URINARY SEDIMENT

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AJKD

Core Curriculum

Urine Sediment Examination in the Diagnosis and Management of Kidney Disease: Core Curriculum 2019

Corey Cavanaugh and Mark A. Perazella

- Automated urine technology and centralized laboratory testing are becoming the standard for providing urinalysis data to clinicians.
- urine sediment examination remains a time-honored test that provides a wealth of information about the patient's underlying Kidney disease.
- Urinary sediment performs as a urinary "biomarker" for a number of acute kidney diseases.

- 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)

- Urinary sediment is especially helpful in assessing AKI, Hematuria, Proteinuria, leukocyturia .

- Importantly, accurately observing urinary cell morphology, identifying cellular and non cellular casts and recognizing endogenous and drug –induced crystalls can enable rapid diagnosis of AKI or CKD.

- Automated systems were inadequate to identify and classify sediment particles such as casts and crystals in highly pathologic samples.

Diagnostic Value of Urine Microscopy for Differential Diagnosis of Acute Kidney Injury in Hospitalized Patients

Mark A. Perazella, Steven G. Coca, Mehmet Kanbay, Ursula C. Brewster, and Chirag R. Parikh

Section of Nephrology, Yale University School of Medicine, New Haven, Connecticut

- Urine sediment examination is a valuable diagnostic tool for confirming the diagnosis of ATN. A score of >2 on an ATN urinary sediment scoring system is an extremely
- strong predictor of ATN.

CLIN J AM SOC NEPHROL 3: 1615–1619, 2008. DOI: 10.2215/CJN.02860608

Diagnostic Value of Urine Microscopy for Differential Diagnosis of Acute Kidney Injury in Hospitalized Patients

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Table 1. Scoring system based on number of granular casts and RTEC seen per high-power field for differentiating ATN from prerenal AKI[a]

Score	Description
1	RTE cells 0 and granular casts 0
2	RTE cells 0 and granular casts 1 to 5 or RTE cells 1 to 5 and granular casts 0
3	RTE cells 1 to 5 and granular casts 1 to 5 or RTE cells 0 and granular casts 6 to 10 or RTE cells 6 to 20 and granular casts 0

[a]ATN, acute tubular necrosis; AKI, acute kidney injury; RTEC, renal tubular epithelial cells.

Clin J Am Soc Nephrol 3: 1615–1619, 2008. DOI: 10.2215/CJN.02860608

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Original paper
Originalni naučni rad

LX-8000R AND URISED 2 FULLY AUTOMATED URINE ANALYZERS COMPARISON TO MANUAL MICROSCOPIC EXAMINATION

POREĐENJE DVA POTPUNO AUTOMATIZOVANA ANALIZATORA LX-8000R I URISED 2 SA MIKROSKOPSKIM MANUELNIM ISPITIVANJEM URINA

Revşa Evin Canpolat Erkan[1], Özgür Aslan[1]

[1]Health Sciences University Diyarbakir Gazi Yaşargil Education and Research Hospital, Department of Medical Biochemistry, Diyarbakir, Turkey

- we suggest that evaluation of automated urinalysis devices together with samples and patient clinical findings in addition to comparing with manual microscopy will be more meaningful.

EXPERIMENTAL AND THERAPEUTIC MEDICINE 21: 538, 2021

Discrepancy in results between dipstick urinalysis and urine sediment microscopy

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- The most common discordant results were: false-negatives for nitrite (72%), followed by false-positives results for red blood cells (22%), false-negative results for leukocytes (16%), false-negative results for red blood cells (4%) and false-positives for leukocytes (4%).

- a small percentage (1.92%) of inconsistencies between urinalysis and microscopic examination .

Table I. Causes of discordant results between between dipstick urinalysis and urine sediment microscopy.

Causes of discordant results	No.	%
Consumption of vitamin C	13	26.0
Infection with *Staphylococcus saprophyticus* (evidenced by urine culture)	5	10.0
Urinary density <1.005	5	10.0
Urinary density >1.030	4	8.0
Infection with *Escherichia coli* (evidenced by urine culture)	4	8.0
Antibiotic treatment (not declared or not known)	4	8.0
Incorrect harvest of urine-urine has been in the bladder for less than 2 h	4	8.0
Enterococcus spp. infection (evidenced by urine culture)	3	6.0
Leukocytes in the urine are lymphocytes, which do not contain leukocyte esterase	2	4.0
Treatment with cephalosporin	2	4.0
Urine with acid pH	2	4.0
Over glycosuria	1	2.0
Urine with alkaline pH	1	2.0
Total	50	100.0

scientific reports

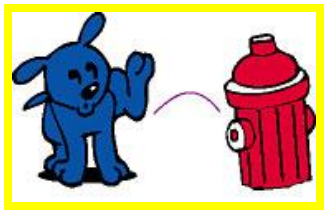
OPEN

Automated urine sediment analyzers underestimate the severity of hematuria in glomerular diseases

Won Seok Yang

- **RBC counting by UF-1000i or Cobas 6500 underestimates**
- **the severity of hematuria in glomerular disease, possibly because dysmorphic RBCs in glomerular disease are**
- **susceptible to hemolysis and/or fail to be properly**
- **recognized.**

Specimen Collection



- First morning voiding (most concentrated)
- Record collection time
- Type of specimen (e.g. “clean catch”)
- Analyzed within 2 hours of collection
- Free of debris or vaginal secretions

Types of Analysis

- Macroscopic Examination
- Chemical Analysis (Urine Dipstick)
- Microscopic Examination
- Culture (not covered in this lecture)
- Cytological Examination

Urine Analysis

Macroscopic Urine Analysis		*Microscopic* W.B.C/Mic.L	2-3
Color	Yellow	R.B.C./Mic.L	0-1
Appearance	Semi-Turbid	Epithelial Cells/hpf	8-10
Specific Gravity	1.020	Bacteria	Rare
pH	6	Mucus	Moderate
Blood/Hgb	Negative	Yeasts	Negative
Protein(mg/dl)	Negative	Casts	Negative
Glucose(mg/dl)	Negative		
Ketone(mg/dl)	Negative		
Bilirubin(mg/dl)	Negative		
Urobilinogen(mg/dl)	Negative		

Macroscopic Examination

Turbidity:

- Typically cells or crystals.
- Cellular elements and bacteria will clear by centrifugation.
- Microscopic examination will determine which is present.

Chemical Analysis

Urine Dipstick

- Glucose
- Bilirubin
- Ketones
- Specific Gravity
- Blood
- pH
- Protein
- Urobilinogen
- Nitrite
- Leukocyte Esterase

Uses and Limitations of Urine Glucose Detection

Significance

- Diabetes mellitus.
- Renal glycosuria.

Limitations

- Interference: reducing agents, ketones.
- Only measures glucose and not other sugars.
- Renal threshold must be passed in order for glucose to spill into the urine.

Other Tests

- $CuSO_4$ test for reducing sugars.

Uses and Limitations of Urine Bilirrubin Detection

Significance

- Increased direct bilirubin (correlates with urobilinogen and serum bilirubin)

Limitations

- Interference: prolonged exposure of sample to light
- Only measures direct bilirubin--will not pick up indirect bilirubin

Other Tests

- Ictotest (more sensitive tablet version of same assay)
- Serum test for total and direct bilirubin is more informative

Uses and Limitations of Urine Ketone Detection

Significance

- Diabetic ketoacidosis
- Prolonged fasting

Limitations

- Interference: expired reagents (degradation with exposure to moisture in air)
- Only measures acetoacetate not other ketone bodies (such as in rebound ketosis).

Other Tests

- Ketostix (more sensitive tablet version of same assay)
- Serum glucose measurement to confirm DKA

Uses and Limitations of Urine Specific Gravity

Significance

- Diabetes insipidus

Limitations

- Interference: alkaline urine
- Does not measure non-ionized solutes (e.g. glucose)

Other Tests

- Refractometry
- Hydrometer
- Osmolality measurement (typically used with water deprivation test)

Uses and Limitations of Urine Blood Detection

Significance

- Hematuria (nephritis, trauma, etc)
- Hemoglobinuria (hemolysis, etc)
- Myoglobinuria (rhabdomyolysis, etc)

Limitations

- Interference: reducing agents, microbial peroxidases
- Cannot distinguish between the above disease processes

Other Tests

- Urine microscopic examination
- Urine cytology

Uses and Limitations of Urine Protein Detection

Significance

- Proteinuria and the nephrotic syndrome.

Limitations

- Interference: highly alkaline urine.
- Much more sensitive to albumin than other proteins (e.g., immunoglobulin light chains).

Other Tests

- Sulfosalicylic acid (SSA) turbidity test.
- Urine protein electrophoresis (UPEP)
- Bence Jones protein

Uses and Limitations of Nitrite Detection

Significance

- Gram negative bacteriuria

Limitations

- Interference: bacterial overgrowth
- Only able to detect bacteria that reduce nitrate to nitrite

Other Tests

- Correlate with leukocyte esterase and
- Urine microscopic examination (bacteria)
- Urine culture

Microscopic Examination

General Aspects

Preservation

- Cells and casts begin to disintegrate in 1 - 2 hrs. at room temp.
- Refrigeration for up to 48 hours (little loss of **cells).**

Specimen concentration

- Ten to twenty-fold concentration by centrifugation.

Types of microscopy

- Phase contrast microscopy
- Polarized microscopy
- Bright field microscopy with special staining (e.g., Sternheimer-Malbin stain)

Microscopic Examination

Abnormal Findings

Per High Power Field (HPF) (400x)

- > 3 erythrocytes
- > 5 leukocytes
- > 2 renal tubular cells
- > 10 bacteria

Per Low Power Field (LPF) (200x)

- > 3 hyaline casts or > 1 granular cast
- > 10 squamous cells (indicative of contaminated specimen)
- Any other cast (RBCs, WBCs)

Presence of:

- Fungal hyphae or yeast, parasite, viral inclusions
- Pathological crystals (cystine, leucine, tyrosine)
- Large number of uric acid or calcium oxalate crystals

Microscopic Examination

Cells

Erythrocytes

- "Dysmorphic" vs. "normal"

Leukocytes

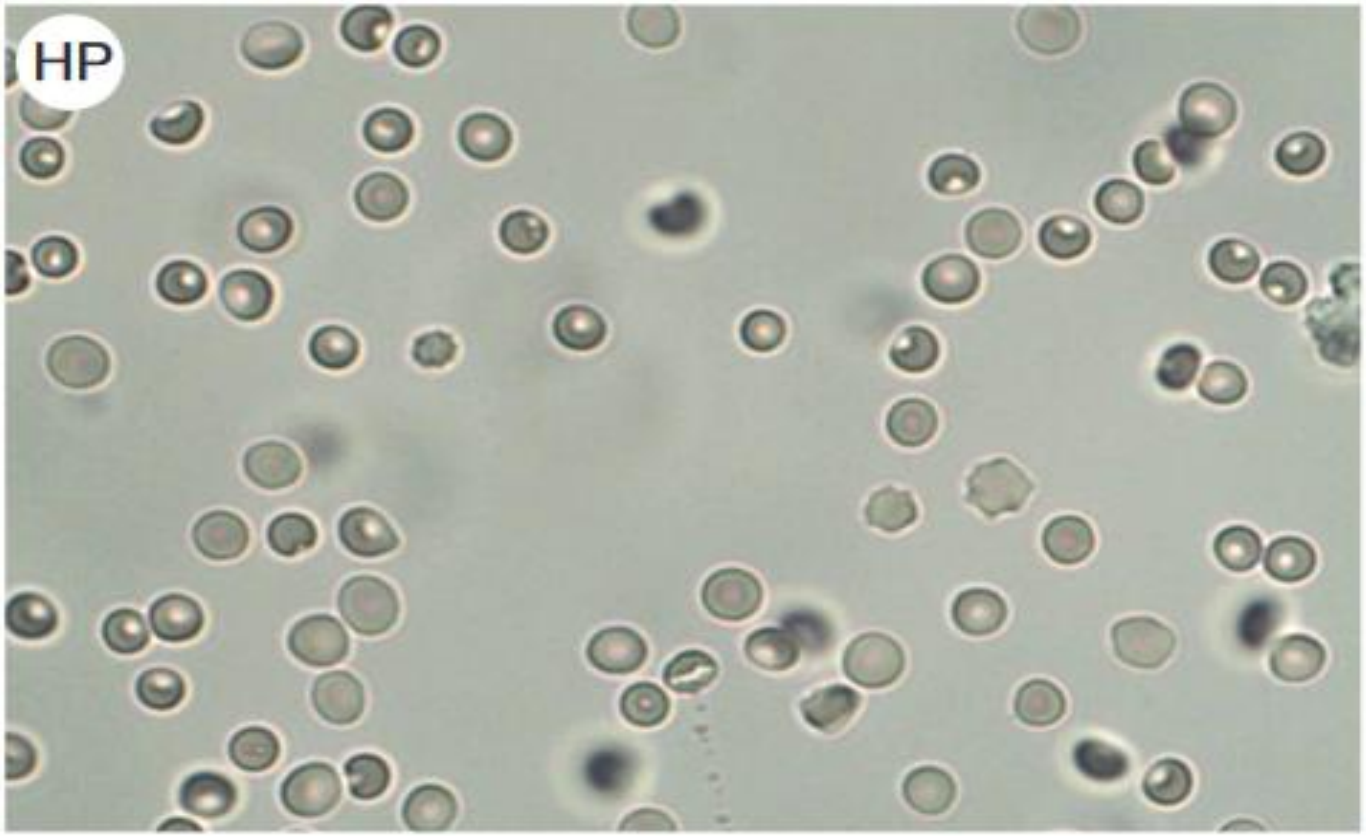
- Neutrophils (glitter cells)
- Eosinophils — Hansel test (special stain)

Epithelial Cells

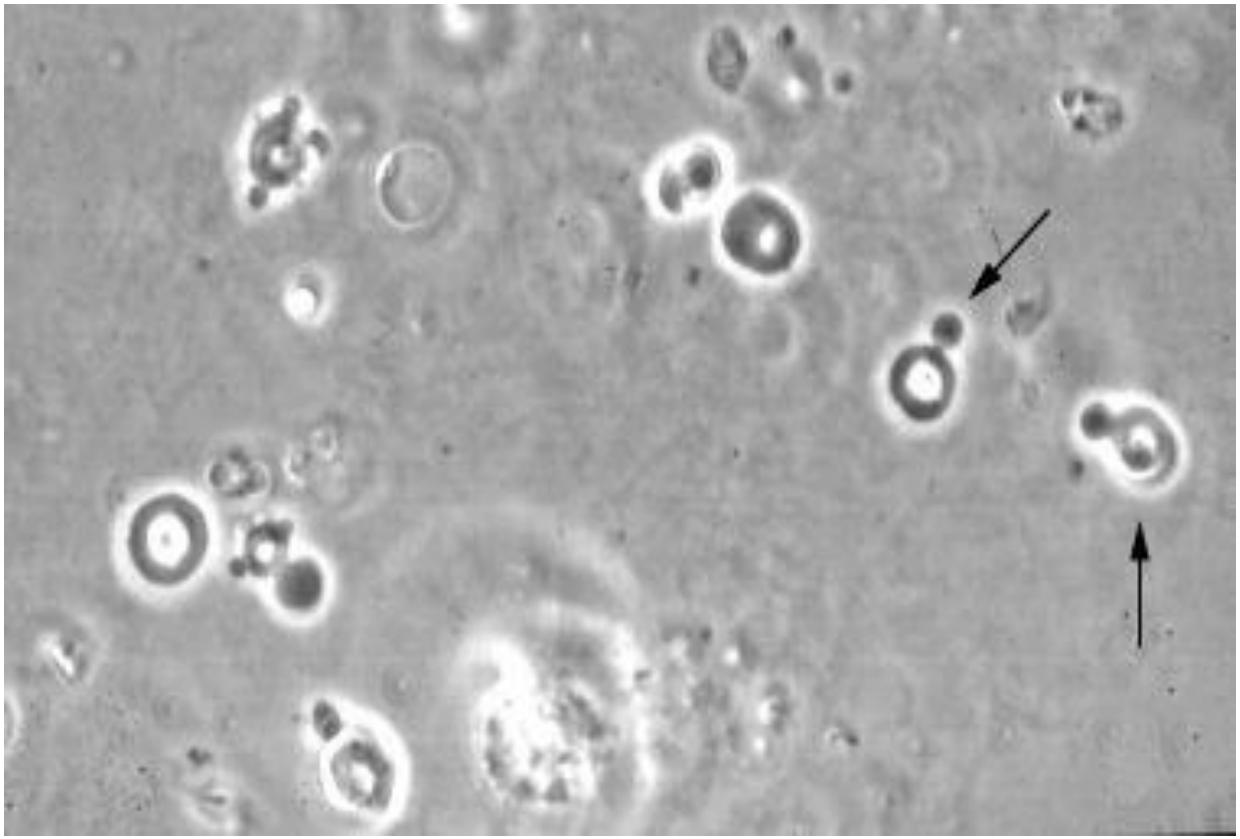
- Squamous cells — Indicate level of contamination
- Renal tubular epithelial cells — Few are normal
- Transitional epithelial cells — Few are normal

