf





Case # 1, Question # 3

Given the HPI, urine dipstick results and urine microscopic findings, what is the most probable diagnosis for this patient?

A. Glomerulonephritis
B. Pyelonephritis
C. Acute kidney injury
D. Chronic kidney disease

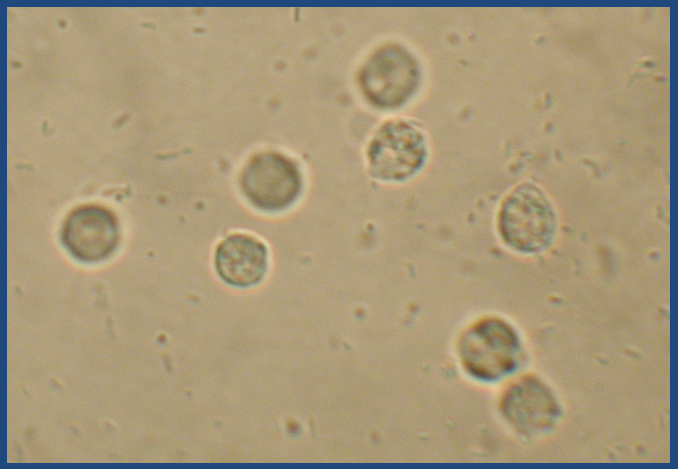
Case 1

- Final diagnosis
  - Pyelonephritis
    - Presence of WBC casts along with WBCs, RBCs, protein and bacteria confirm diagnosis
    - Presence of transitional and renal tubular epithelial cells indicates infection beyond bladder
- Culture positive for E. coli

Lee M. *Basic Skills in Interpreting Laboratory Data*. American Society Of Health System Pharmacists; 2017, 247-260.

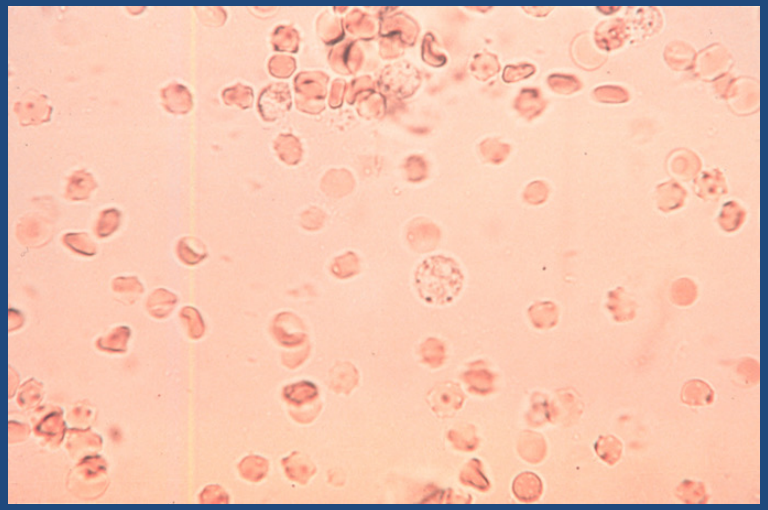
White Blood Cells in Urine

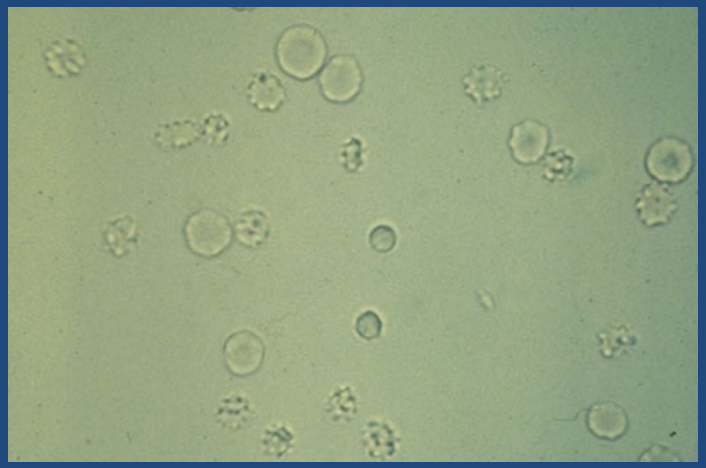
- Normal = 0-3/hpf
- Pyuria (usually segmented neutrophils)
- Any renal or urinary tract disease or infection (acute pyelonephritis, cystitis, prostatitis, urethritis)
- Often in clumps and accompanied by bacteria in infection



Red Blood Cells in Urine

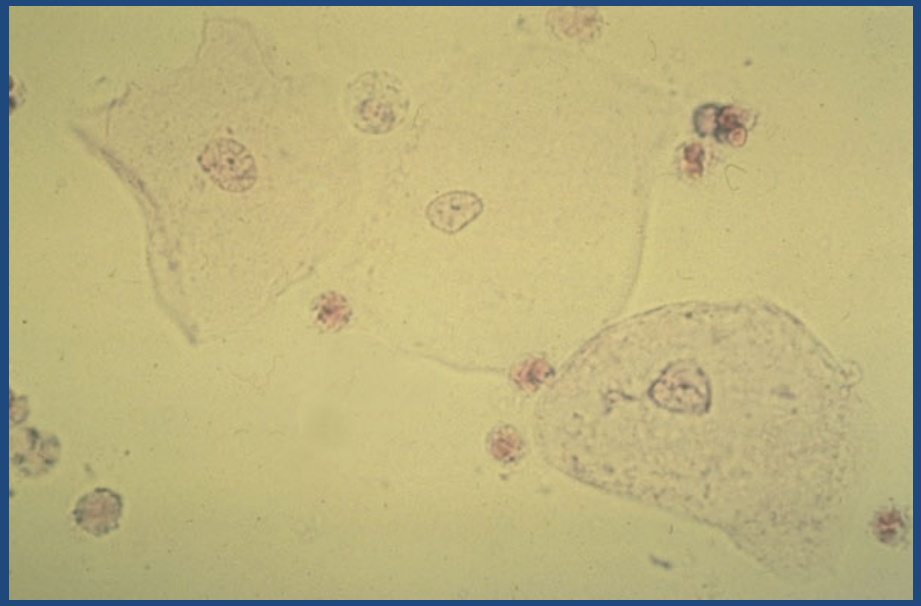
- Normal = 0-3/hpf
- May be seen following strenuous exercise, but disappear with rest
- Increased with damage to glomerular membrane (dysmorphic RBCs) or vascular injury





