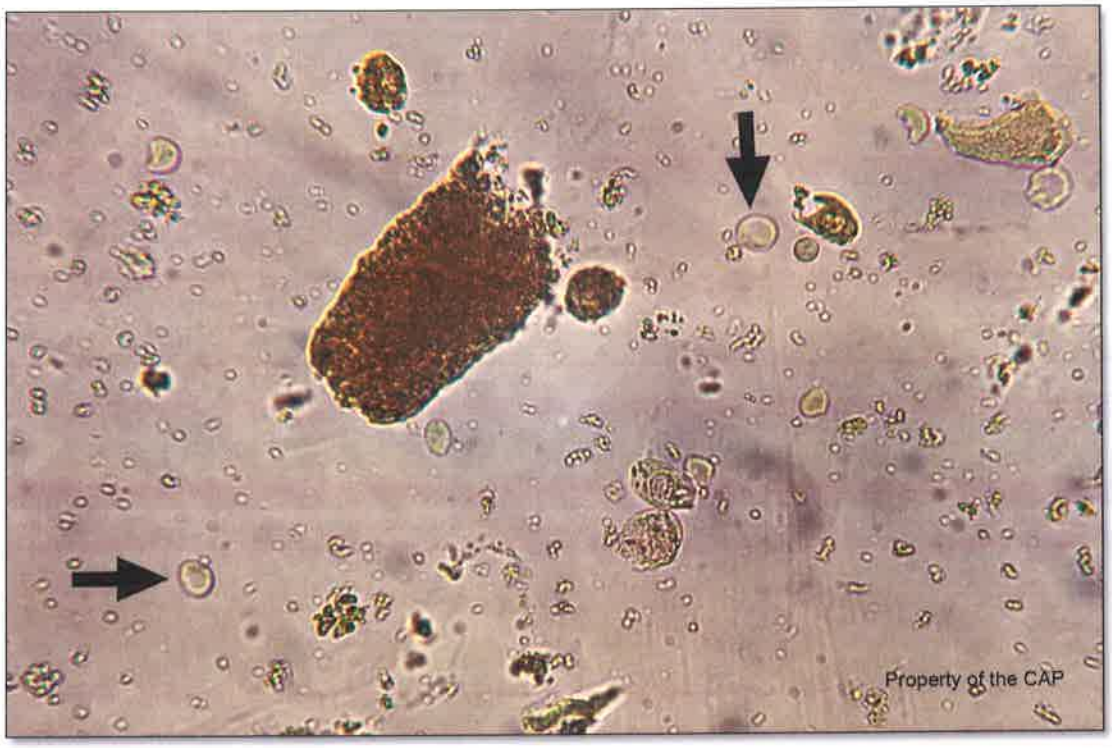
Urine Sediment Photographs

Case History CMP-04 through CMP-06
This urine sample is obtained from a 46-year-old man with MRSA pneumonia and vancomycin-induced acute tubular necrosis. Laboratory data include: specific gravity = 1.012; pH = 6.5; protein, blood, and leukocyte esterase = positive; glucose, ketones, and nitrite = negative. Identify the arrowed object(s) on each image.

(URINE, UNSTAINED, HIGH POWER)