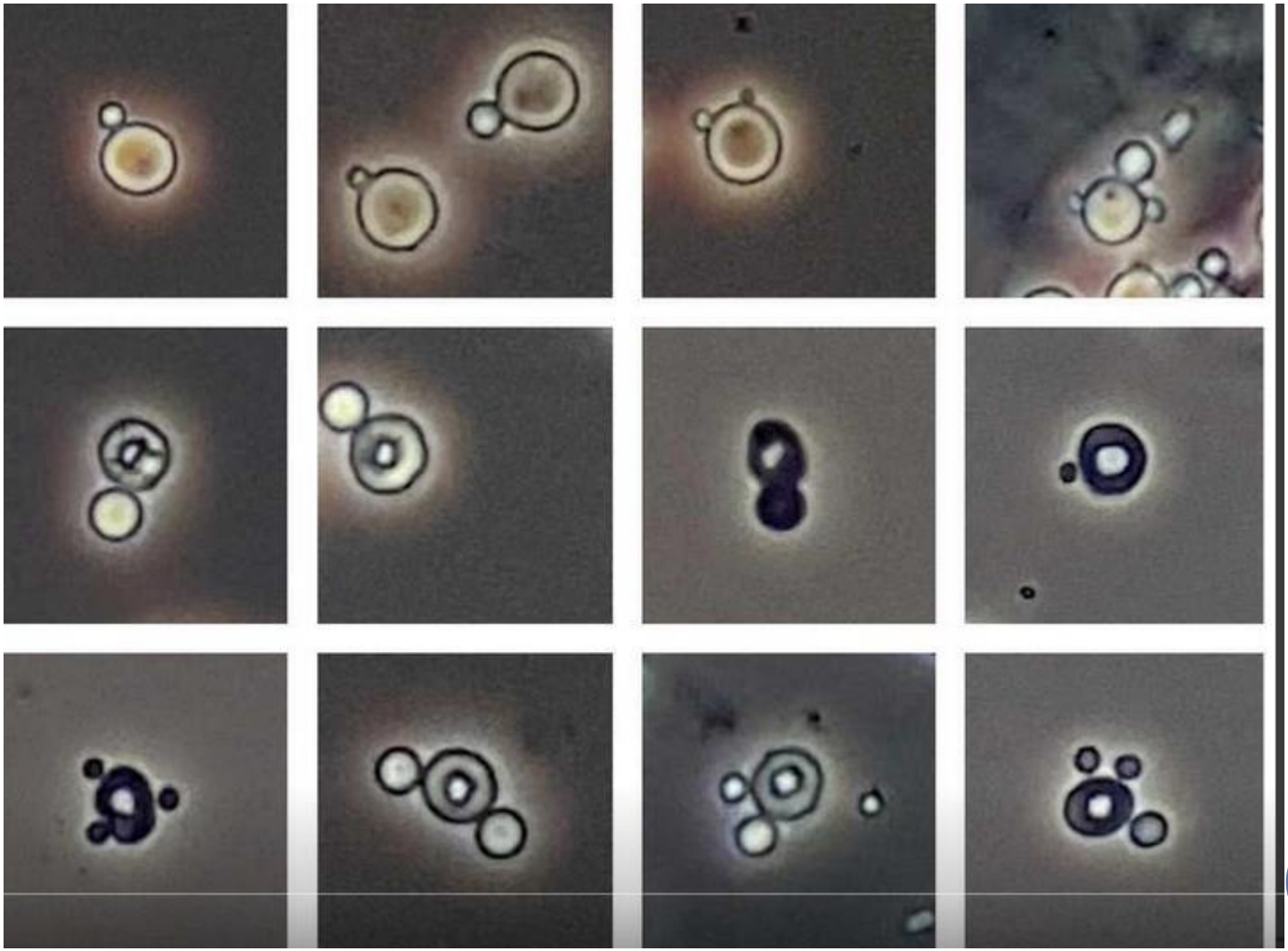
- Oval fat bodies — Abnormal, indicate Nephrosis

RBC

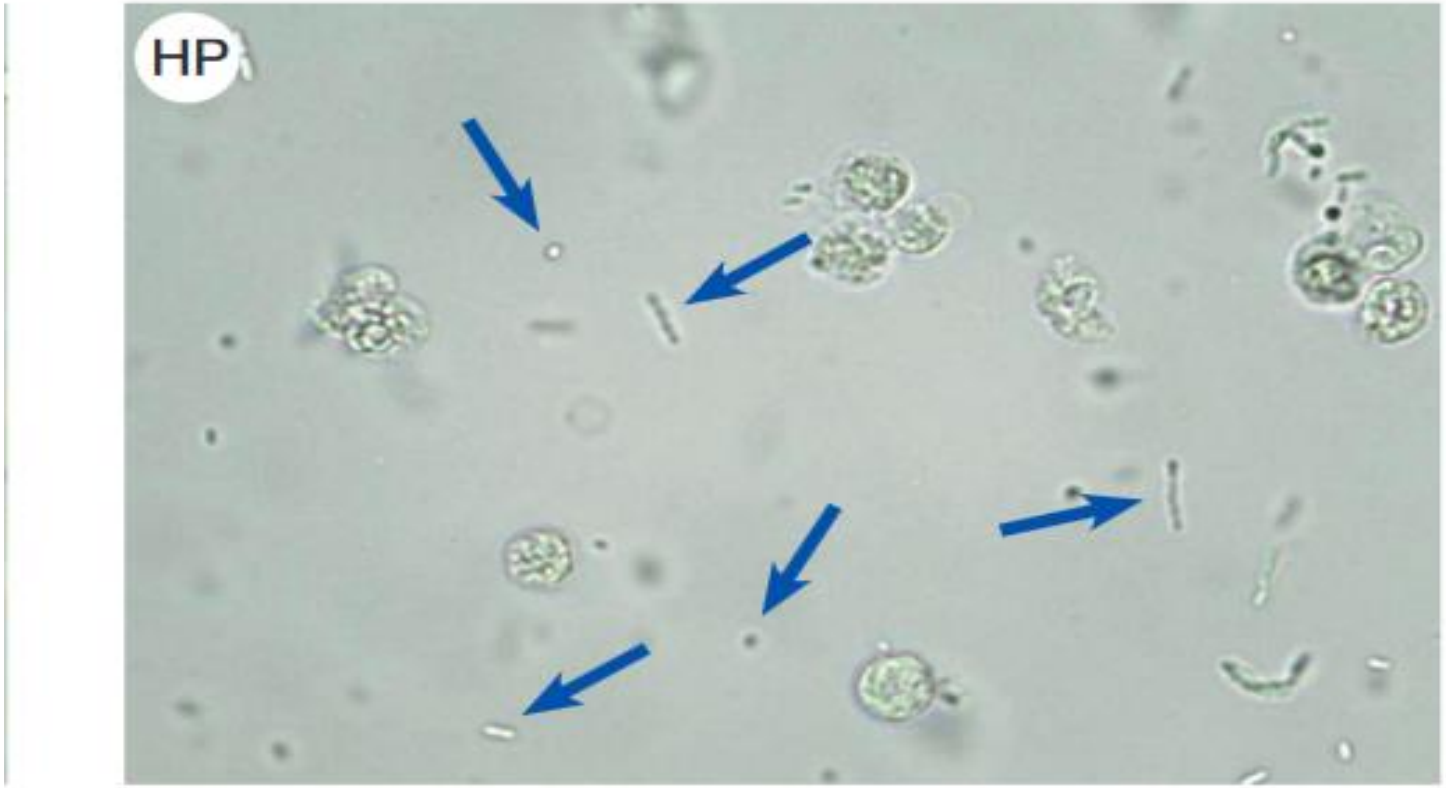


RBC - Dysmorphic



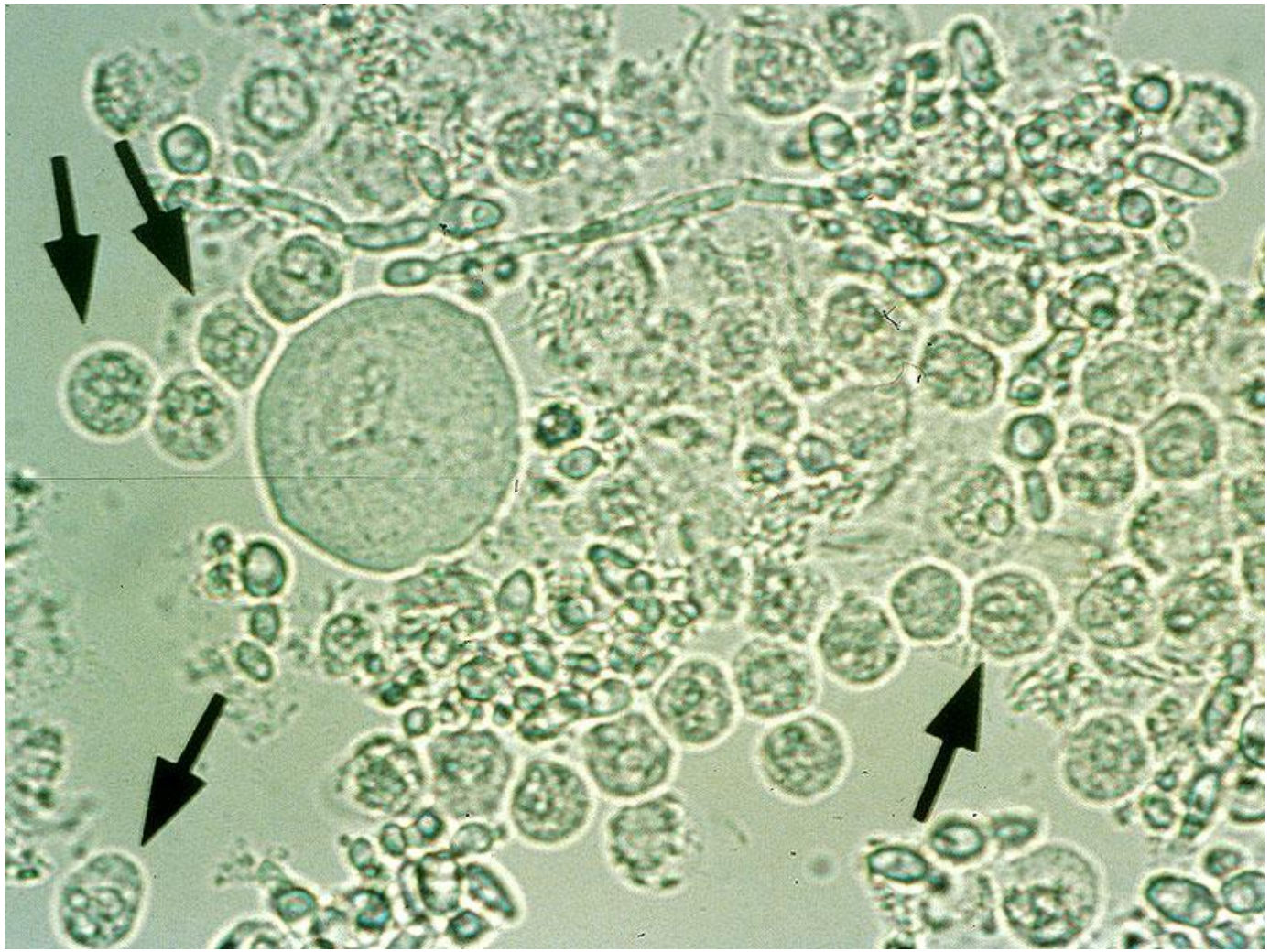


WBC and Bacteria



Microscopic Examination

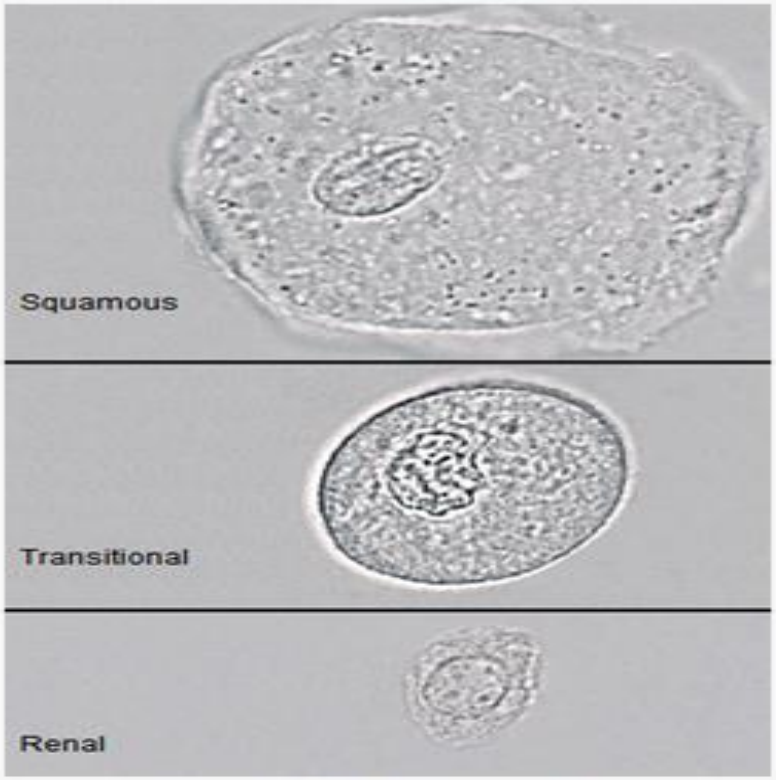
WBCs



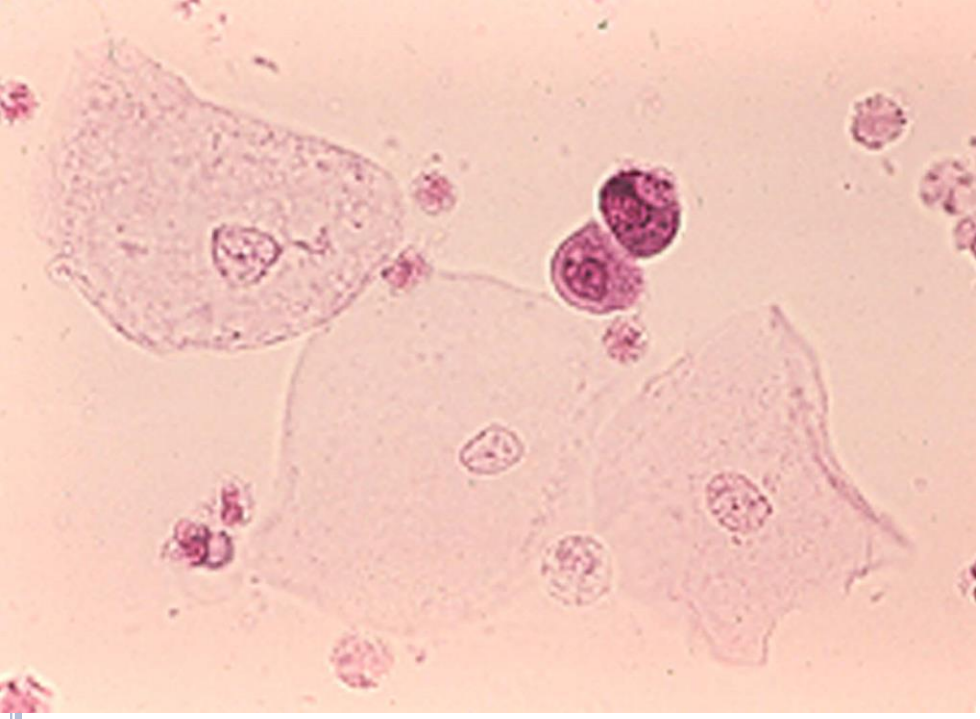
Three types of epithelial cells

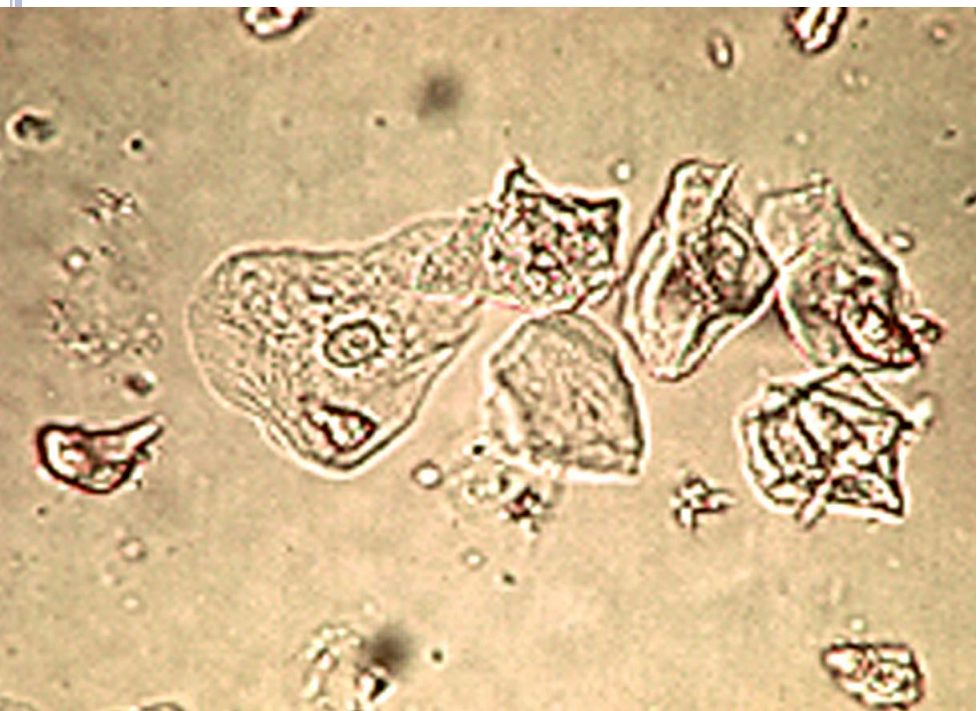
There are 3 types of epithelial cells that can be found in urine:

1. Squamous Epithelial cells
2. Transitional Epithelial cells
3. Renal Tubular Epithelial (RTE) cells



epithelial cells found in urine

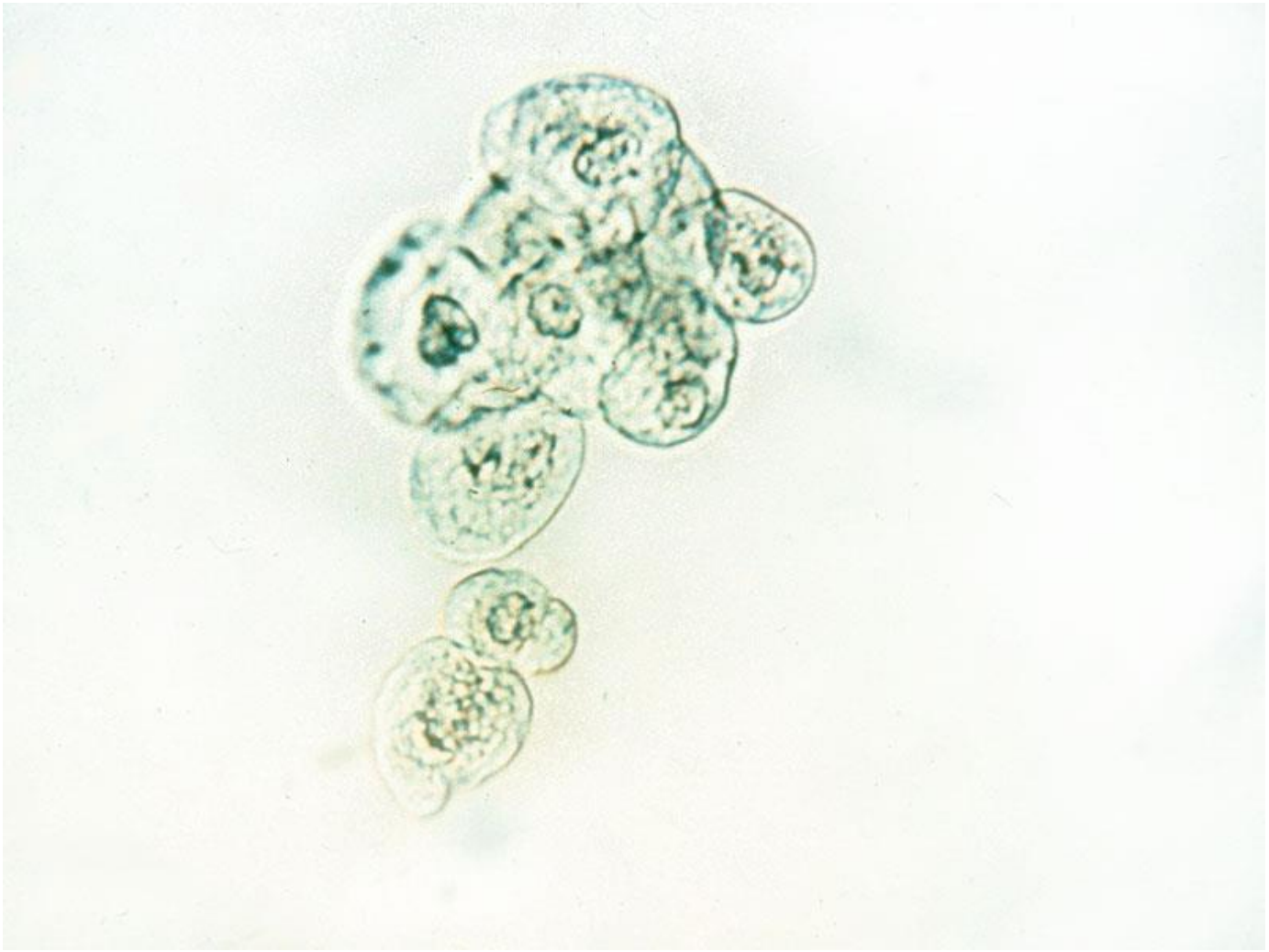




Squamous Epithelial

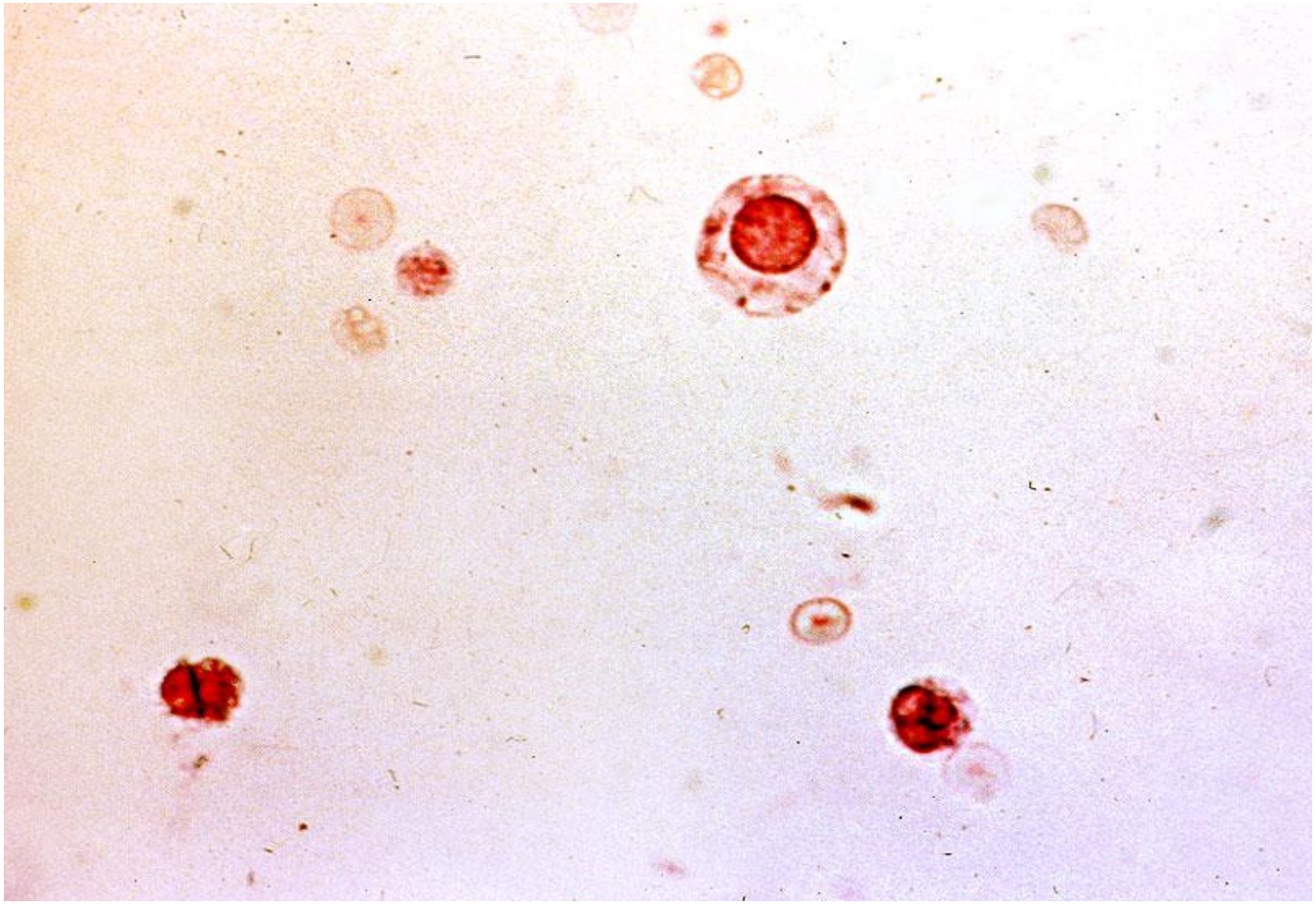
Microscopic Examination

Transitional Cells

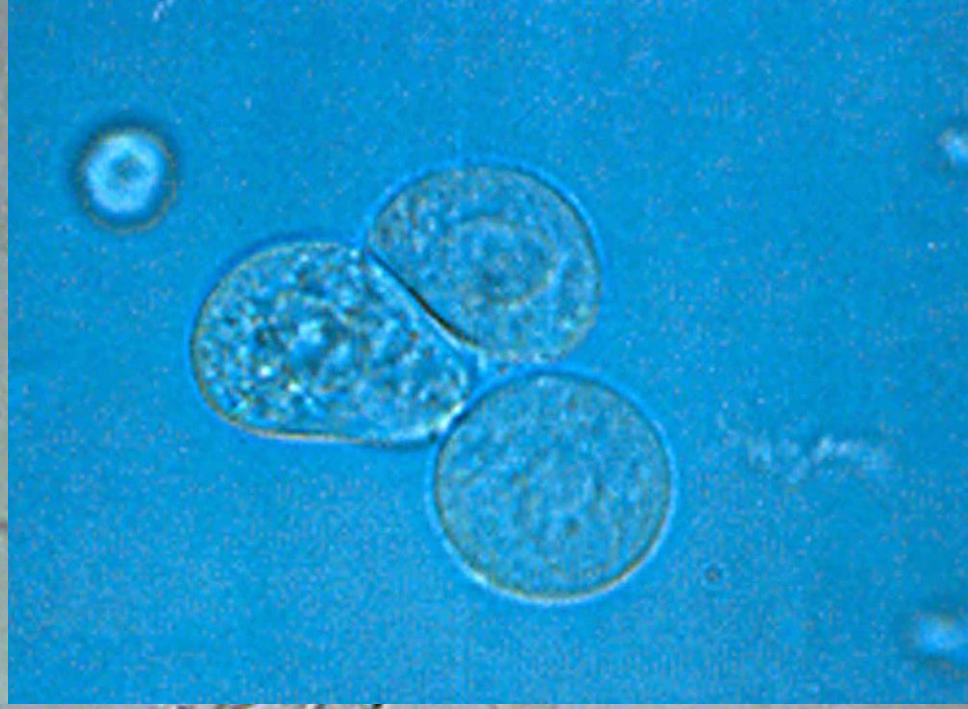


Microscopic Examination

Tubular Epithelial Cells

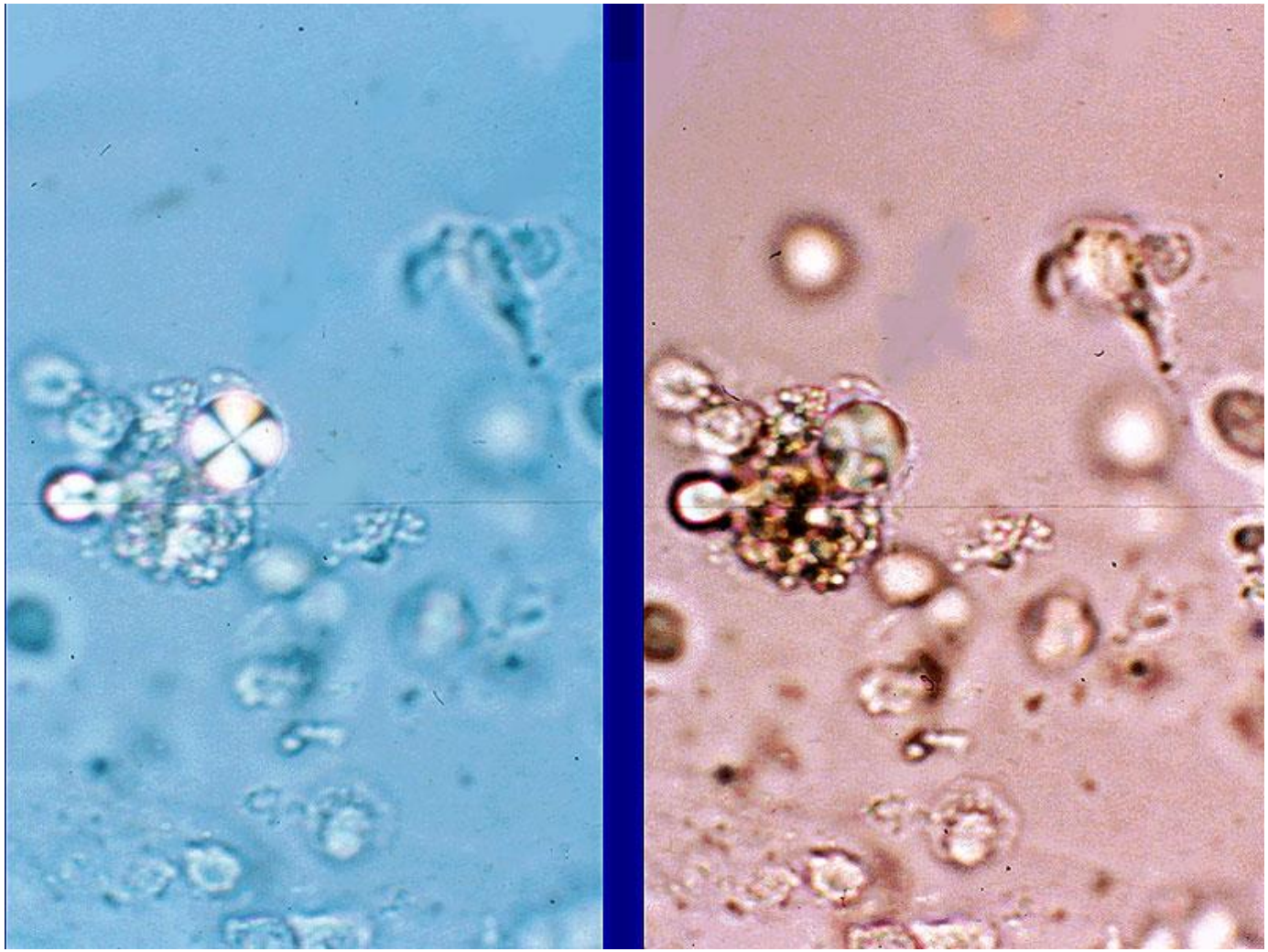



Renal Tubular Epithelial



Microscopic Examination

Oval Fat Body



Microscopic Examination

Bacteria & Yeasts

Bacteria

- Bacteriuria	More than 10 per HPF

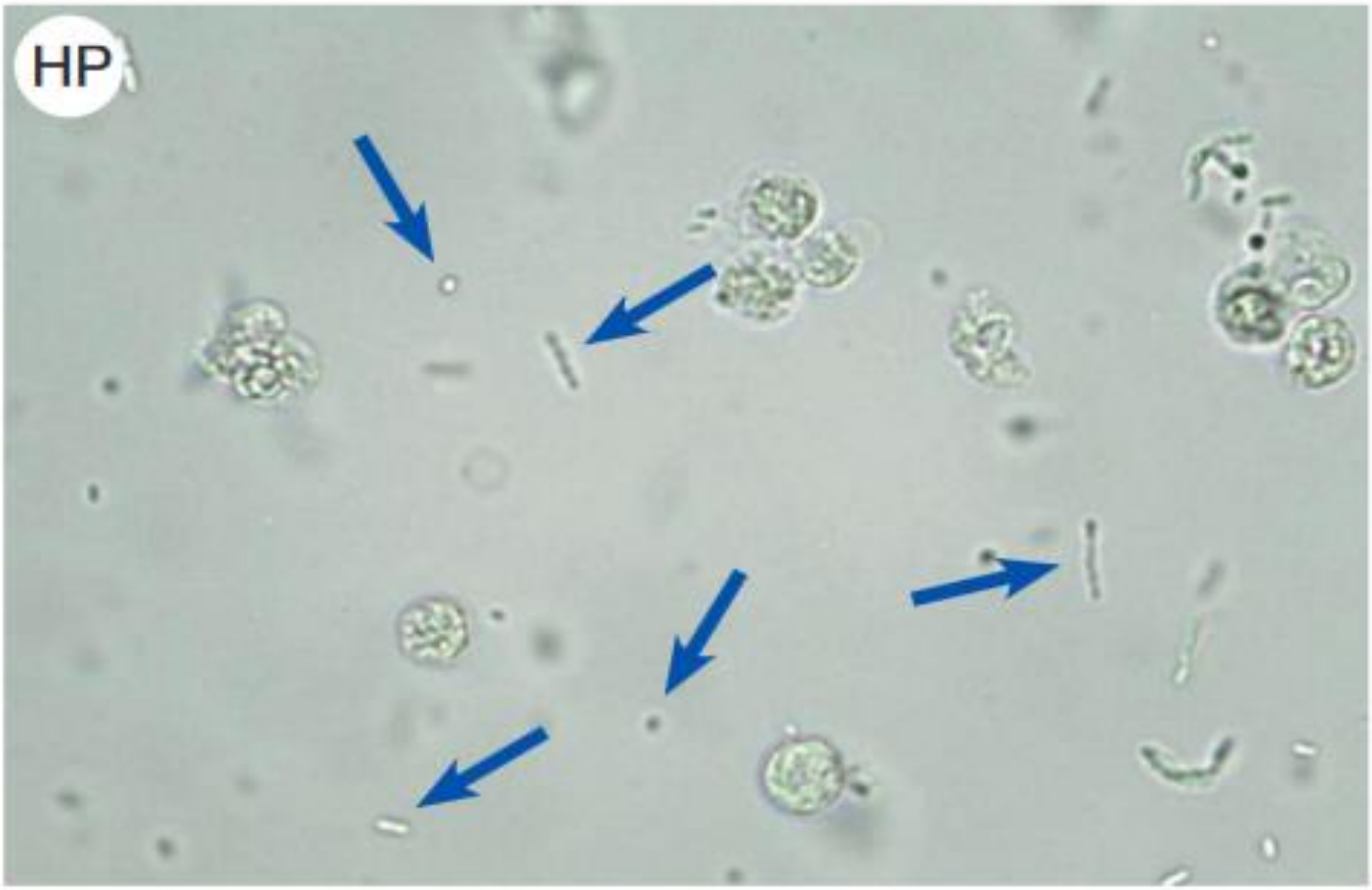
Yeasts

- Candidiasis	Most likely a contaminant but should correlate with clinical picture.

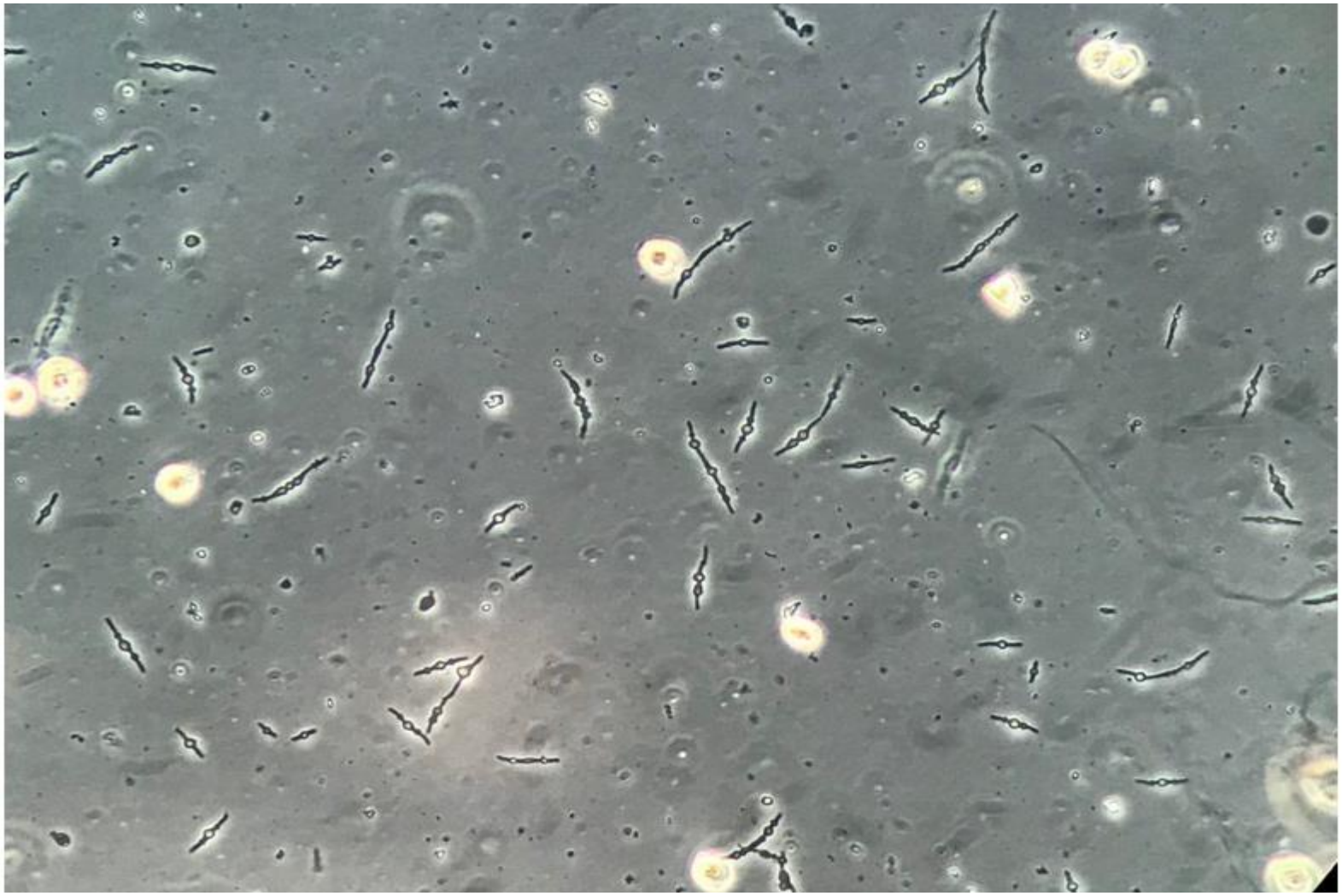
Viruses

- CMV inclusions	Probable viral cystitis.