Epithelial Cells in Urine

- Squamous
  - Large with irregular cytoplasm & central nucleus
  - From lower urinary tract; vaginal contamination

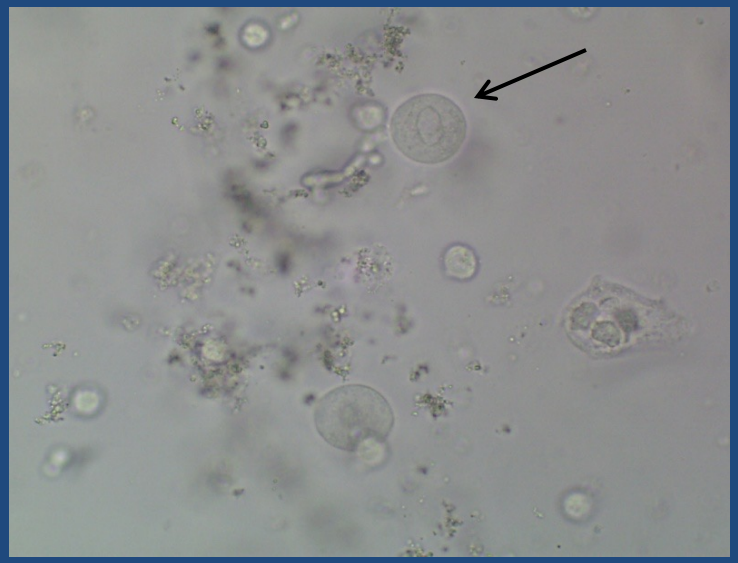


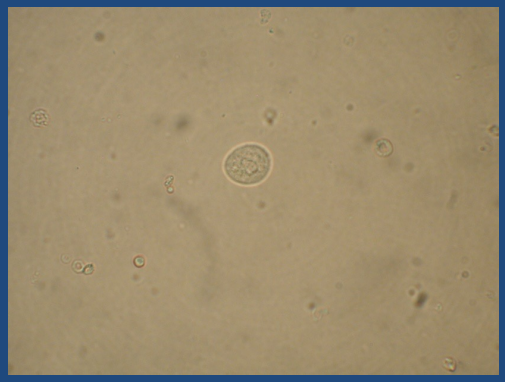
Epithelial Cells in Urine

- Transitional
  - Smaller than squamous; round/pear shaped; central nucleus
  - From renal pelvis, bladder, upper urethra

Epithelial Cells in Urine

- Renal Tubular (RTE)
  - Round, 2x size of WBC, single round nucleus centrally located
  - From renal tubules
  - Increased in kidney inflammation and tubular necrosis





Case 2

- A 17-year-old male has had respiratory tract infections intermittently for the past few months. His mother has made an appt. to see you because he has been complaining of headaches and “fuzzy” vision for the past few days. Upon exam, he appears slightly edematous.

Case 2 - Urinalysis

- Color – light brown
- Appearance – cloudy
- Glucose - negative
- Bilirubin - negative
- Ketones - negative
- Sp. Gr. - 1.025
- Blood – 3+
- pH – 5.0
- Protein – 4+
- Urobilinogen – normal
- Nitrites – negative
- Leukocyte esterase - trace

Case #2, Question #1

What can the presence of a trace of leukocyte esterase in this urine be attributed to?

A. Presence of 3+ blood
B. Low-grade infection
C. False positive dipstick reading
D. High urine specific gravity

Case # 2, Question # 1 Rationale

Remember: Leukocyte esterase produced by WBCs

- Presence of 3+ blood
  - Ratio of RBCs to WBCs in whole blood = 20:1
- Low-grade infection
  - Possible, but no nitrites or indications of infection
- False positive dipstick reading
  - No false positives, only false negatives from ↑ urine concentration
- High urine specific gravity
  - False negatives from ↑ urine concentration

Case #2, Question #2

What can the presence of 4+ protein in this urine be attributed to?

A. Presence of 3+ blood
B. Low-grade infection
C. Damage to the glomerulus
D. High protein diet

Case # 2, Question # 2 Rationale

Remember: Albumin (protein) typically not filtered out at glomerulus

- Presence of 3+ blood
  - Too much protein for amount of blood present
- Low-grade infection
  - Too much protein for low-grade infection
- Damage to the glomerulus
  - Allows more high-molecular weight substances to pass through the glomerular filter
- High protein diet
  - Protein not filtered out in urine if no glomerular damage