CMP-04

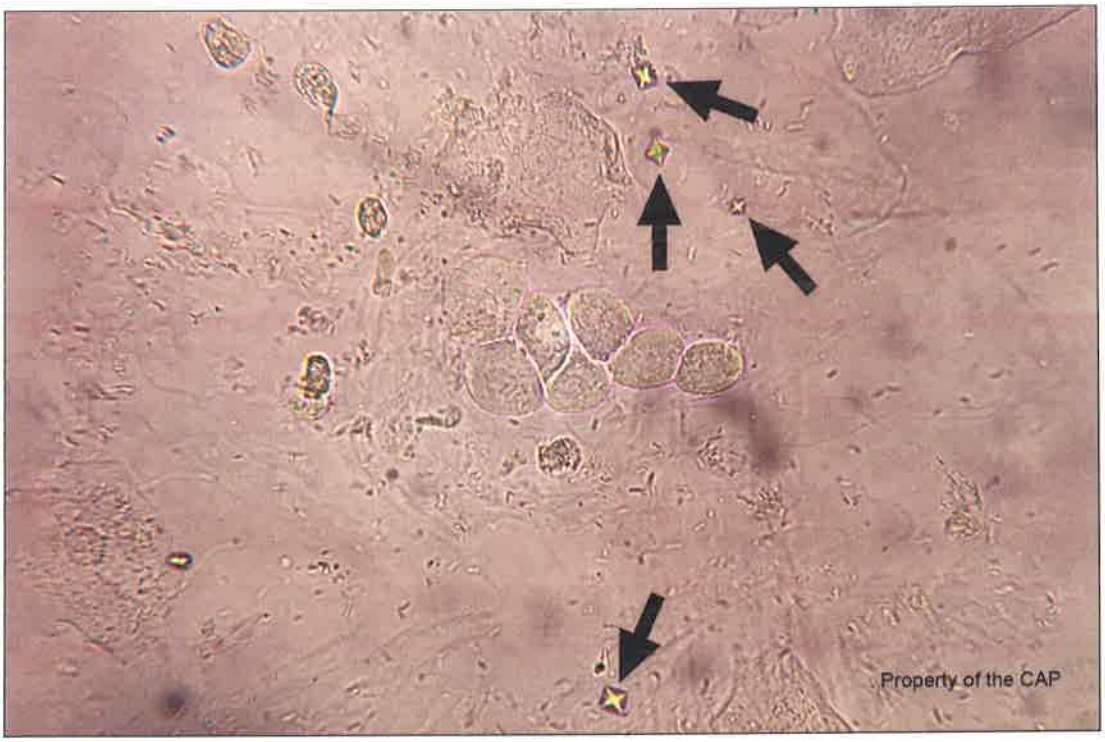


Identification	Participants		Evaluation
	Freq	%	
Erythrocyte	5929	98.2	Good

The arrowed cells are erythrocytes, as correctly identified by 98.2% of participants. The cells are non-nucleated cells approximately 7 µm in diameter with the classic biconcave disc shape. Erythrocytes contain hemoglobin and appear slightly orange in this image. A central zone of pallor is seen in both cells due to the biconcavity of the cell which is most prominent in the lower left arrowed cell.

Urine Sediment Photographs

CMP-05

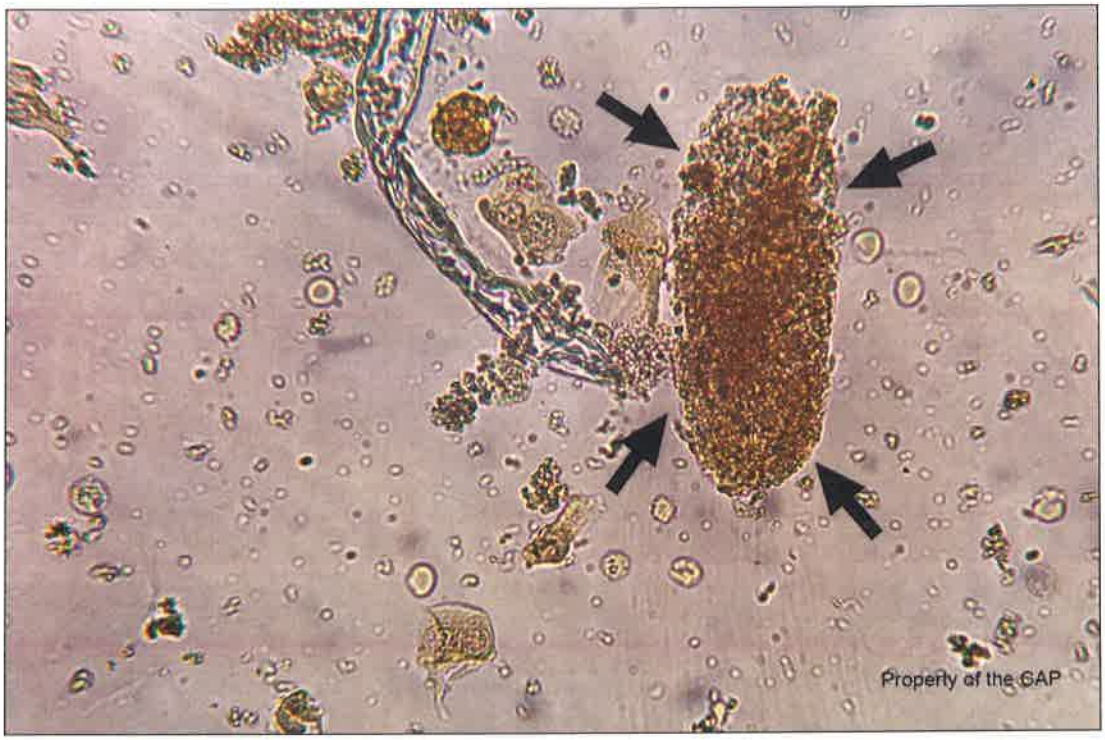


Identification	Participants		Evaluation
	Freq	%	
Calcium oxalate crystals	5962	99.4	Good

The arrowed crystals are calcium oxalate crystals, as correctly identified by 99.4% of participants. Their appearance as squares with a cross is due to the eight-sided octahedron shape often described as envelopes. Although calcium oxalate crystals are sometimes mistaken for red blood cells, they are typically smaller than red blood cells and are colorless. The crystals seen in this image are the common dihydrate form which are usually not an abnormal finding, although they can suggest the cause of renal calculi.