WBC and Bacteria



Spheroplasts



Microscopic Examination

Yeasts

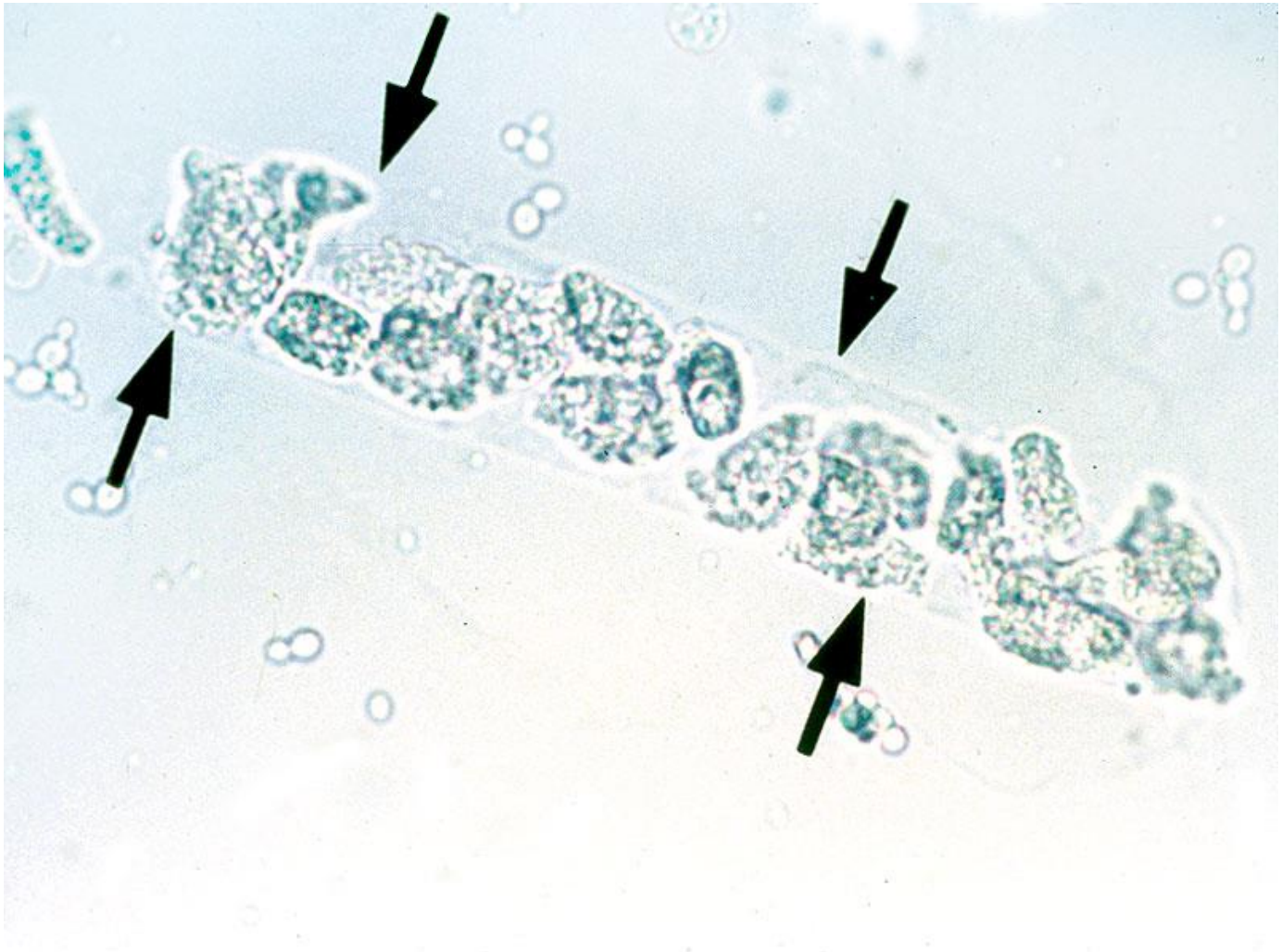
Casts

- Hyaline
- Granular
- Cellular
- Billirubin

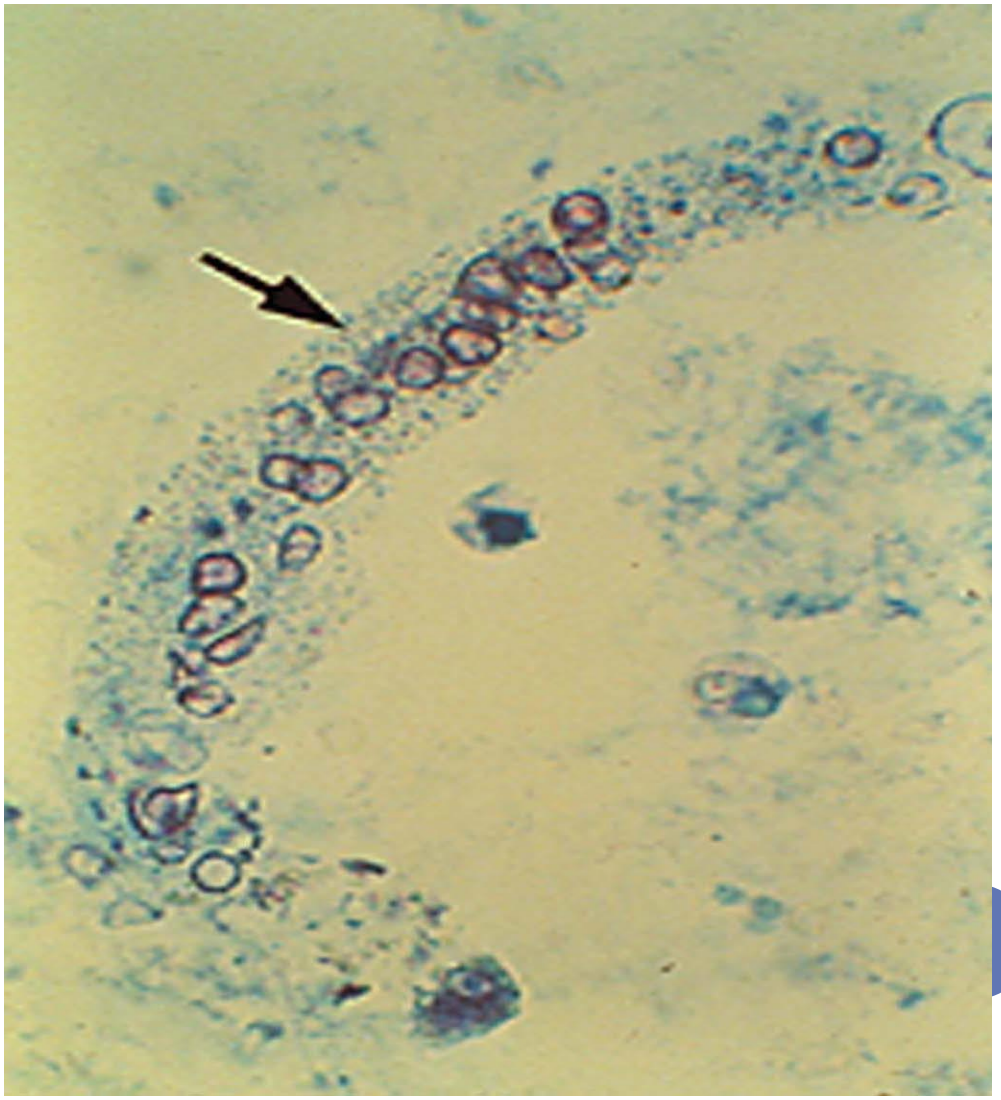

How many casts do you see?