Case # 2, Question # 3

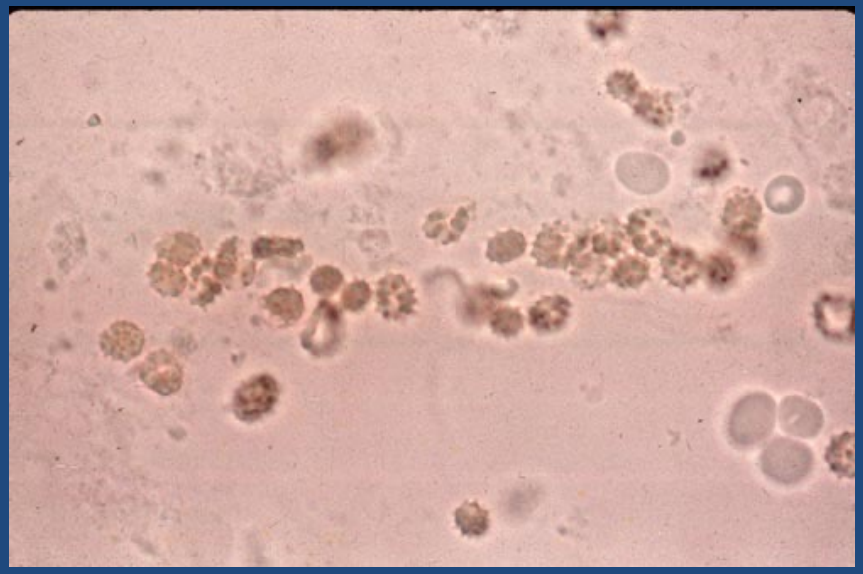
Given this patient's HPI and urinalysis report, what type of casts would you expect to see on the microscopic analysis of the urine sediment?

A. Hyaline
B. Red blood cell
C. White blood cell
D. Waxy

Microscopic – Case 2

Microscopic:

- WBCs:
  - 5-10 / hpf
- RBCs:
  - 50-100 / hpf (or TNTC)
  - Dysmorphic RBCs present
- Casts:
  - 2-5 granular casts / lpf
  - 0-2 red cell casts / lpf



Case # 2, Question # 4

Given the HPI, urine dipstick results and urine microscopic findings, what is the most probable diagnosis for this patient?

A. Glomerulonephritis
B. Pyelonephritis
C. Exercise-induced proteinuria
D. Chronic kidney disease

Case 2, Question #4 Rationale

- Diagnosis
  - Acute Kidney Injury (AKI) probably due to post-streptococcal glomerulonephritis, particularly with presence of dysmorphic RBCs
  - Positive protein due to inflammation to glomerulus and presence of blood
  - Granular and RBC casts due to glomerulonephritis and prolonged AKI

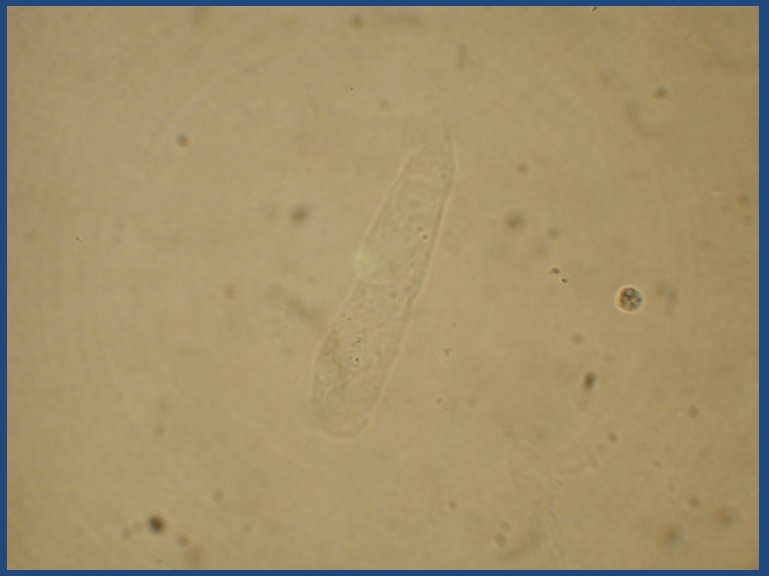
Eison, T. Matthew, et al. “Post-Streptococcal Acute Glomerulonephritis in Children: Clinical Features and Pathogenesis.” *Pediatric Nephrology*, vol. 26, no. 2, 2010, pp. 165–180.

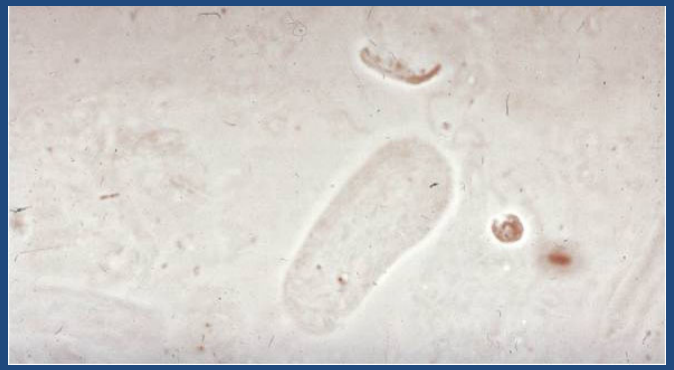
Casts

- Casts - protein gels or fibers of protein mold to lumina of kidney tubule
- Formation favored by: oliguria, acid pH, high specific gravity, and presence of protein.
- Any particulate or cellular material present in abnormal tubular conditions readily adheres to the sticky protein matrix.
- Major constituent of casts = Tamm-Horsfall protein
- Reported as:
  number per low power field

Hyaline Casts

- Hyaline Cast
  - Tubular secretion of Tamm-Horsfall protein that aggregates into fibrils
  - Low refractive index
  - Small numbers not abnormal
  - Increased with fever, exercise
  - Normal = 0-2/hpf