Urine Sediment Photographs

CMP-06



Identification	Participants		Evaluation
	Freq	%	
Granular cast	5109	84.6	Good
RBC/muddy brown cast	855	14.2	Unacceptable

The arrowed element is a granular cast, as correctly identified by 84.6% of participants. The granules within the cast are coarse and evenly dispersed over the cast. This cast has taken the form of a renal tubule usually indicating a pathological process within the kidney. For this patient, the finding is consistent with vancomycin-induced acute tubular necrosis which can help confirm the diagnosis. The granules seen within the cast are from degenerated cells within a matrix of aggregated protein. In this case, the cells have degraded to a point where the cell type can no longer be identified and therefore is referred to as a granular cast.

14.2% of participants incorrectly identified the images as an RBC/muddy brown cast. This type of case is rare but always clinically significant. RBC/muddy brown casts contain intact erythrocytes, densely or loosely covering the hyaline or granular matrix. The red blood cells may be shrunken or crenated when compared with those in the surrounding urine. This image lacks intact erythrocytes.

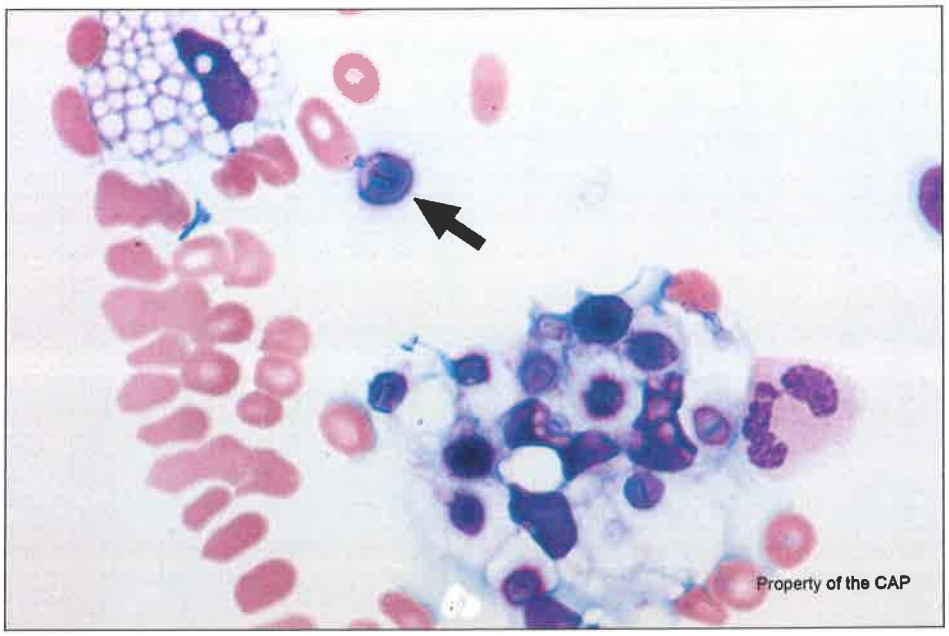
Body Fluid Photographs

Case History CMP-07 through CMP-09

This patient is a 60-year-old man with HIV with a suspicion of a cryptococcal infection. Cerebrospinal fluid sample laboratory findings include: TNC = 58 cells/µL (0.058 x 10E3/µL); RBC = 891 cells/µL (0.891 x 10E3/µL). Identify the arrowed object(s) on each image.

(CSF, CYTOCENTRIFUGE, WRIGHT-GIEMSA, 100X)

CMP-07



Identification	Referees		Participants		Evaluation
	Freq	%	Freq	%	
Yeast/fungi, extracellular	40	78.4	2574	69.5	Non-consensus
Lymphocyte	1	2.0	467	12.6	Non-consensus
Pneumocystis jirovecii	2	3.9	257	6.9	Non-consensus
Starch granule	3	5.9	78	2.1	Non-consensus
Immature or abnormal cell, would refer for identification	1	2.0	70	1.7	Non-consensus
Neutrophil/macrophage containing fungi	1	2.0	23	0.6	Non-consensus
Parasite	1	2.0	22	0.6	Non-consensus
Stain precipitate	1	2.0	23	0.6	Non-consensus
Ventricular lining cell (ependymal or choroid cell)	1	2.0	13	0.3	Non-consensus

The arrowed cell is a cryptococcus fungal form, as correctly identified by 69.5% of participants. The microorganisms can be readily identified as single or multiple, uniform, cytoplasmic inclusions with a central basophilic core and surrounding pale capsule, all of which are classic features of *Cryptococcus*.