Microscopic Examination

WBCs Cast

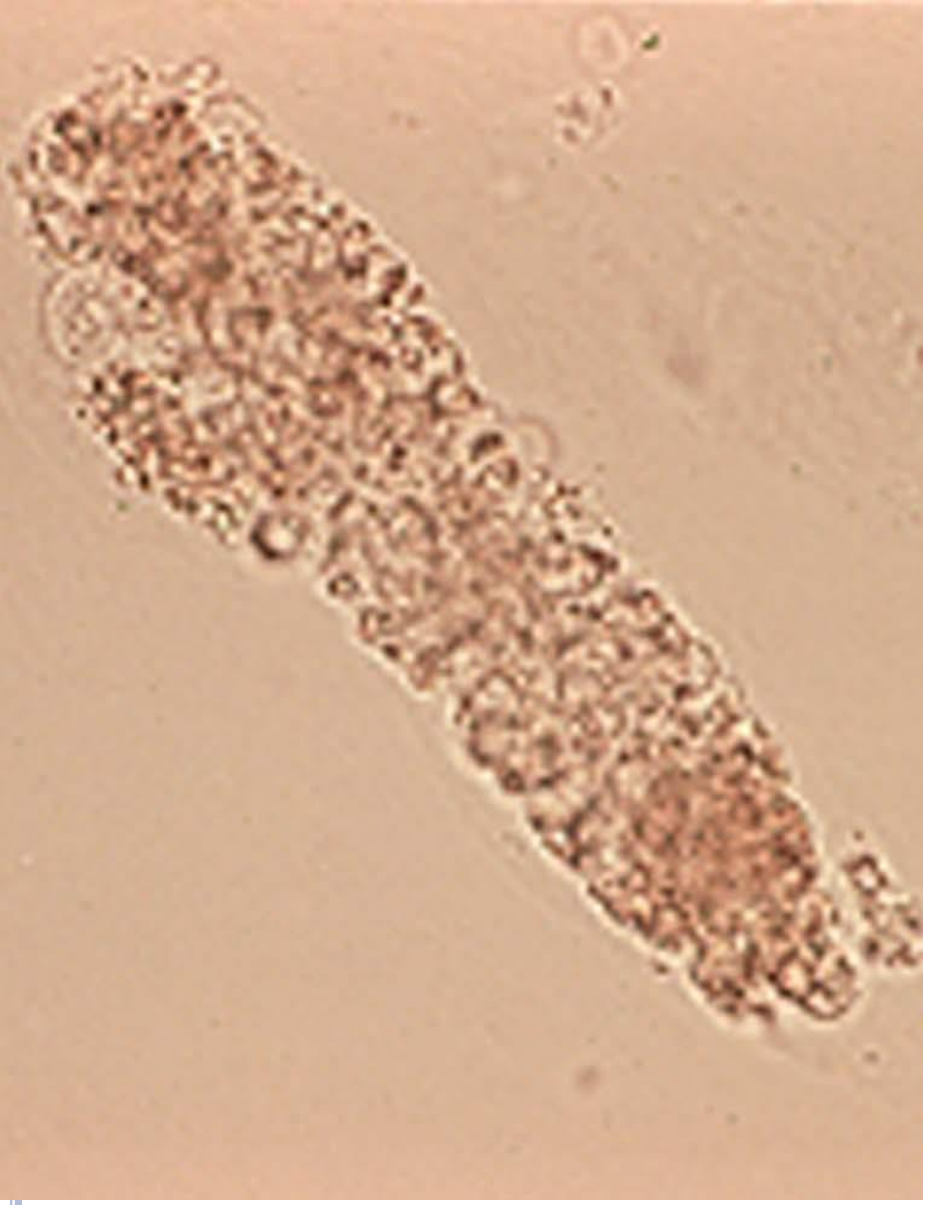


RBC cast

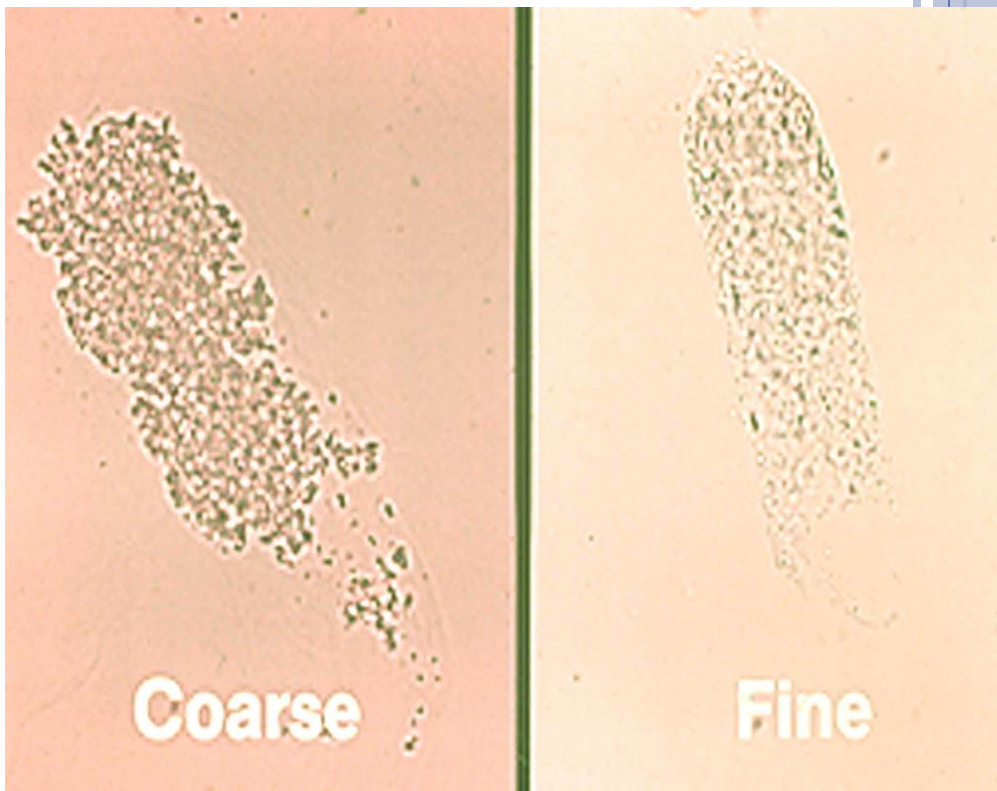


Microscopic Examination

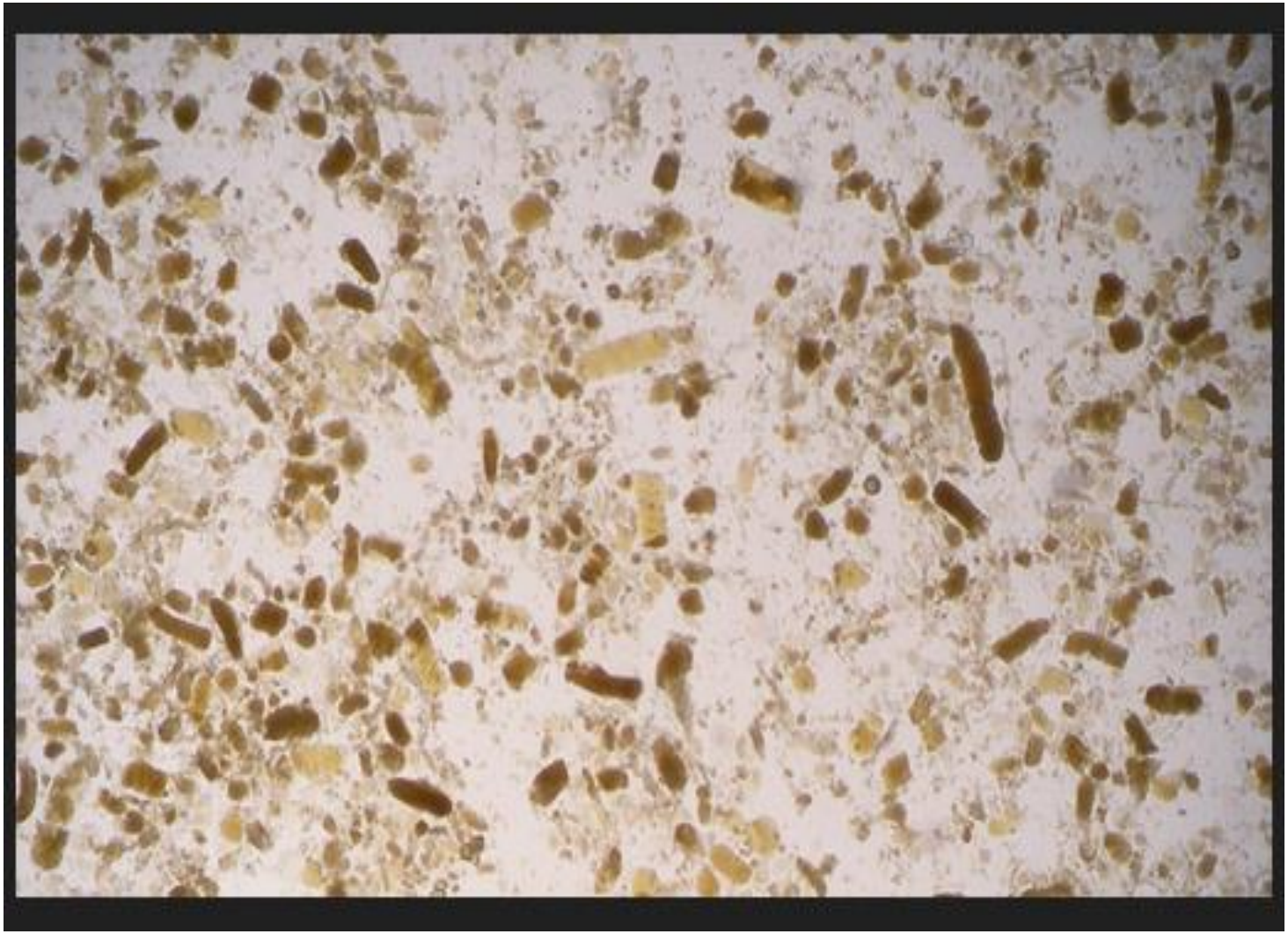
Tubular Epith. Cast



Coarse Granular Cast

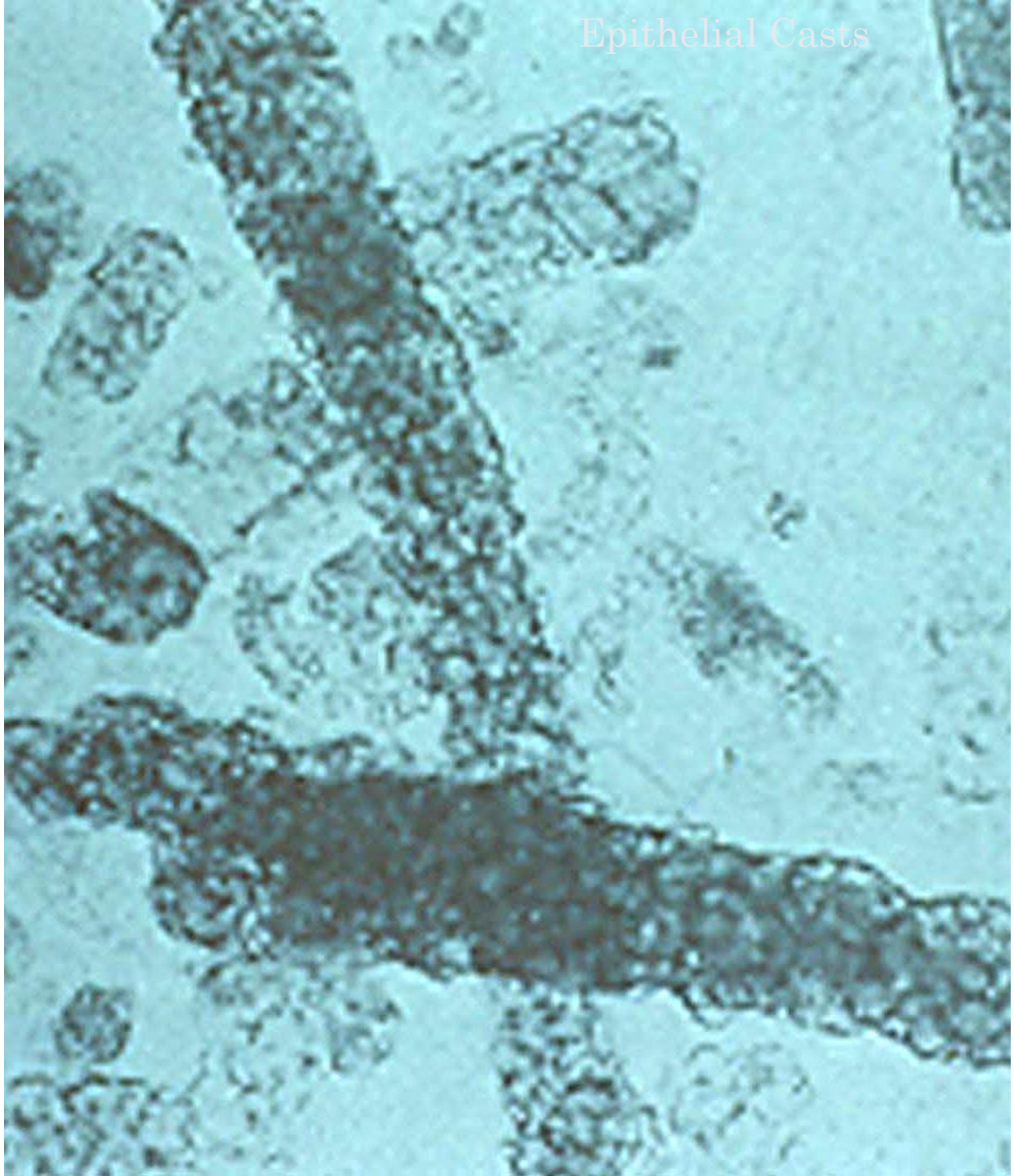


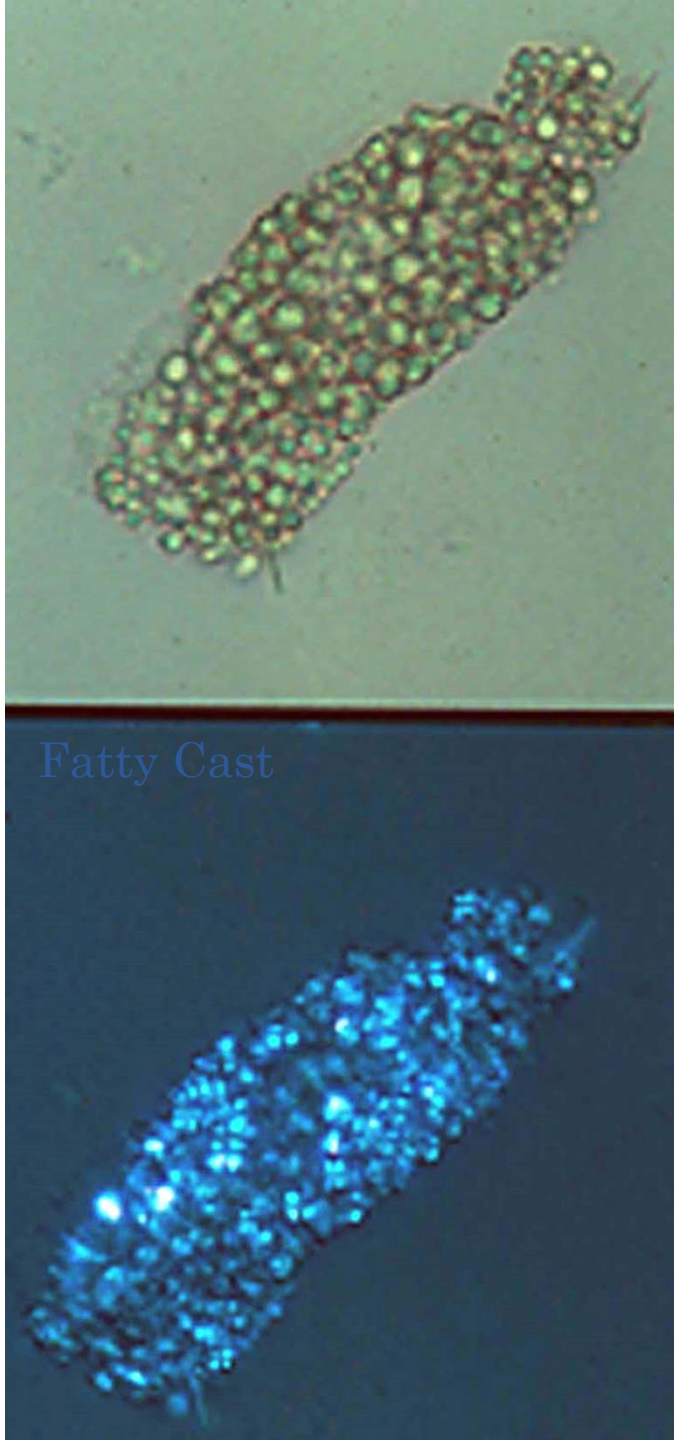
Muddy Brown Casts



Microscopic Examination

Waxy Cast


Epithelial Casts


Fatty Cast

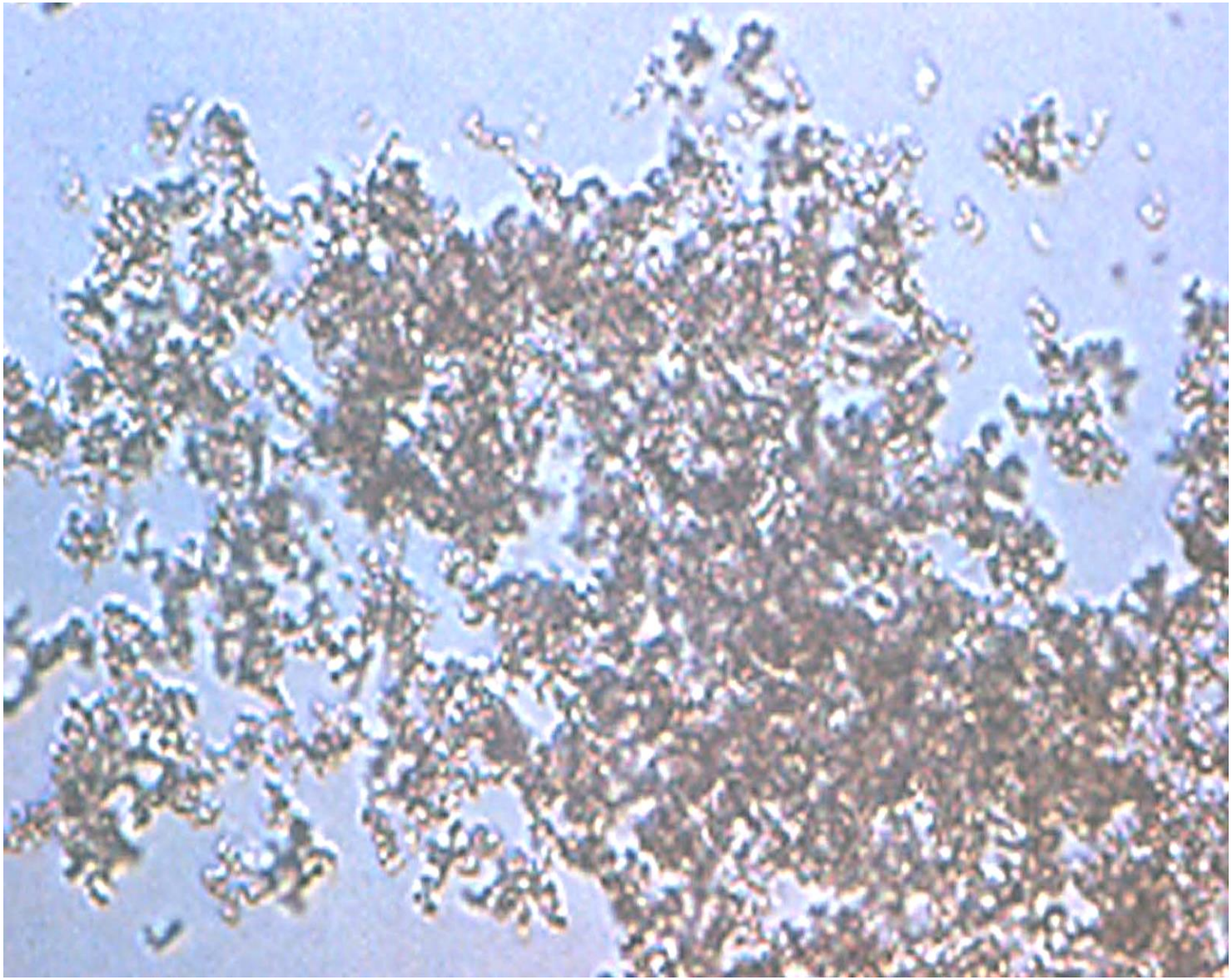
Bilirubin cast

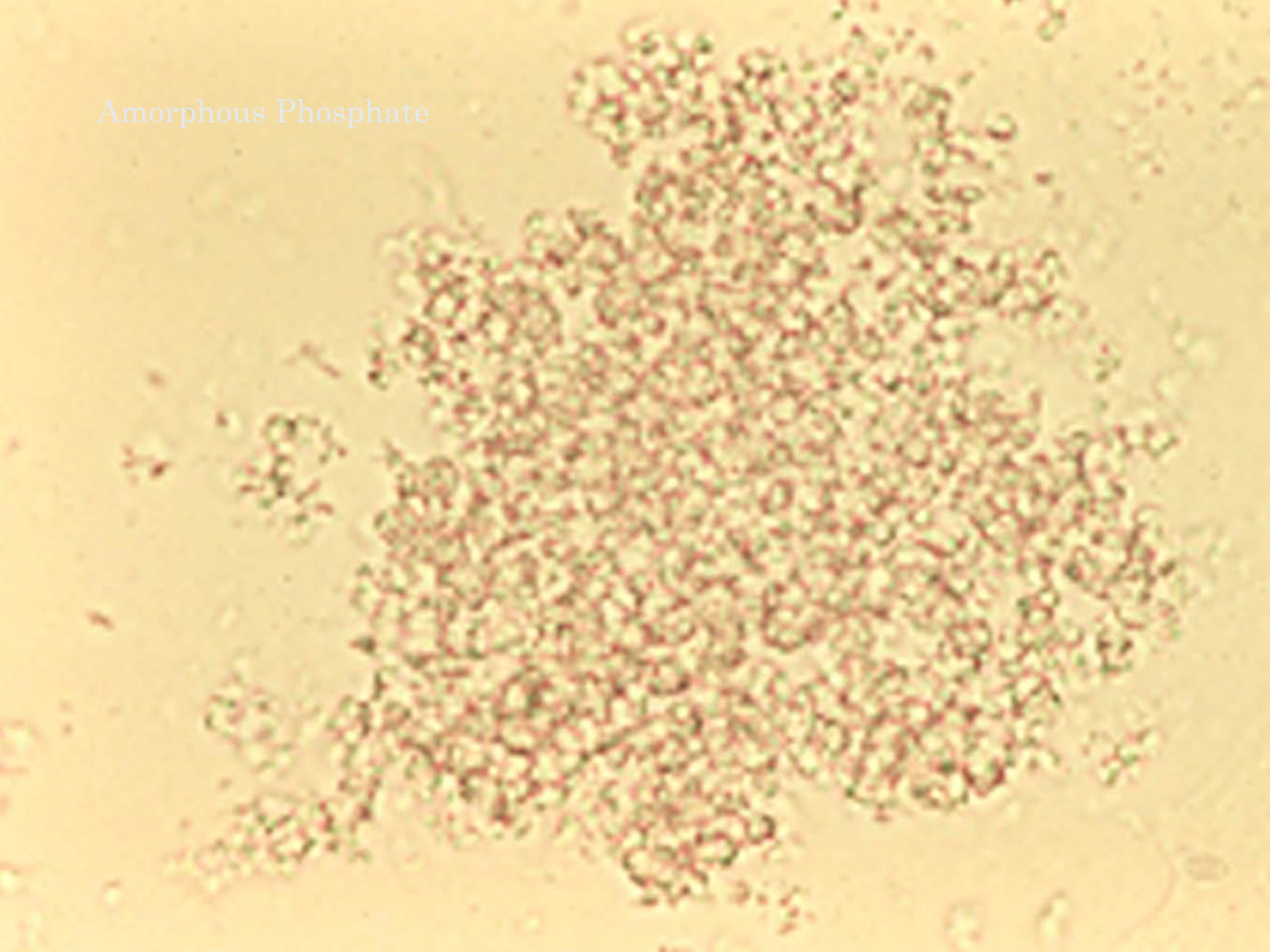
Microscopic Examination

Crystals

- Urate
  - Ammonium biurate
  - Uric acid
- Triple Phosphate
- Calcium Oxalate
- Amino Acids
  - Cystine
  - Leucine
  - Tyrosine
- Drugs (Sulfonamide,…)