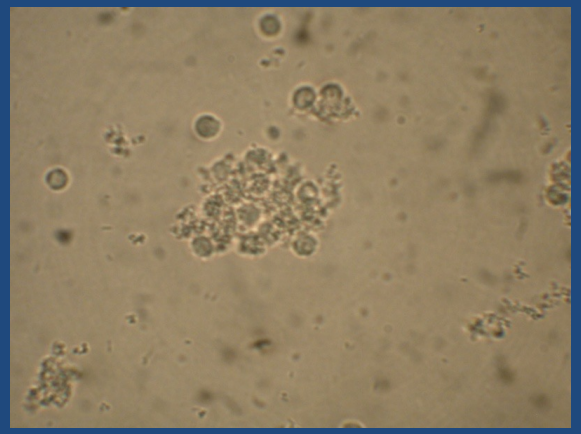


Granular Casts

- Coarse and fine granular casts
  - Nonpathologic – plasma proteins, bacteria, or crystals precipitated in T-H protein following stress/strenuous exercise
  - Pathologic – degenerated cellular casts
- Muddy brown granular cast
  - Seen in acute renal failure

WBC Casts

- WBC Cast
  - WBCs enmeshed in or attached to Tamm-Horsfall protein matrix
  - Seen in acute pyelonephritis
- Not to be confused with clumps of WBCs seen in ascending urinary tract infections

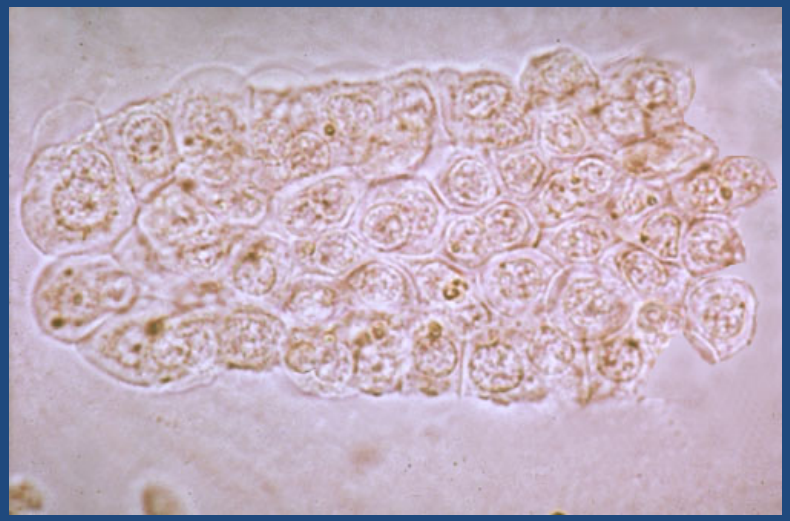


RBC Casts

- RBC cast
  - RBCs enmeshed in or attached to Tamm-Horsfall protein matrix
  - Seen in acute glomerulonephritis
  - Also seen in strenuous exercise

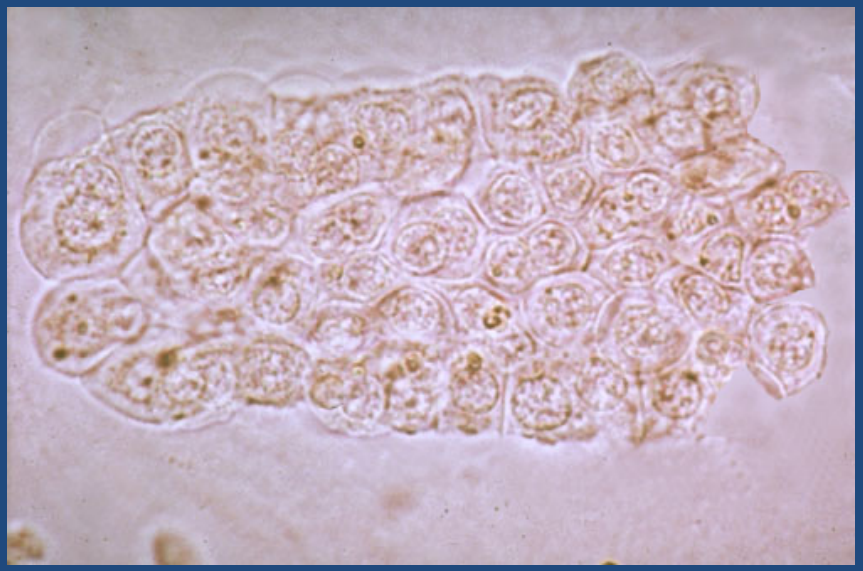
RTE Casts

- RTE Cast
  - Renal tubular cells attached to Tamm-Horsfall protein matrix
  - Seen in tubular necrosis



RTE Casts

- RTE Cast
  - Renal tubular cells attached to Tamm-Horsfall protein matrix
  - Seen in tubular necrosis



Waxy Casts

- Waxy Cast
  - Final stage of a hyaline cast
  - High refractive index
  - Implies
    - Oliguria
    - Renal failure

Case 3

- 50-year-old male presents with severe left flank pain and gross hematuria.
  - Denies fever or chills
  - Mild nausea without vomiting

Case 3

- T 37.6°C; P 96/min; RR 16/min; BP 135/85 mmHg
- Patient is well developed and well nourished
- Abdominal and genital exam is normal
- Left costovertebral angle tenderness is noted

Case 3

Laboratory

- WBC 8,900/µL
- Hgb/Hct 15.0 g/dl/45%
- PLT 290,000/µL
- Sodium 135 mEq/L
- Potassium 3.5 mEq/L
- Chloride 100 mEq/L
- Carbon dioxide 25 mEq/L
- BUN 13 mg/dl
- Creatinine 0.9 mg/dl

Urinalysis

- Color – red
- Appearance – cloudy
- Specific gravity - 1.018
- pH - 5.5
- Glucose - Negative
- Protein - 1+
- Blood - 3+
- Bilirubin - Negative
- Nitrite - Negative
- Leukocyte esterase – Negative

Case #3, Question #1

What is the most probable cause for the presence of blood in this urine sample?