2.0% of referees and 12.6% of the participants incorrectly identified the cells as lymphocyte. While lymphocytes in body fluids can look slightly larger than its counterpart on blood smears, it often has even more abundant cytoplasm.

3.9% of referees and 6.9% of the participants incorrectly identified the cells as *Pneumocystis jirovecii*. *Pneumocystis jirovecii* typically present as flattened, contact lens shape forms with no capsule. This image shows a *Cryptococcus* yeast form which is encapsulated.

5.9% of referees and 2.1% of the participants incorrectly identified the cells as starch granule. Starch granules are contaminants that vary in size from red blood cell to six times larger in size. On the Wright-Giemsa stain, they are blue to purple and are irregularly formed with indentation. The image provided shows background that contains nearly identical organisms.

2.0% of referees and 1.9% of the participants identified the cells as immature/abnormal cells, would refer for ID is an acceptable answer if sent to an outside laboratory with another CLIA number. However, this is an extracellular microorganism without typical features of a human immature cell that show round to ovoid nucleus with high nucleus to cytoplasmic ratio.

2.0% of referees and 0.6% of the participants incorrectly identified the cells as neutrophil/macrophage with fungi. A neutrophil has several nuclear lobes, often with granules. A macrophage is larger with abundant cytoplasm, often showing vacuoles. Both these cells can demonstrate active phagocytosis, with the fungi evidence in their cytoplasm. However, in this image, only the yeast/fungus is present in extracellular space.

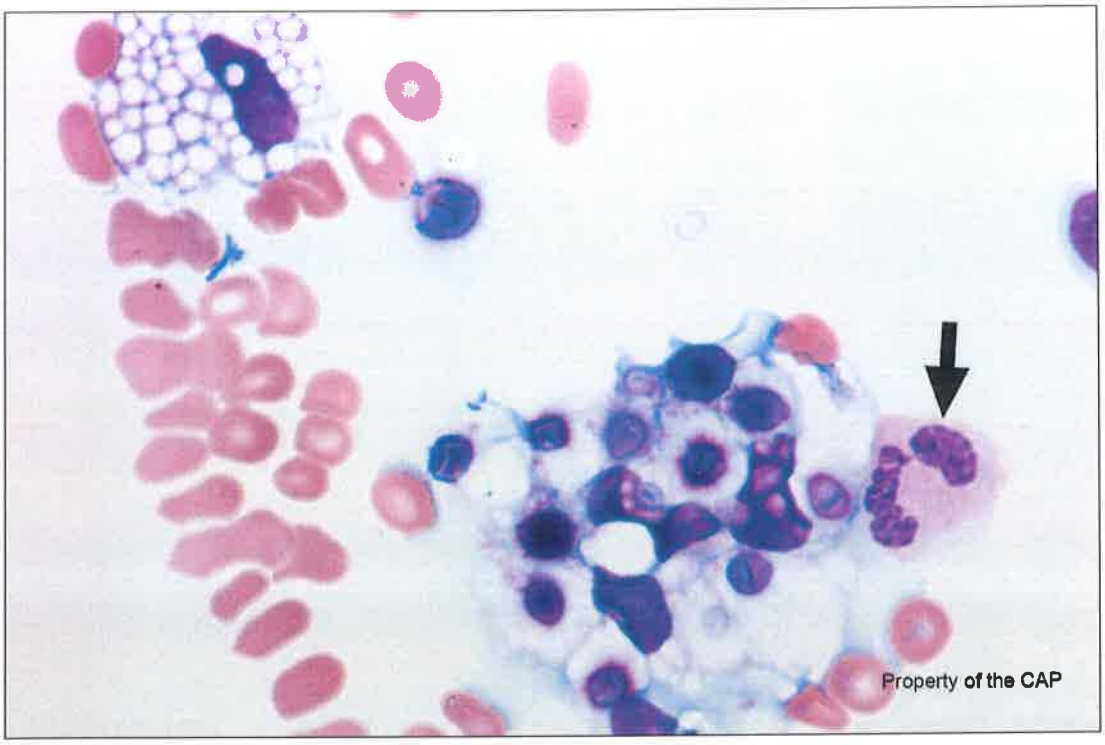
2.0% of referees and 0.6% of the participants incorrectly identified the cells as parasite. While a wide variety of parasites can be found in body fluids, such as giardia or tapeworms, this image shows Cryptococcus, which are fungi.