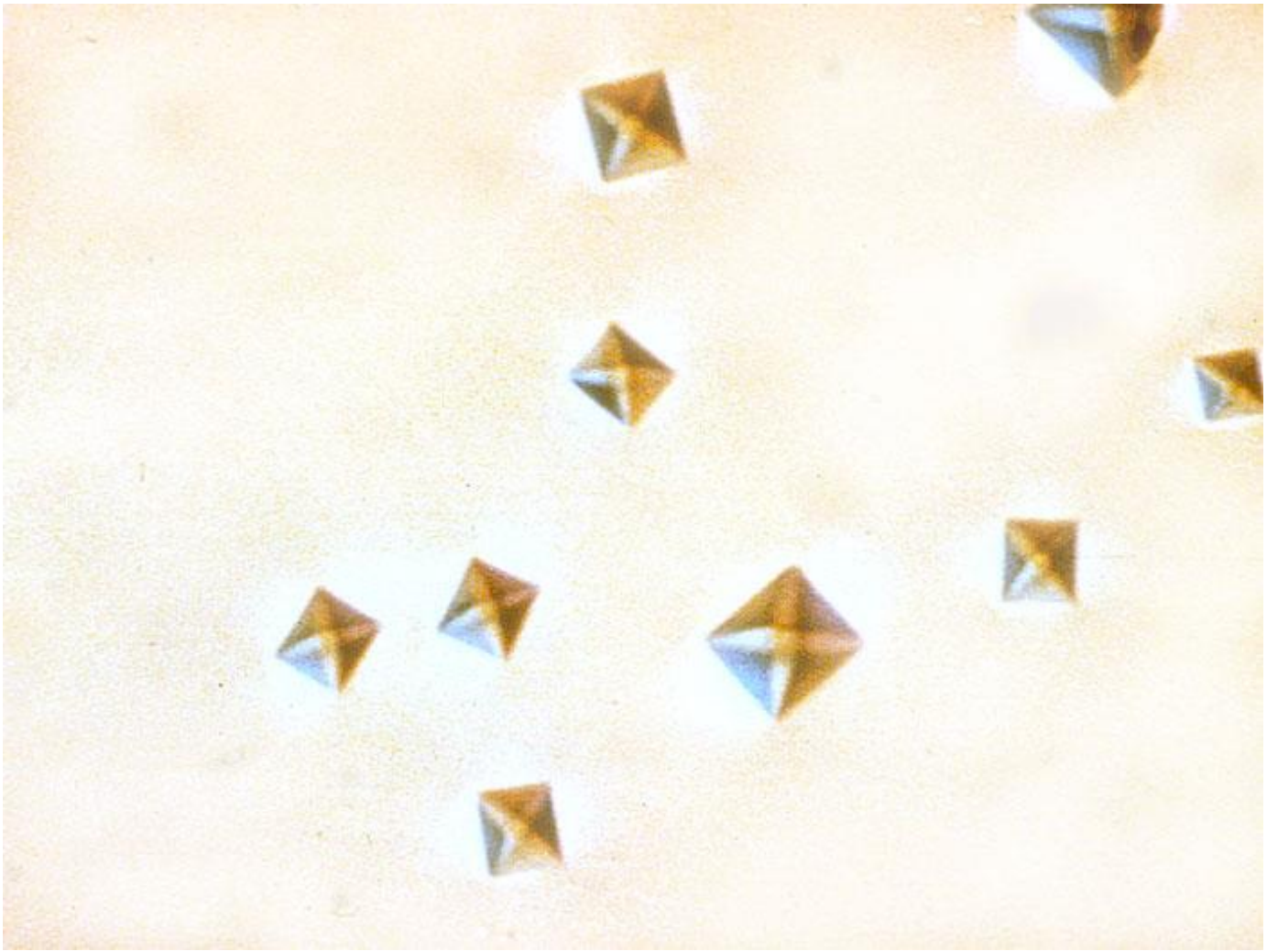
Amorphous Urate

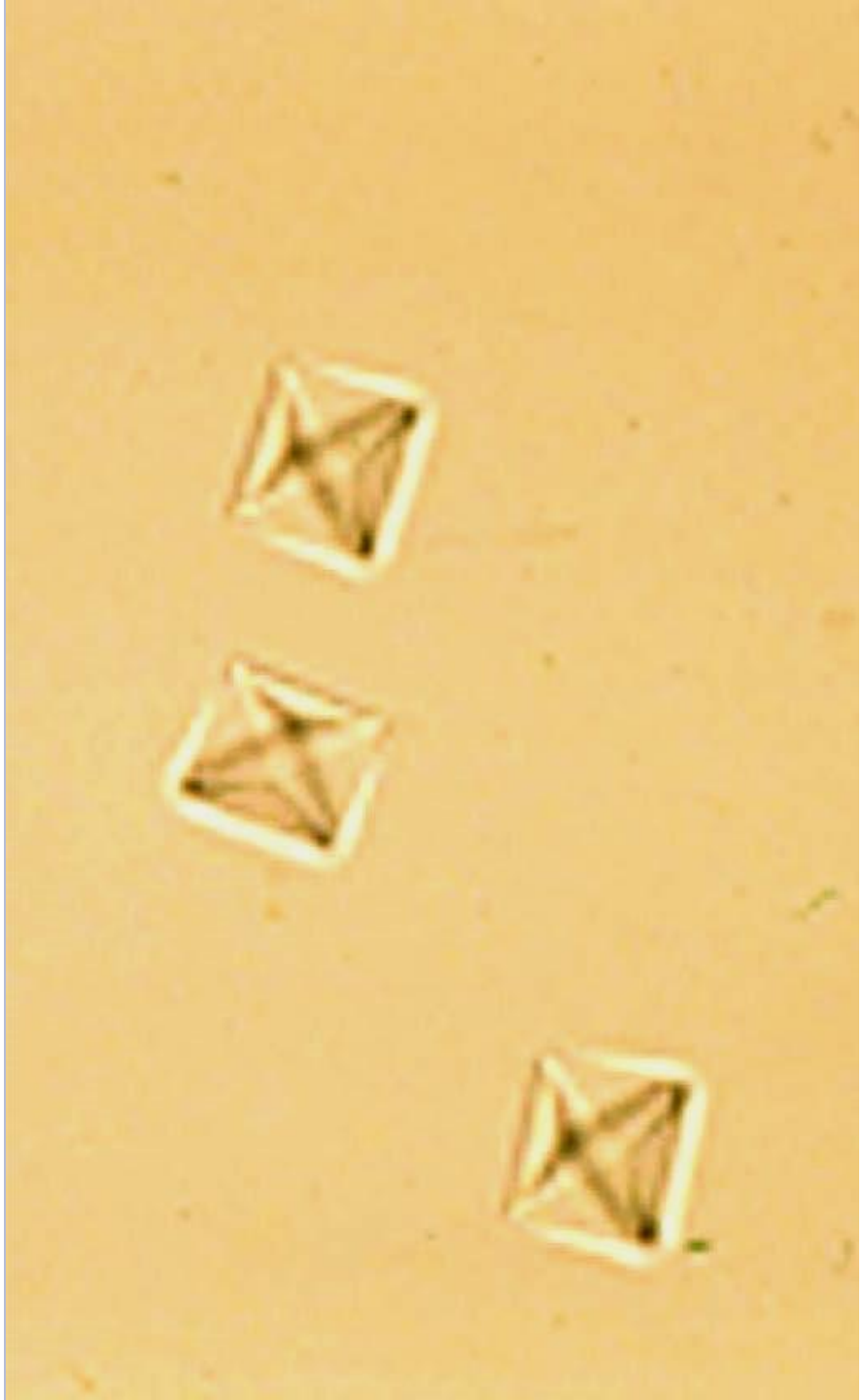



Amorphous Phosphate

Microscopic Examination

Calcium Oxalate Crystals





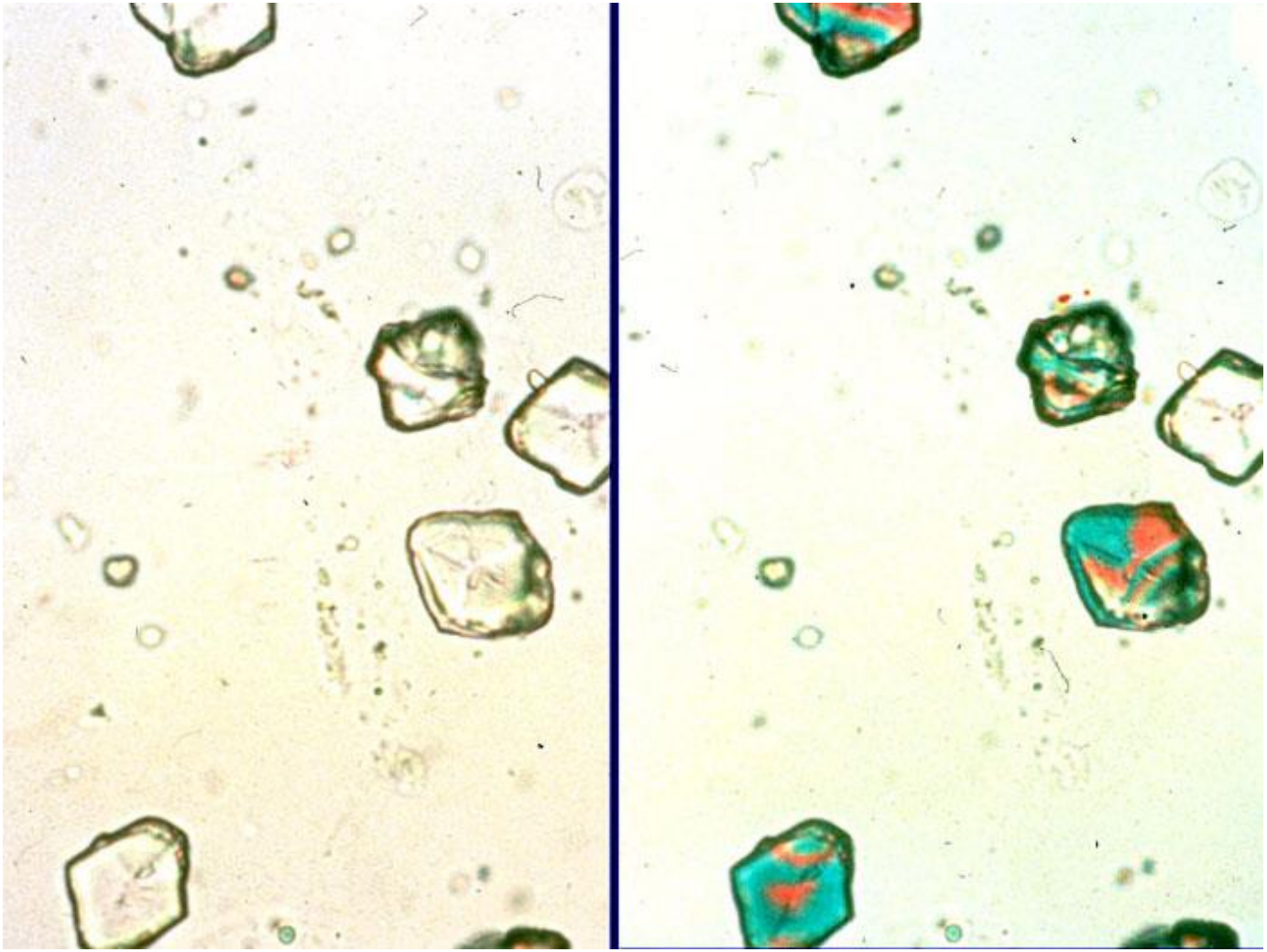

Calcium Oxalate

Microscopic Examination

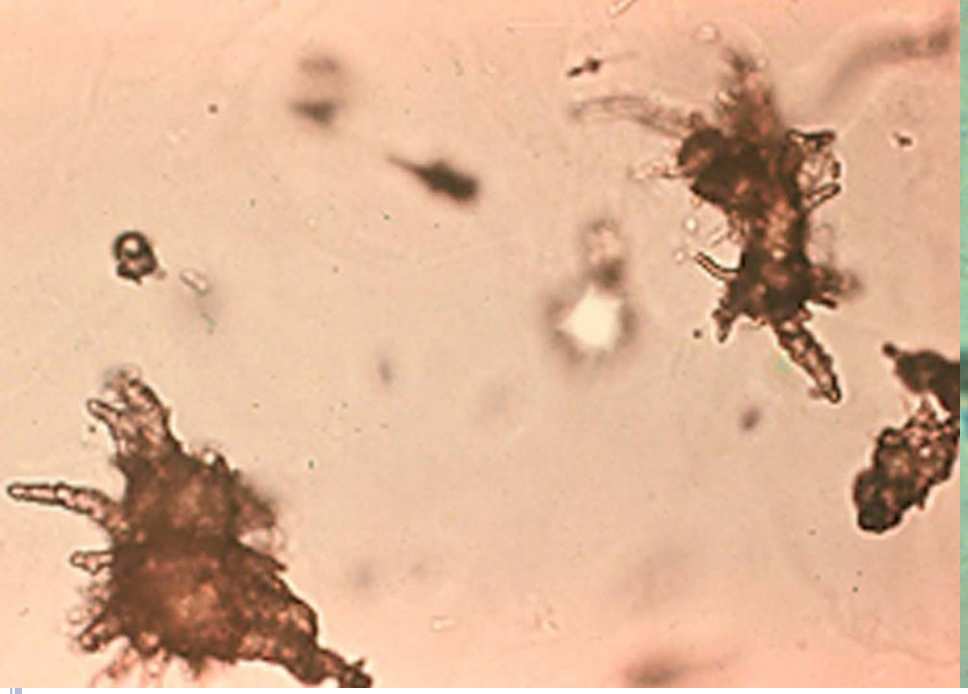
Triple Phosphate Crystals

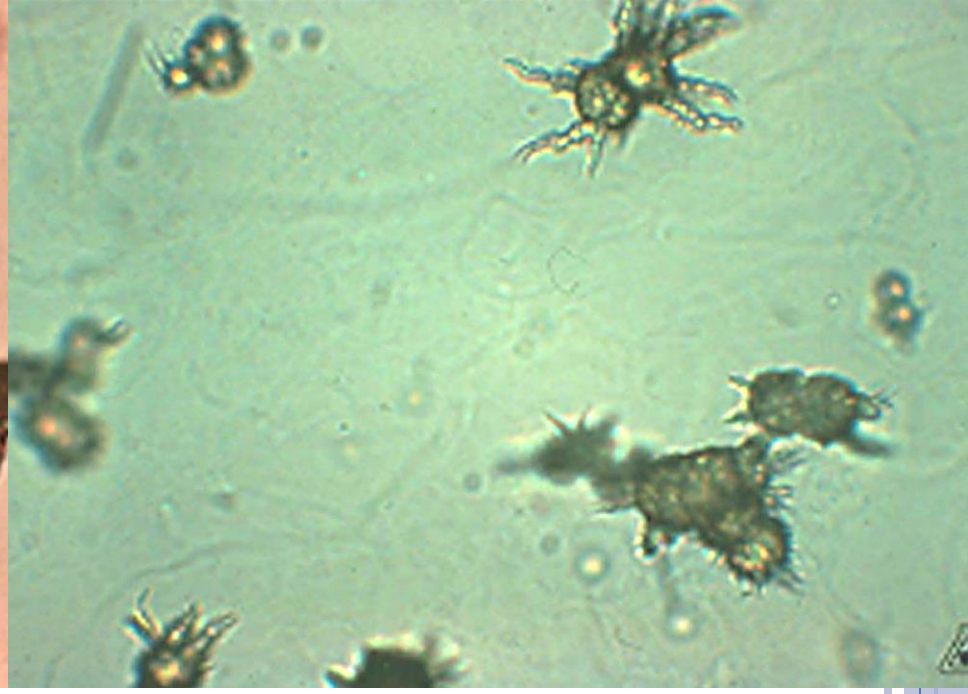
Microscopic Examination

Urate Crystals



Uric Acid

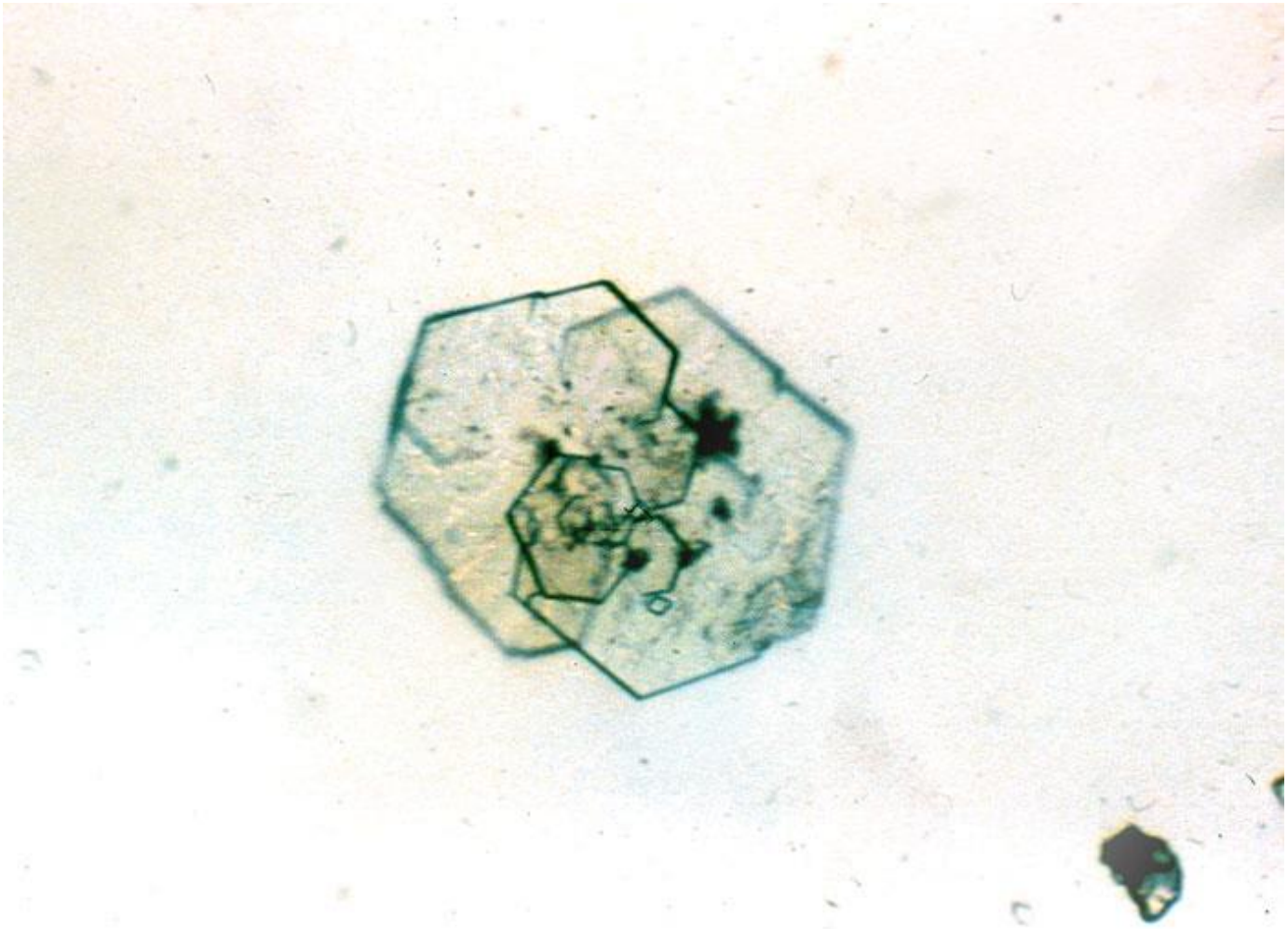




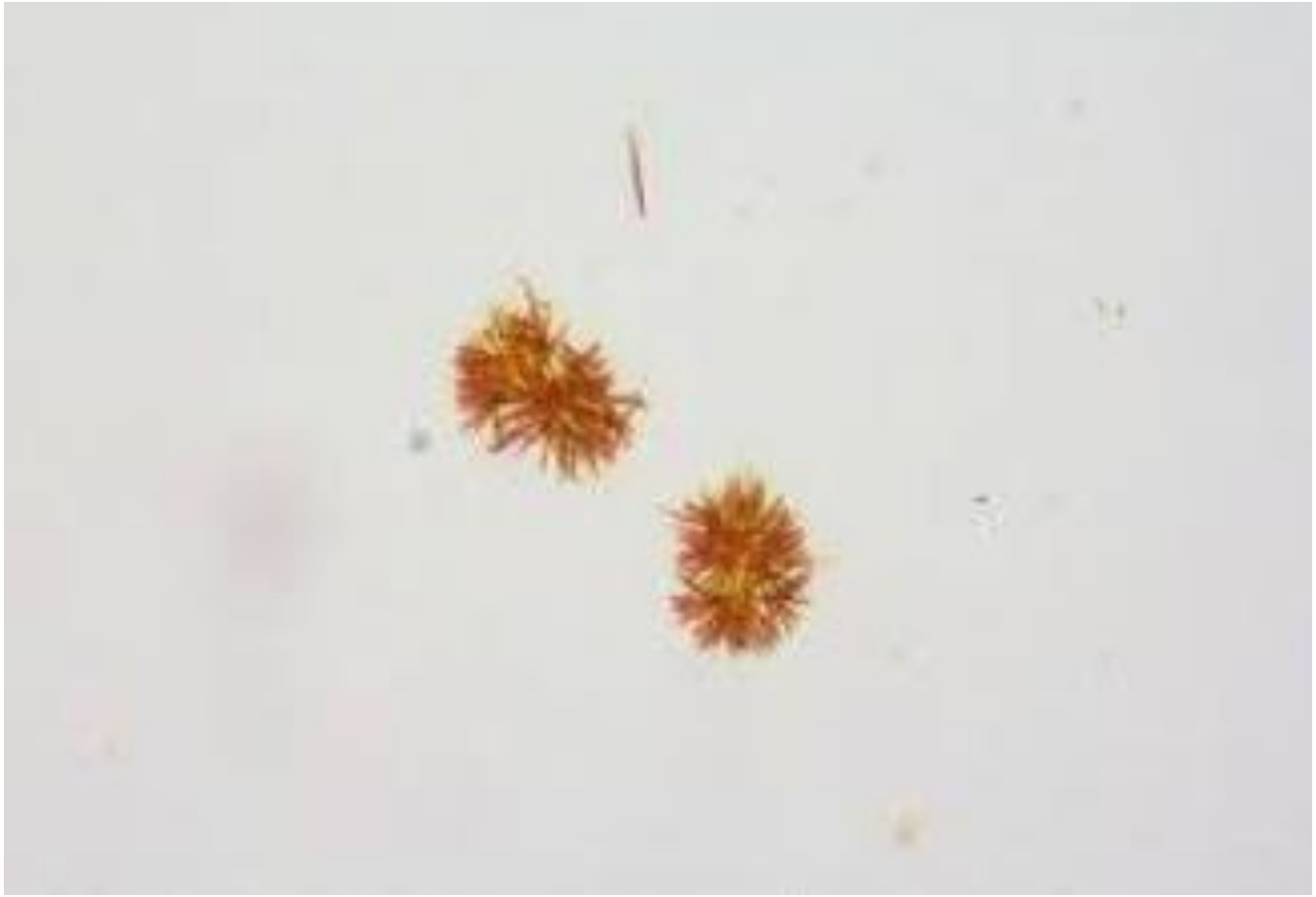
Ammonium Biurate

Microscopic Examination

Cystine Crystals

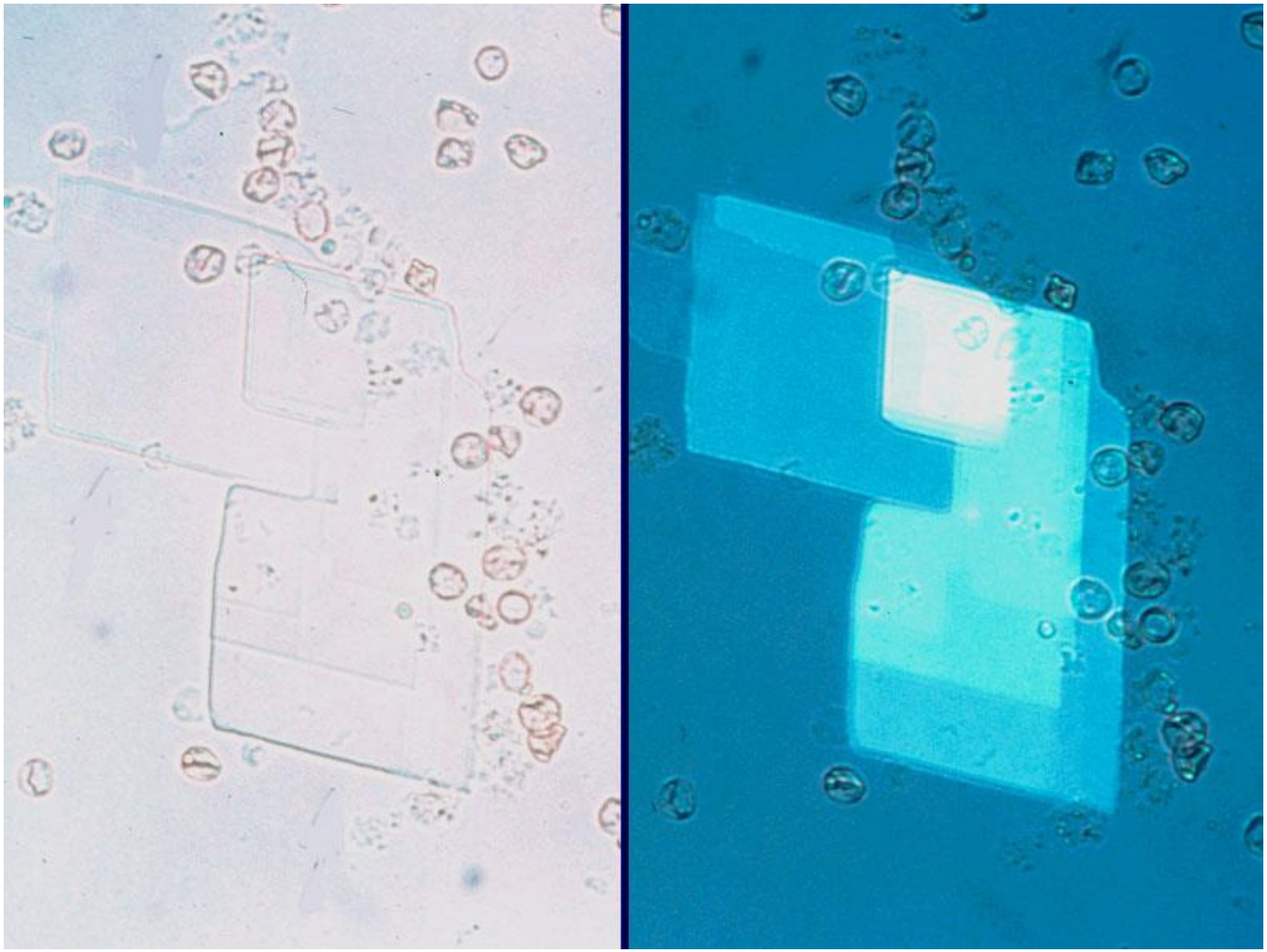


Bilirubin crystals



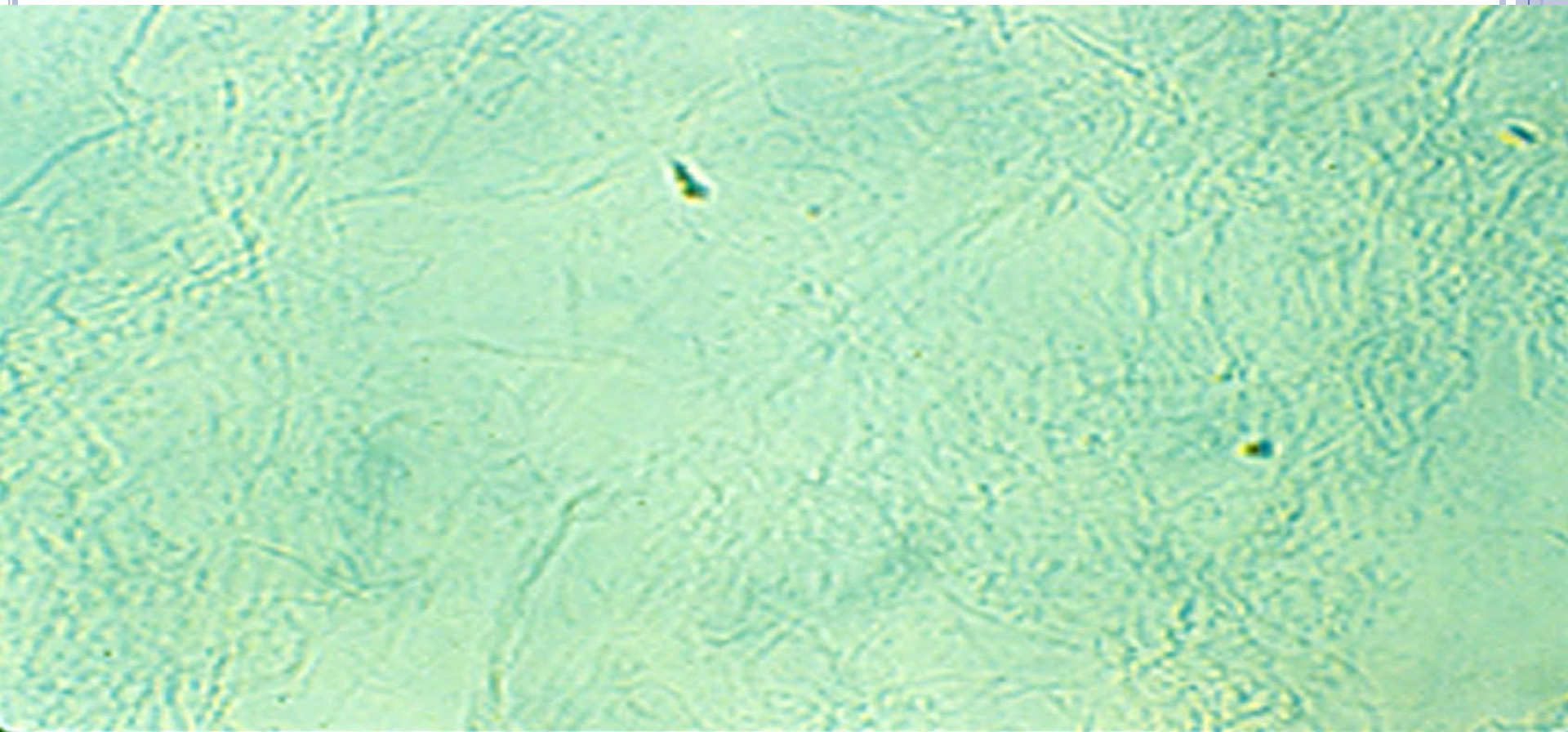
Microscopic Examination

Cholesterol Crystals



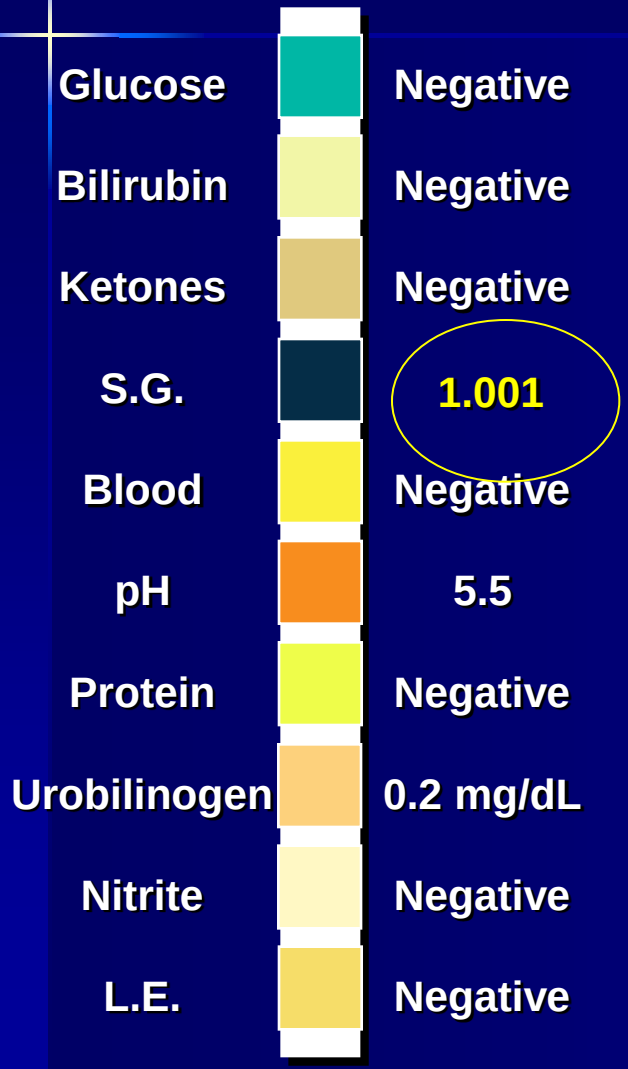
Mucus

- Usually of no clinical significance



Case 1

Diluted urine, request a voided urine in the morning
If persisting low SG, possible diabetes insipidus
A microscopic may give negative results



A 35-year old man undergoing routine pre employment drug screening.

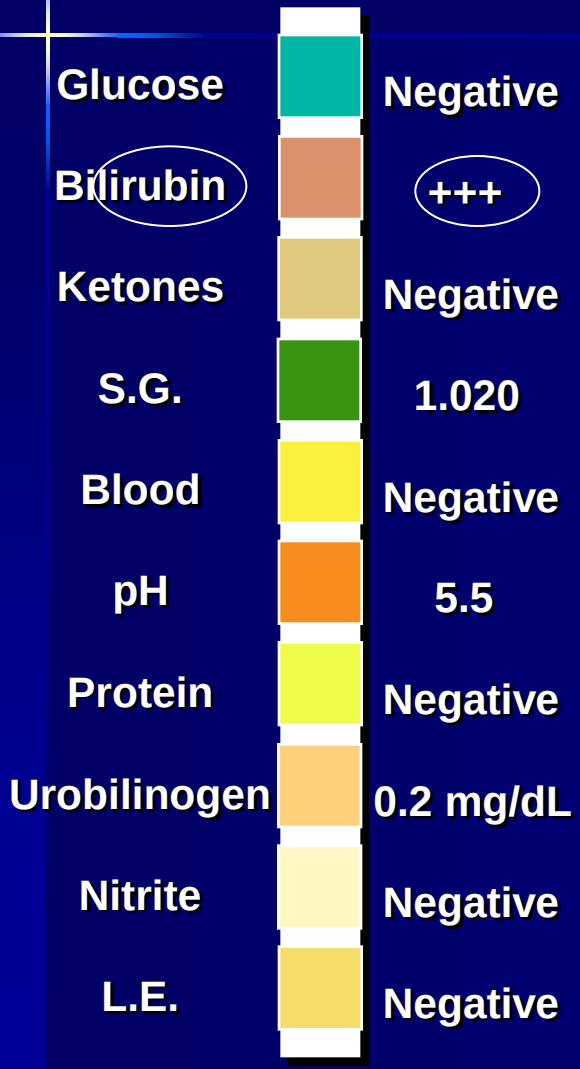
Physical characteristics: Clear.
Microscopic: Not performed.
Drugs Identified: None.

Questions:

- What is your differential diagnosis?
- What would you do next to confirm your suspicion?