A. Exercise
B. Infection
C. Injury to the kidney or ureters
D. Damage to the glomerular membrane

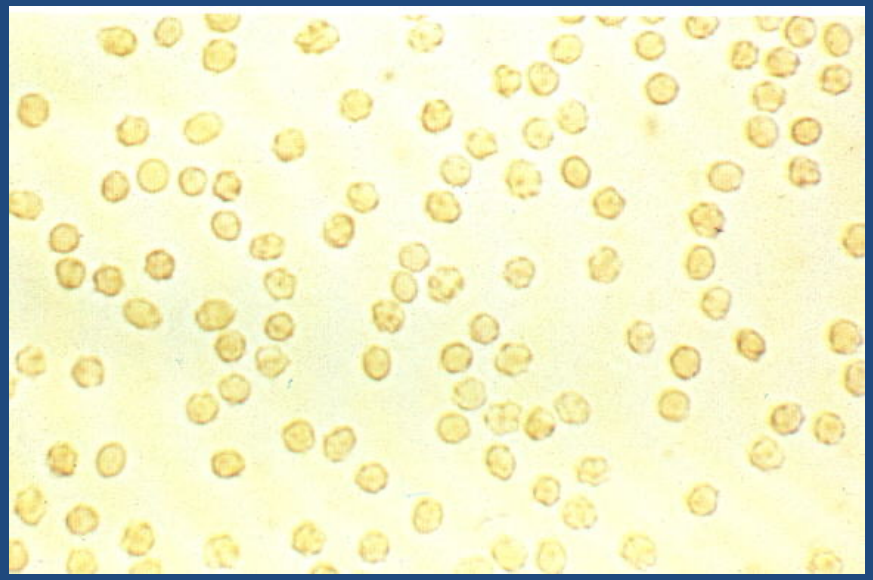
Case # 3, Question # 1 Rationale

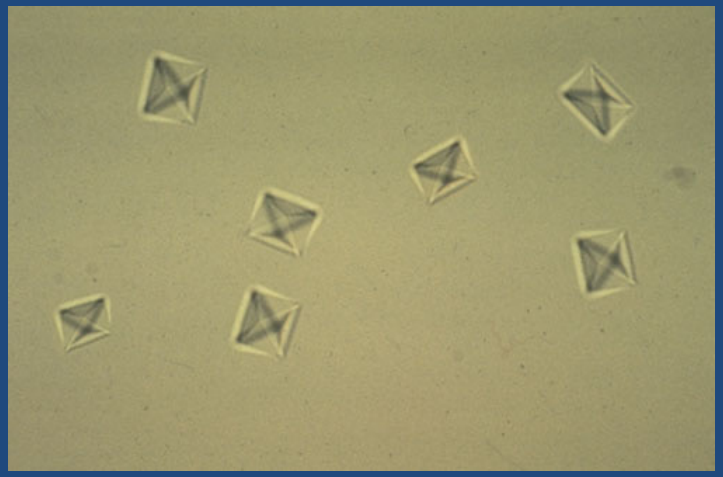
- Exercise
  - Exercise typically yields only small amounts of blood in urine
- Infection
  - Only small amounts of blood resulting from infection
- Injury to the kidney or ureters
  - Most likely cause, from injury or trauma
- Damage to the glomerular membrane
  - Results in dysmorphic RBCs

Case 3 – Urine Microscopic

Microscopic:

- WBCs:
  - 2-4 / hpf
- RBCs:
  - 50-100 / hpf (or TNTC)
- Crystals:
  - Many calcium oxalate crystals





Case #3, Question #2

What do the presence of calcium oxalate crystals in the urine indicate?

A. Gout
B. Kidney stones
C. Chronic Cystitis
D. Liver failure

Case # 3, Question # 2 Rationale

- Gout
  - Uric acid crystals
- Kidney stones
  - Calcium oxalate crystals
- Chronic cystitis
  - Triple phosphate crystals
- Liver failure
  - Bilirubin or tyrosine crystals

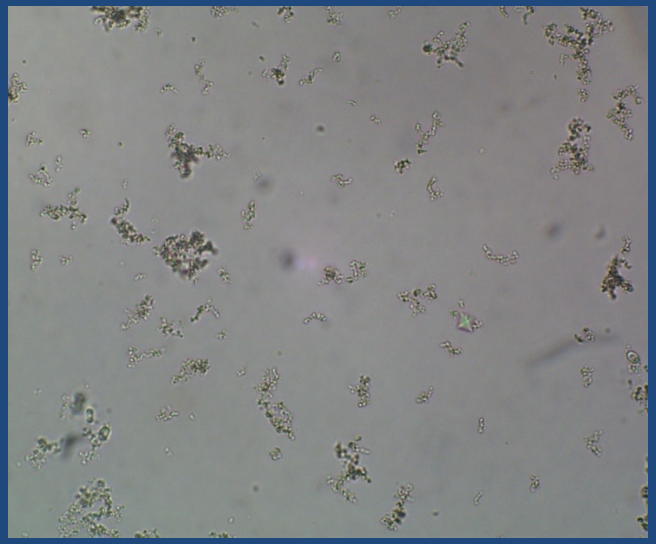
Case 3

Case 3

- Final Diagnosis
  - Nephrolithiasis

Kazi, Saifullah N., and Robert L. Benz. “Work-up of Hematuria.” *Primary Care: Clinics in Office Practice*, vol. 41, no. 4, 2014, pp. 737–748.