2.0% of referees and 0.6% of the participants incorrectly identified the cells as stain precipitate. Stain precipitates are metachromatic granular deposits that typically show a range of sizes. This is in contrast to the fungi shown here, which are of uniform morphology.

2.0% of referees and 0.3% of the participants incorrectly identified the cells as ventricular lining cell. Ventricular lining cells are cells that normally line the ventricles or choroid plexus which can be shed into the CSF. These cells are large (20-40μm) and can occur in loose clumps. Their nuclei are eccentrically placed with smooth nuclear membrane and abundant amphophilic cytoplasm.

Body Fluid Photographs

CMP-08

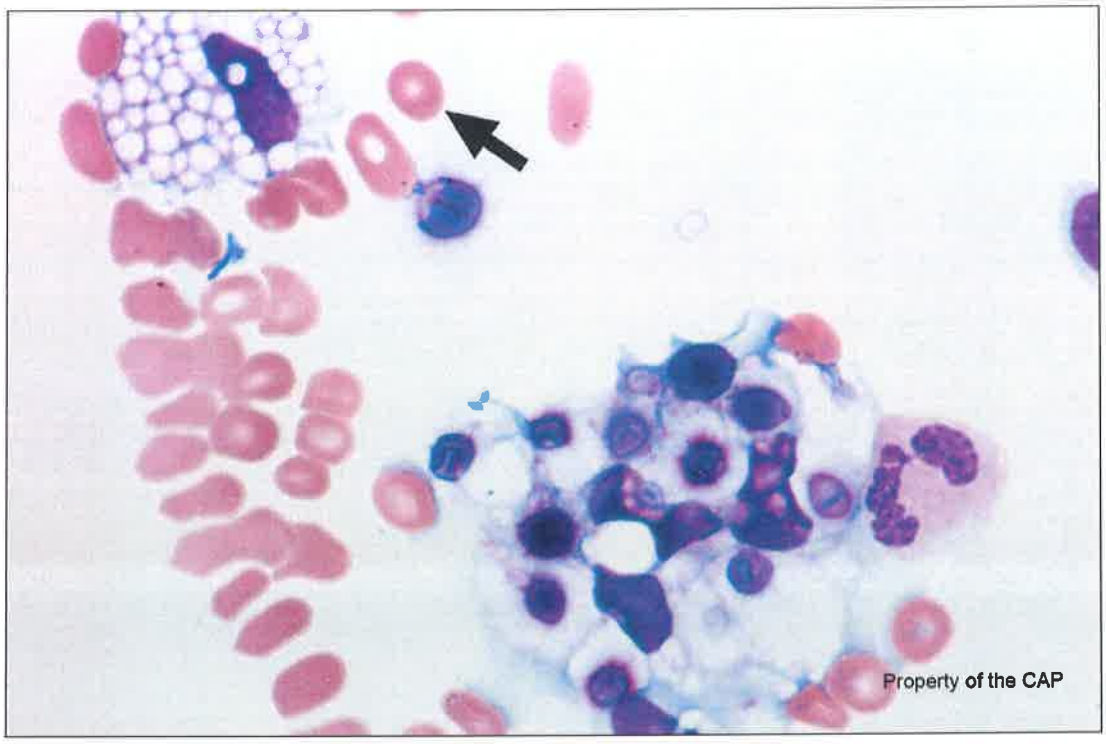


Identification	Participants		Evaluation
	Freq	%	
Neutrophil, segmented or band	3737	97.4	Good

The arrowed cell is a neutrophil, segmented or band, as correctly identified by 97.4% of participants. Neutrophils are 10 - 15 µm in size and contain moderate pale pink cytoplasm with specific granules. The nucleus is segmented or lobated (with a normal range of three to five lobes). The lobes are connected by a thin filament that contains no internal chromatin, giving it the appearance of a solid, dark, thread-like line. The appearance of neutrophils in body fluids may be similar to those seen in peripheral blood, although in some cases degenerative changes may also be present.