- Would you order a microscopic analysis on this sample?

Case 2

Possible gallbladder or hepatic disease.
No hemolytic anemia. Perform bilirubins in serum
Microscopic unlikely to provide additional info



A 42-year old woman presents with “dark urine”

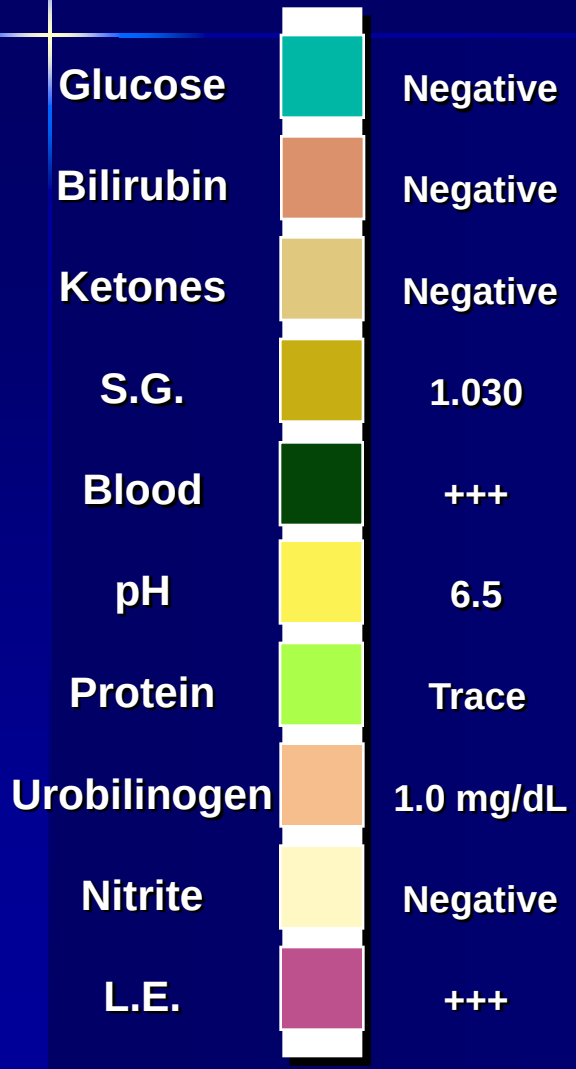
Physical characteristics: Red-brown.
Microscopic: Not performed.

Questions:

- What is your differential diagnosis?
- Could this be a case of hemolytic anemia?
- How would you rule it out?
- What tests would you order next? Why?
- Would you order a microscopic analysis?

Case 3

Possible UTI, request culture and antibiotic sensitivity
Negative Nitrite test: Gram positive bacteria
Lower SG may show less number of cells and bacteria
Un-common diagnosis in this type of patient



A 42-year old man presents painful urination

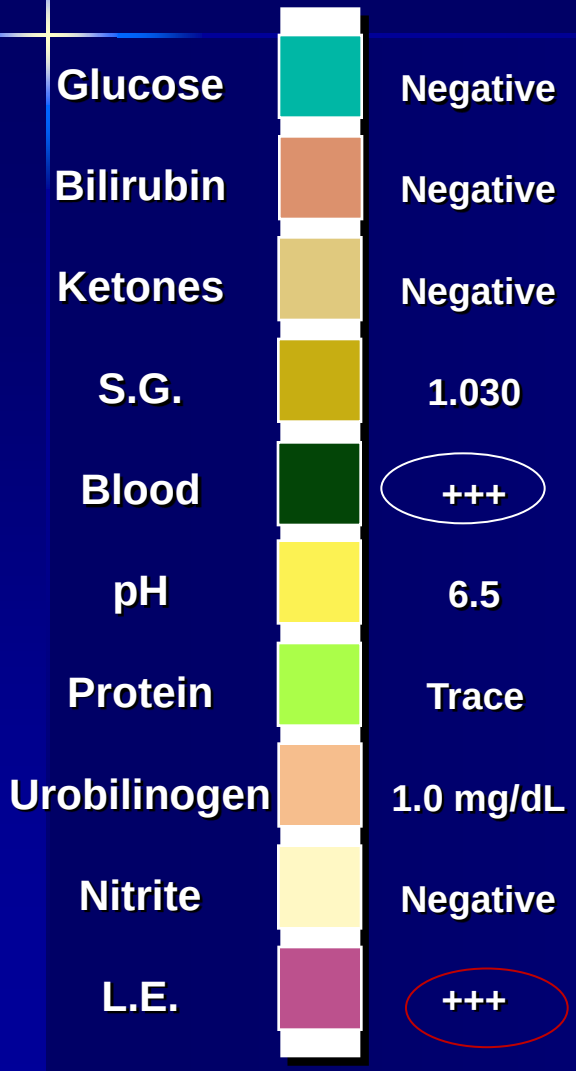
Physical characteristics: dark red, turbid
Microscopic: leukocytes = 30 per HPF
RBCs = >100 per HPF
Bacteria = >100 per HPF

Questions:

- What is your suspected diagnosis?
- What would you do next?
- What do you make of the nitrite test?
- How would the microscopic exam differ if the S.G. were 1.003?
- Is this a common diagnosis for this type of patient?