Common Crystals in Acid Urine



- Amorphous urates
  - Granular not crystalline
  - Pink sediment when refrigerated

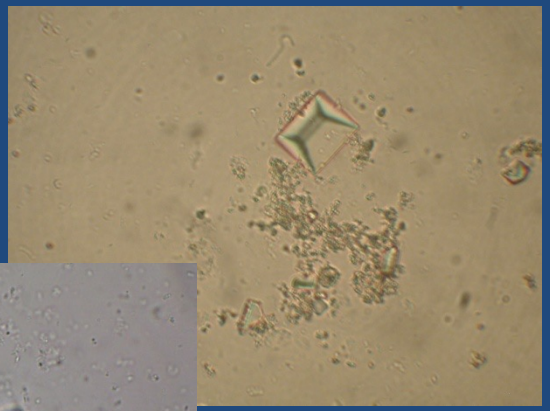
- Uric acid
  - Yellow, brown, or colorless
  - Rhomboid, barrel, or rosette
  - Seen in gout or high nucleic acid turnover

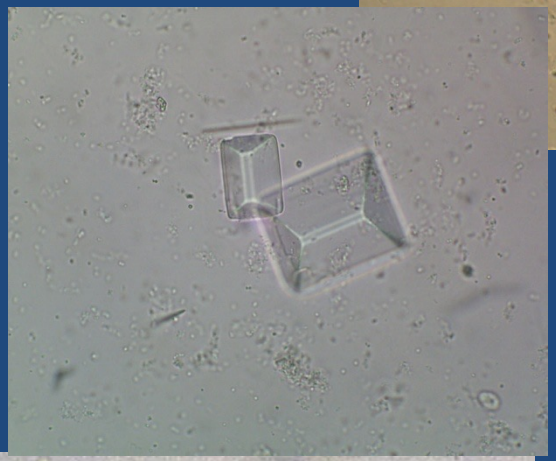
Common Crystal in Acid/Neutral Urine

- Calcium oxalate
  - Small, colorless envelope
  - Tomatoes, spinach, cocoa, ethylene glycol
  - Renal calculi

Common Crystals in Alkaline Urine

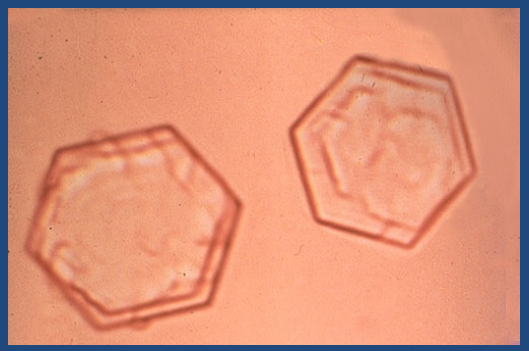
- Amorphous phosphates
  - Granular not crystalline
  - Identical to amorphous urates (pH determines)
- Triple phosphate
  - Coffin lid, colorless
  - Large 3-6 sided prisms
  - Chronic cystitis
- Ammonium biurates
  - thorn apples
  - Yellow, brown spheres with spikes

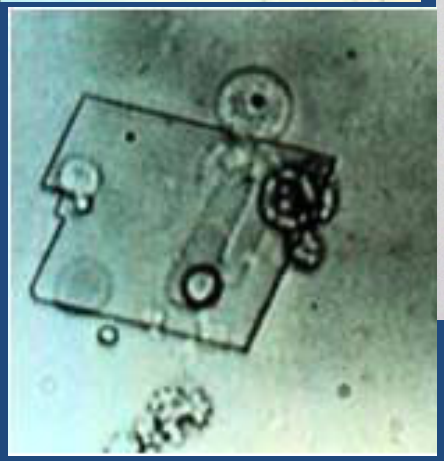


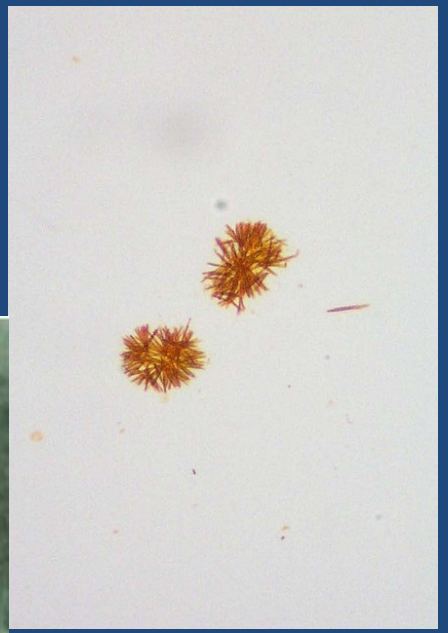


Abnormal Crystals

- Cystine
  - Colorless, flat hexagons
  - Cystinuria
- Tyrosine
  - Fine needles in sheaves
  - Liver disease
- Bilirubin
  - Red, brown needles
- Cholesterol
  - Large, flat, transparent plates, notched corners
  - Lipiduria