Body Fluid Photographs

CMP-09



Identification	Participants		Evaluation
	Freq	%	
Erythrocyte	3798	99.0	Good

The arrowed cell is an erythrocyte, as correctly identified by 99.0% of participants. Erythrocytes are anucleate and are the most mature cell in the lineage of erythroid elements. While in peripheral blood smears, they show central pallor that comprises a third of the diameter of the cell, there is more variable morphology in fluids. The red blood cell morphology in fluids is not a reliable feature since the cytospin process can introduce artifacts. There is no feathered edge in body fluids for morphologic evaluation.

Clinical Presentation:
This patient is a 60-year-old man with HIV with a suspicion of a cryptococcal infection. Cerebrospinal fluid sample laboratory findings include: TNC = 58 cells/µL (0.058 x 10E3/µL); RBC = 891 cells/µL (0.891 x 10E3/µL).

(CSF, CYTOCENTRIFUGE, WRIGHT-GIEMSA, 100X)

CASE DISCUSSION: *Cryptococcus* in cerebrospinal fluid

Cryptococcus is a common world-wide fungus, present in soil and bird droppings, that rarely causes disease in healthy individuals. However, in immunocompromised patients, inhalation of the fungi, particularly the species *neoformans,* can cause life-threatening pneumonia and meningitis. Rarely, the infection becomes disseminated, and can involve skin and internal organs. As such, identification of *Cryptococcus* is clinically important to guide early and effective therapy.

Acquired Immune Deficiency Syndrome (AIDS) is caused by untreated Human Immunodeficiency Virus (HIV) infection, and clinically manifests with increased risk of infection and cancer in the setting of progressive immune system dysfunction. While implementation of antiretroviral therapy has dramatically improved long-term outcomes of HIV-infected individuals, cryptococcal meningitis remains am important cause of morbidity and mortality in this population world-wide. However, *Cryptococcus* infection is not limited to the HIV infected, as patients on chronic corticosteroid therapy, cancer patients receiving chemotherapy, and those after solid organ transplantation are also at risk. Another *Cryptococcus* species, *C. gattii,* can cause similar manifestations in immunocompetent people.

The diagnosis of cryptococcal meningitis is suspected by clinical manifestations and patient history. Diagnosis is confirmed by a comprehensive cerebrospinal fluid (CSF) evaluation, which typically shows increased nucleated cells, composed primarily of monocytes. The cytologic preparation can occasionally demonstrate monocytes containing fungal organism, and the morphologic features are highly specific for *Cryptococcus*. However, the sensitivity of detection by microscopy is relatively low and *Cryptococcus* antigen testing and culture remain the primary modes of detection.

The morphologic identification of extracellular *C. neoformans* in the CSF is also aided by the use of India ink staining. As the fungus has a prominent mucopolysaccharide capsule that is not penetrated by ink particles, the yeast appears to be surrounded by a "halo" when stained with black India ink. When tissue is biopsied for the diagnosis of disseminated disease, the capsule can be specifically highlighted with mucicarmine stain.

Patients diagnosed with cryptococcal meningitis are immediately started on antifungal therapy.

Yuri D. Fedoriw, MD
Hematology and Clinical Microscopy Committee

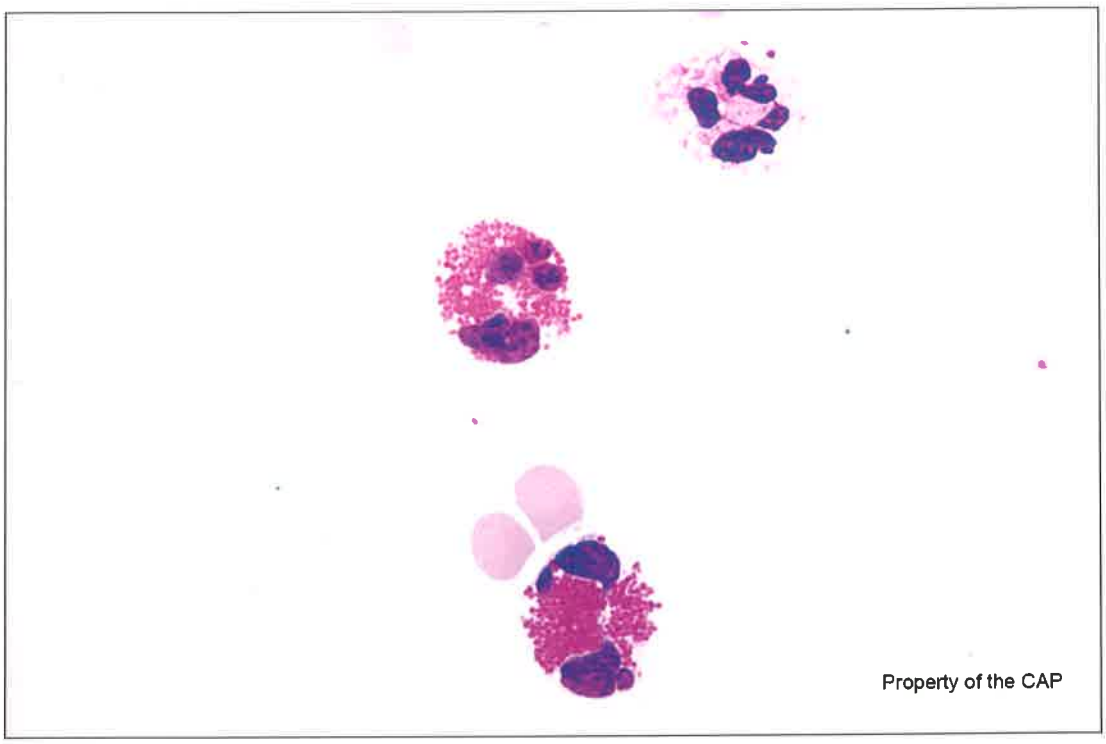
REFERENCES:

1. Abassi M, Boulware DR, Rhein J. Cryptococcal meningitis: diagnosis and management update. *Curr Trop Med Rep.* 2015;2(2):90-99.
2. McHugh KE, Gersey M, Rhoads DD, et al. Sensitivity of cerebrospinal fluid cytology for the diagnosis of cryptococcal infections: A 21-year single-institution retrospective review. *Am J Clin Pathol.* 2019;151(2):198-204.
3. Park BJ, Wannemuehler KA, Marston BJ, Govender N, Pappas PG, Chiller TM. Estimation of the current global burden of cryptococcal meningitis among persons living with HIV/AIDS. *AIDS.* 2009;23(4):525-530.

CMMP – Clinical Microscopy Miscellaneous Photographs

(NASAL, WRIGHT-GIEMSA)

CMMP-22



Identification	Participants		Evaluation
	Freq	%	
Eosinophils are present	1998	99.8	Good

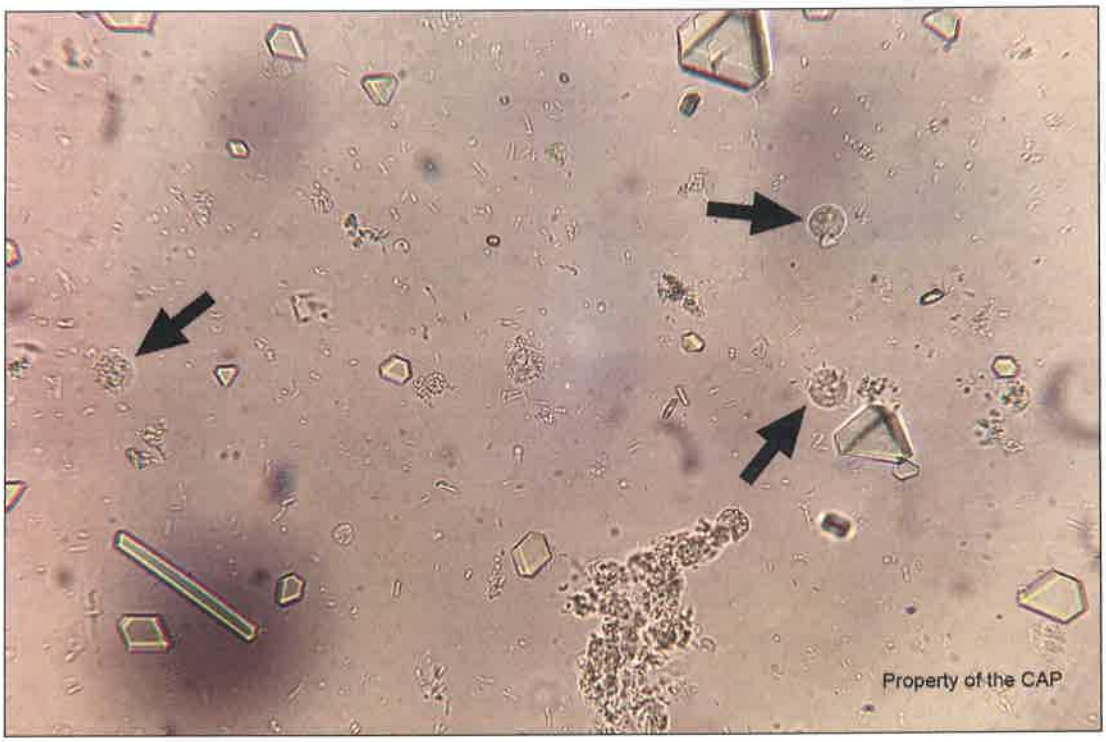
This nasal smear has eosinophils present, which exhibit the typical bilobed nucleus and numerous cytoplasmic eosinophilic granules. Nasal smears for eosinophils are an aid to distinguishing allergic rhinitis, where eosinophils are present, from non-allergic rhinitis. The clinical differential diagnosis of non-allergic rhinitis and allergic rhinitis is difficult due to the significant overlap of clinical symptomatology. In addition to the nasal smear, skin prick tests, serum IgE levels, and RAST tests may be used in conjunction with the clinical presentation to differentiate allergic and non-allergic rhinitis.