Case 3

Possible UTI, request culture and antibiotic sensitivity
Negative Nitrite test: Gram positive bacteria
Lower SG may show less number of cells and bacteria
Un-common diagnosis in this type of patient



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Physical characteristics: dark red, turbid
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RBCs = >100 per HPF
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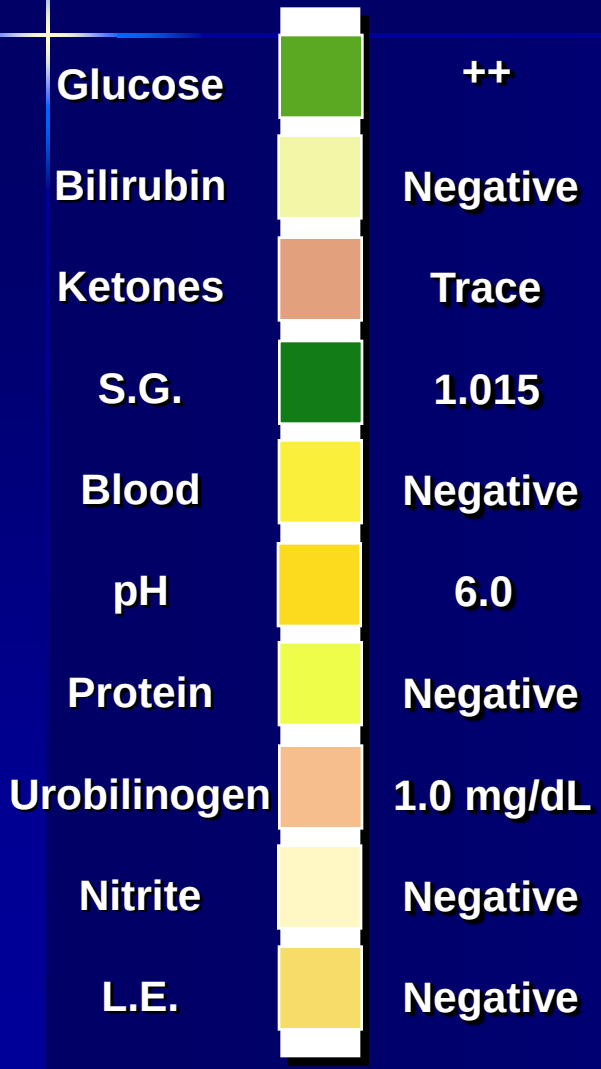
Questions:

- What is your suspected diagnosis?
- What would you do next?
- What do you make of the nitrite test?
- How would the microscopic exam differ if the S.G. were 1.003?
- Is this a common diagnosis for this type of patient?

Case 4

Diabetes
May be decompensated and with ketoacidosis
Ketones should become negative after treatment



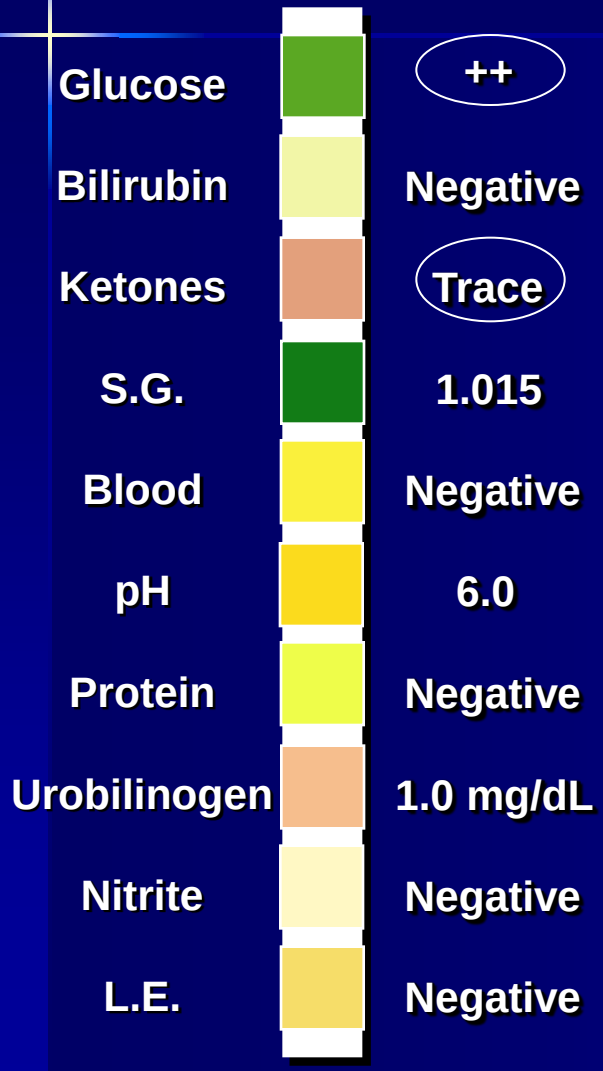
A 27-year old woman presents with severe abdominal pain.

Physical characteristics: clear-yellow.
Microscopic: Not performed.

Questions:
- What is the most likely diagnosis?
- What do you make of the ketone result?
- What do you expect to happen to the ketone measurement when treatment begins?

Case 4

Diabetes
May be decompensated and with ketoacidosis
Ketones should become negative after treatment



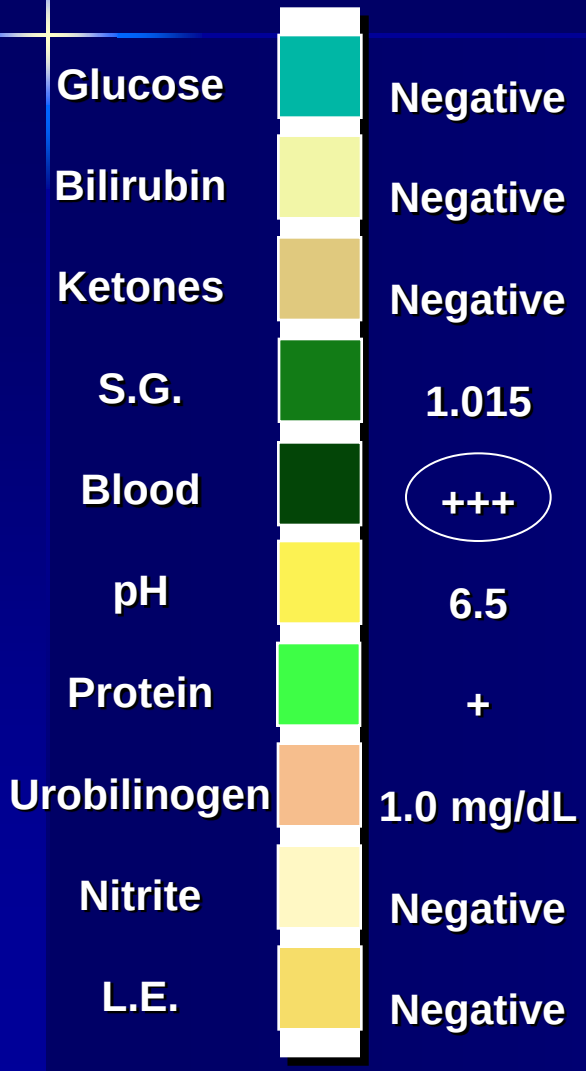
A 27-year old woman presents with severe abdominal pain.

Physical characteristics: clear-yellow.
Microscopic: Not performed.

Questions:
- What is the most likely diagnosis?
- What do you make of the ketone result?
- What do you expect to happen to the ketone measurement when treatment begins?

Case 5

Glomerulonephritis
RBC casts reveals renal cortex involvement
RBC cast are not always present in GN



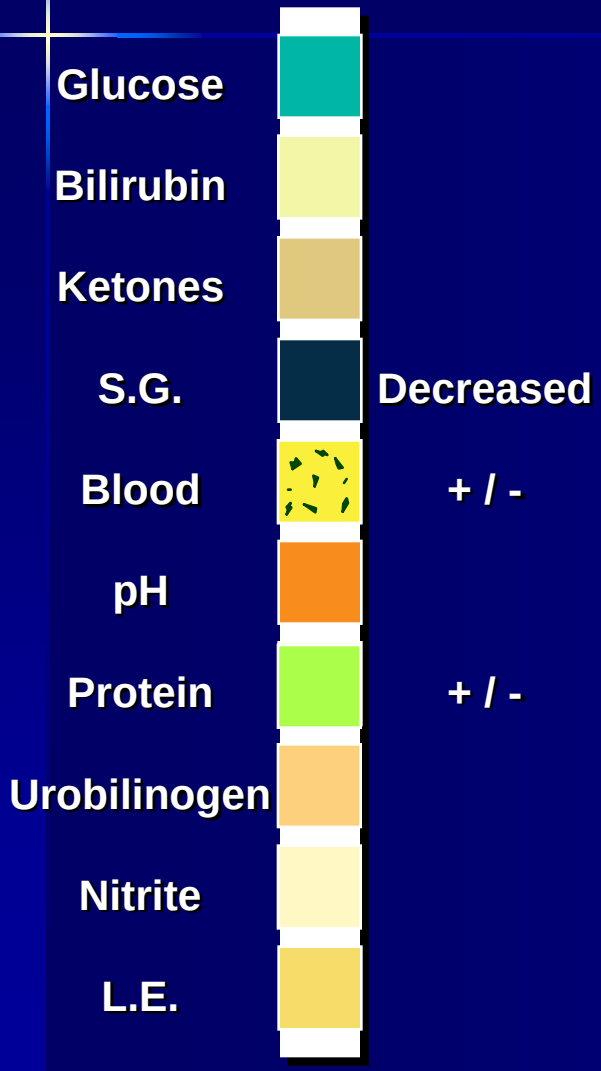
8-year old boy presents with discolored urine

Physical characteristics: Red, turbid.
Microscopic: erythrocytes = >100 per HPF (almost all dysmorphic)
Red cell casts present.

Questions:

- What is the most likely diagnosis in this case?
- Does the presence of red cell casts help you in any way?
- If the erythrocytes were not dysmorphic would that change your diagnosis?

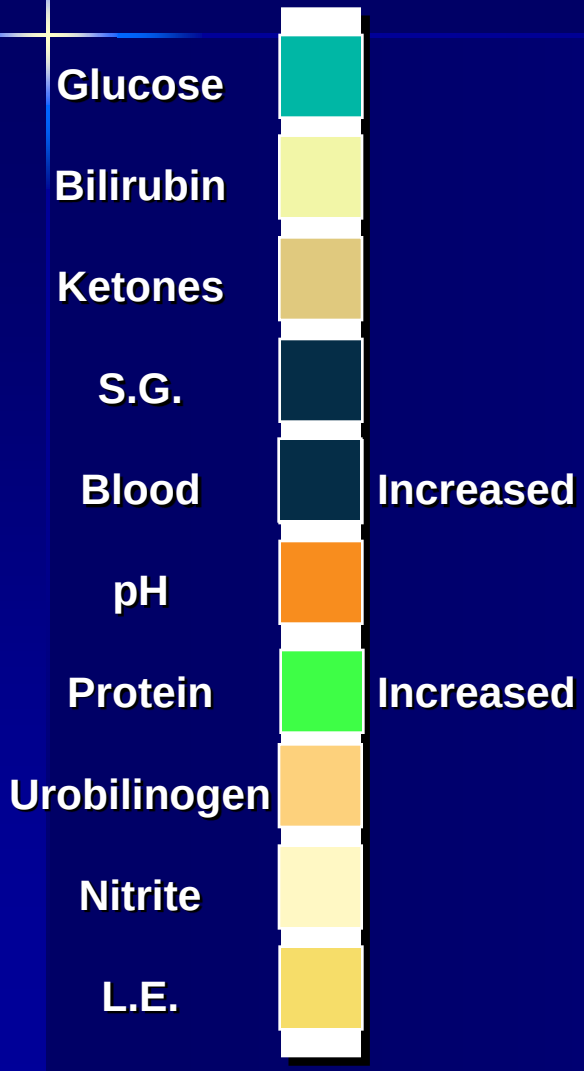
Common Findings in: Acute Tubular Necrosis



Microscopic:

- Renal tubular epithelial cells
- Pathological casts

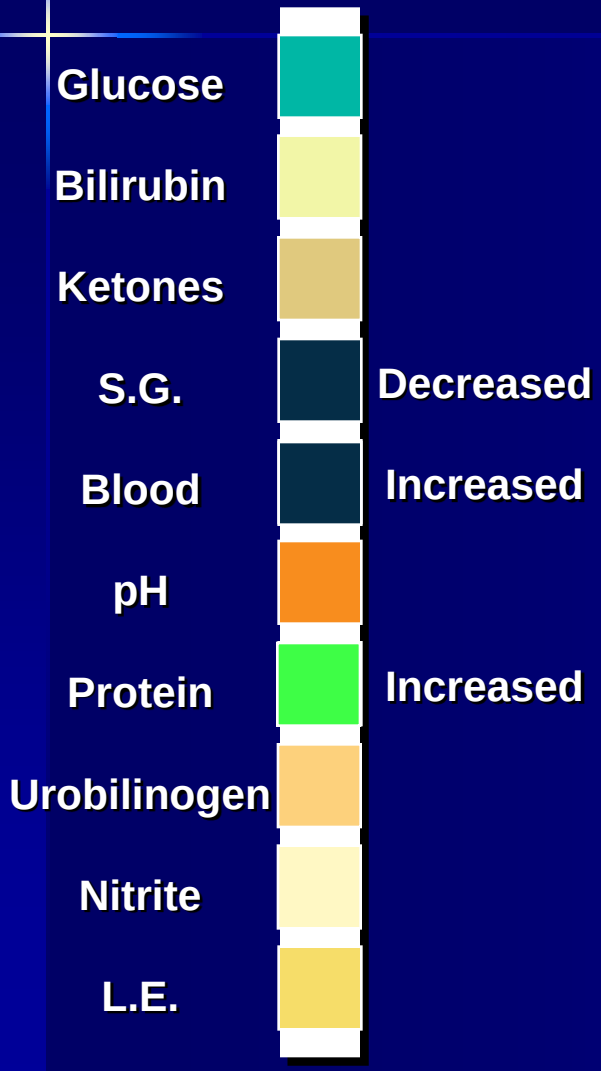
Common Findings in: Acute Glomerulonephritis



Microscopic:

- Erythrocytes (dysmorphic)
- Erythrocyte casts
- Mixed cellular casts

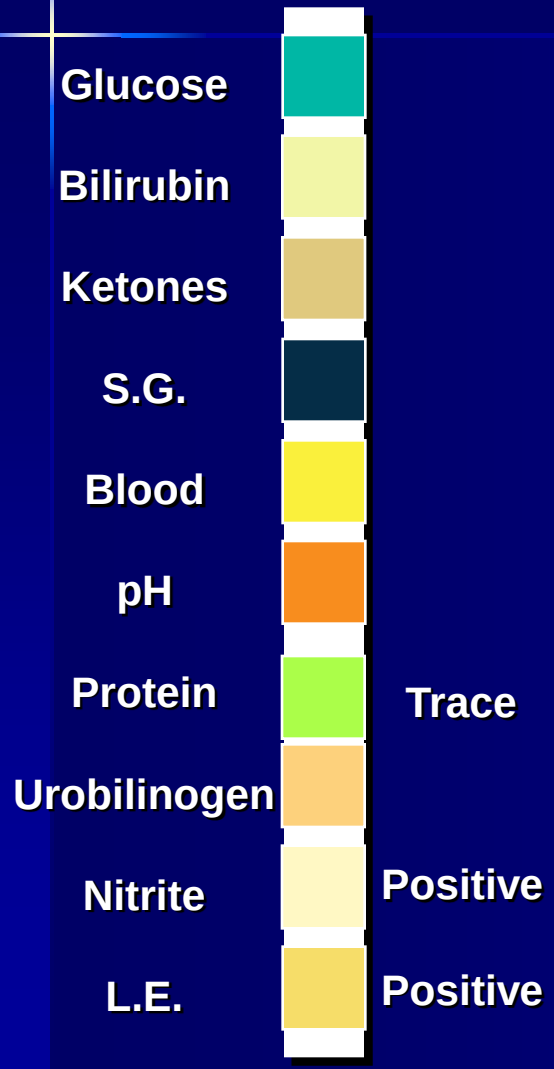
Common Findings in: Chronic Glomerulonephritis



Microscopic:

- **Pathological casts (broad waxy casts, RBCs)**

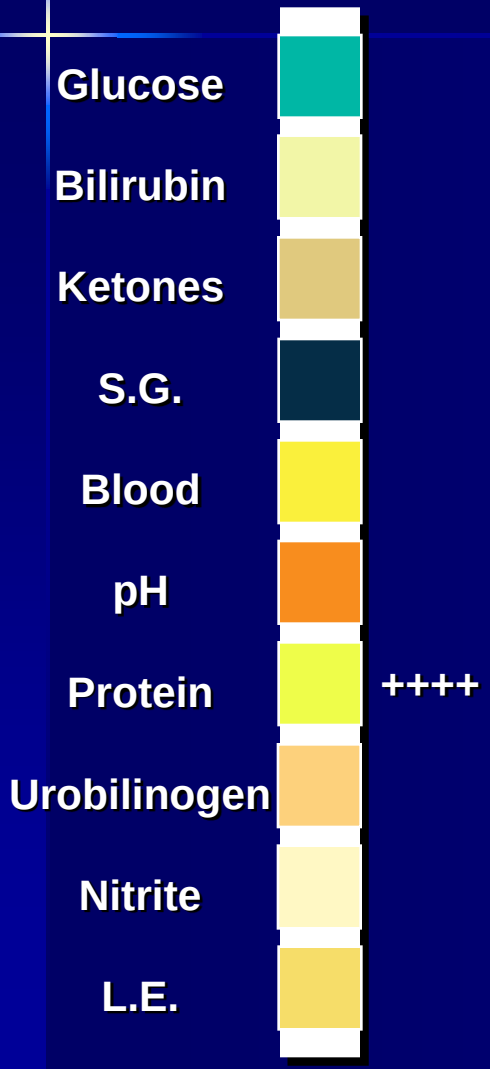
Common Findings in: Acute Pyelonephritis



Microscopic:

- Bacteria
- Leukocytes
- Leukocyte, granular, and waxy casts
- Renal tubular epithelial cell casts

Common Findings in: Nephrotic Syndrome



Microscopic:

- Oval fat bodies
- Fatty casts
- Waxy casts

Take Home Message

- Urinary sediment is an important key to diagnosis of kidney diseases.
- In AKI , after sonography , urinary sediment should be examined.
- In hematuria , evaluation of RBC morphology by microscopic examination is very important.
- Urinary WBCs may indicate TIN and association with bacteria indicate pyelonephritis.
- Urinary RTE can be seen in ATN or ATIN.
- Urinary casts (muddy brown casts in ATN) ,and urinary crystals (uric acid crystals ,Calcium oxalate crystals, Billirubin crystals) can be clues for diagnosis of etiology of AKI.