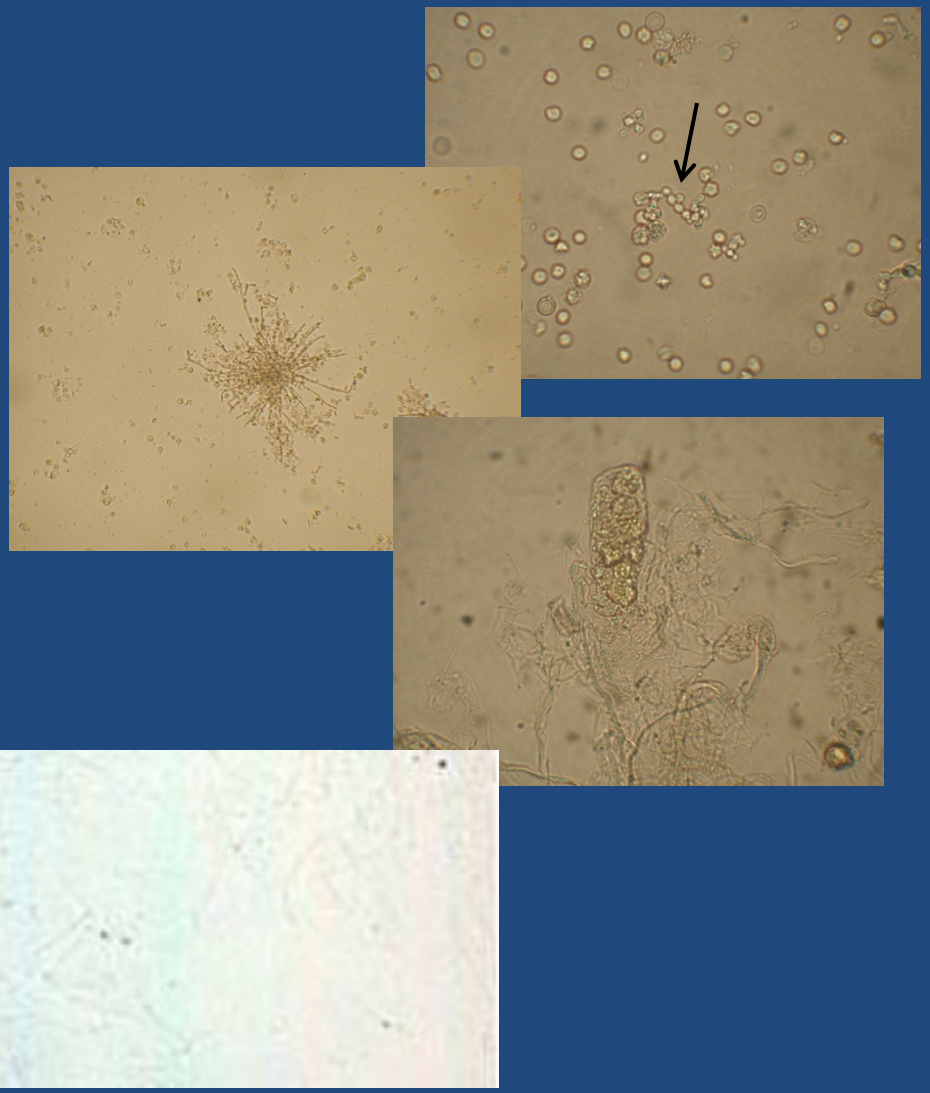






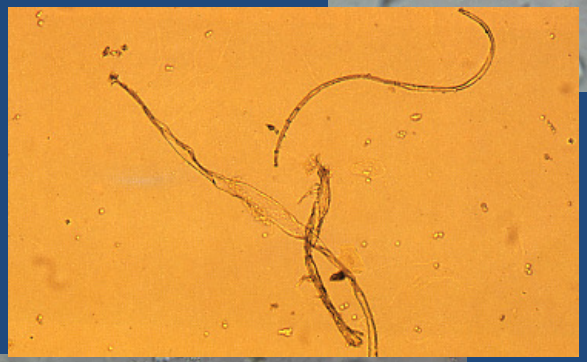
Yeast and Mucous

- Yeast
  - Budding and hyphae
  - Diabetics or in women with vaginal yeast infections
  - Easily confused with RBCs
- Mucous
  - Protein produced by glands and epithelial cells in the GU tract
  - Not clinically significant
  - Threadlike structures, low refractive index



Artifacts

- Artifacts
  - Oil
  - Cloth fibers
  - Fecal fibers
  - Hair
  - Cornstarch and talcum
- Starch granules (crystals) easily confused with RBCs



Case 4

- 65-year-old female presents with RUQ pain that radiates around to the back, nausea, and vomiting.
  - On admission the patient is orthostatic and spikes a fever to 39°C
  - She is treated with IV antibiotics
- No prior history of renal dysfunction

Case 4

Admission

- Sodium - 146 mEq/L
- Potassium - 4.1 mEq/L
- Chloride - 111 mEq/L
- Carbon dioxide - 22 mEq/L
- Glucose - 195 mg/dl
- BUN - 35 mg/dl
- Creatinine - 1.6 mg/dl

- Elevated WBC with left shift

Day 1 post admission

- Sodium - 140 mEq/L
- Potassium - 5.0 mEq/L
- Chloride - 100 mEq/L
- Carbon dioxide - 15 mEq/L
- Glucose - 130 mg/dl
- BUN - 40 mg/dl
- Creatinine - 2.5 mg/dl
- Urine output:
  100cc/12 hours

Case #4, Question #1

Given this patient's BUN and Creatinine values, as well as her urine output, what type of epithelial cells would you expect to find in her urine sediment?

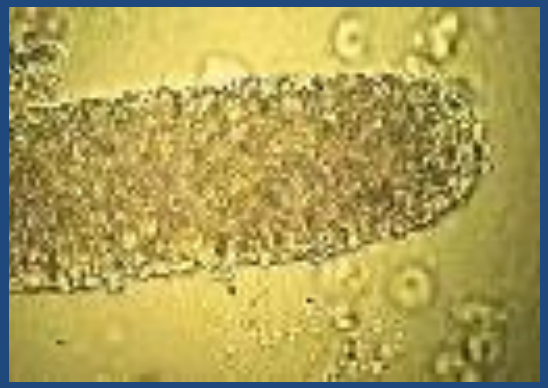
A. Squamous
B. Transitional
C. Renal tubular
D. Oval fat bodies

Case #4, Question #1 Rationale

- Squamous
  - Lower urinary tract and vaginal contamination
- Transitional
  - Renal pelvis, bladder, upper urethra
- Renal tubular
  - Renal tubules; increased in kidney inflammation
- Oval fat bodies
  - Free fat droplets within renal tubular cells

Case 4 - Urinalysis

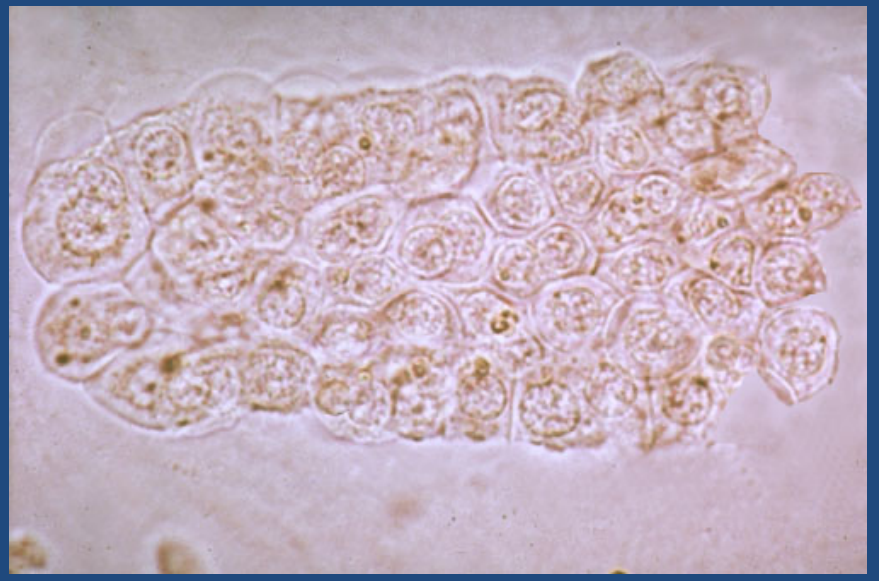
- Specific gravity - 1.010
- pH - 5.0
- Glucose - Negative
- Protein - 1+
- Blood - 1+
- Bilirubin - Negative
- Nitrite - Negative
- Leukocyte esterase - Negative



Case 4

3 Days Later

- Oliguria continues
- Bun 100 mg/dl
- Creatinine 5.5 mg/dl



Case #4, Question #2

If this patient's oliguria continues, what type of cast would you expect to find in the microscopic examination of her urine sediment?

A. Hyaline
B. White blood cell
C. Red blood cell
D. Waxy

Case #4, Question #2 Rationale

- Hyaline
  - Can be normal
  - increased with fever/exercise
- White blood cell
  - Pyelonephritis
- Red blood cell
  - Glomerulonephritis
- Waxy
  - Implies oliguria and renal failure

Case #4, Question #3

What is the most likely diagnosis for this patient?

A. Acute tubular necrosis
B. Chronic kidney disease
C. Dehydration
D. Urethral obstruction

Case #4, Question #3 Rationale

- Acute tubular necrosis
  - 2012 KDIGO guidelines[1]
    - Rise in creatinine of 0.3 mg/dL in 24 hrs
    - Rise in creatinine of >1.5 over 7-day period
    - Urine volume ≤0.5 mL/kg per hour for 6 hours
- Chronic kidney disease
  - Patient presented acutely (3 days)
- Dehydration
  - Prerenal disease
- Urethral obstruction
  - Post-renal disease

[1]Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract 2012; 120:c179.

Case 4

- Final Diagnosis
  - –Acute kidney injury
  - –Acute tubular necrosis

Perazella, M. A., et al. “Diagnostic Value of Urine Microscopy for Differential Diagnosis of Acute Kidney Injury in Hospitalized Patients.” *Clinical Journal of the American Society of Nephrology*, vol. 3, no. 6, Oct. 2008, pp. 1615–1619.

Clinical Utility of Urine Dipstick Testing

Urine Dipstick Test	Disease Process
Leukocytes Nitrites	Urinary Tract Infection
pH Occult Blood	Renal Cancer Kidney Stones Bladder Cancer
Protein Leukocytes Blood	Chronic Kidney Disease
Glucose Ketones	Diabetes Gestational Diabetes Eating Disorders
Bilirubin Urobilinogen	Liver Function

Should you order a microscopic on a urine with negative dipstick readings?

Things to Consider

- Patient presentation
- Appearance of urine
- Specific gravity of urine
- pH of urine

Question #1

In which of the following conditions are white blood cell casts commonly noted in the microscopic analysis of the urine?

A. Urethral syndrome
B. Chronic cystitis
C. Renal tuberculosis
D. Acute pyelonephritis

Question #2

Which of the following urine microscopic findings are indicative of glomerulonephritis?

A. Waxy casts
B. Dysmorphic RBCs
C. Calcium oxalate crystals
D. Renal tubular epithelial cells

Question #3

In which of the following conditions would a patient present with decreased glomerular filtration rate, the presence of protein in the urine, and a urine microscopic that notes the presence of broad waxy casts?

A. Tubular necrosis
B. Urinary tract infection
C. Advanced renal failure
D. Acute glomerulonephritis

Take Home Points

- Urine microscopy can be combined with urine chemistry results to make a more accurate clinical diagnosis.
- Understanding the significance of microscopic elements found in urine can provide a better understanding of renal disease.
- Specific combinations of pathologic urine microscopic elements are associated with various stages of renal disease.

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Questions?

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