Urine Sediment Color Photographs

Case History USP-01 through USP-03
This urine sample is obtained from a 77-year-old man with chronic kidney disease and history of bladder cancer. Laboratory data include: specific gravity = 1.014; pH = 8.0; protein, glucose, and leukocyte esterase = positive; ketones, blood, and nitrite = negative. Identify the arrowed object(s) on each image.

(URINE, UNSTAINED, HIGH POWER)

USP-01

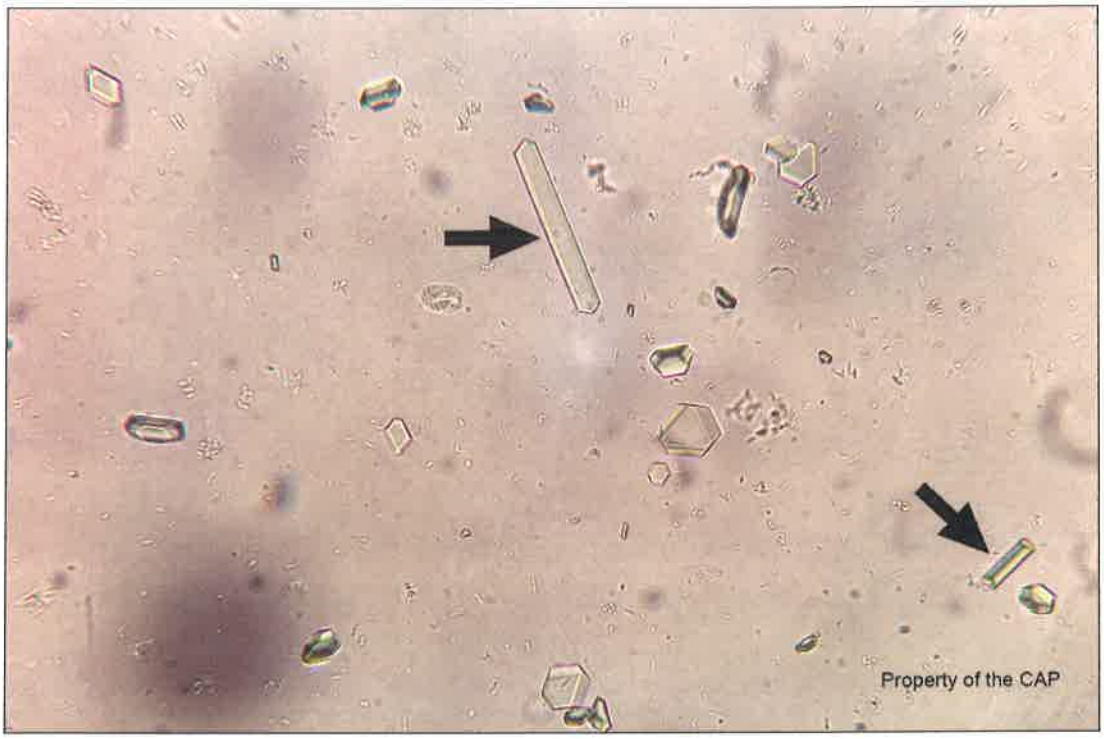


Identification	Participants		Evaluation
	Freq	%	
Leukocyte (neutrophil, eosinophil, lymphocyte)	3950	99.0	Good

The arrowed cells in this image are leukocytes. The cells are round nucleated cells with granular appearance approximately 10 – 12 µm in diameter. Leukocytes are larger than red blood cells and smaller than renal tubular cells. The presence of five or more leukocytes per high power field indicates inflammation in the urinary tract and is termed pyuria. The combined presence of both leukocytes and bacteria is an important indicator of bacterial urinary tract infection.

Urine Sediment Photographs

USP-02



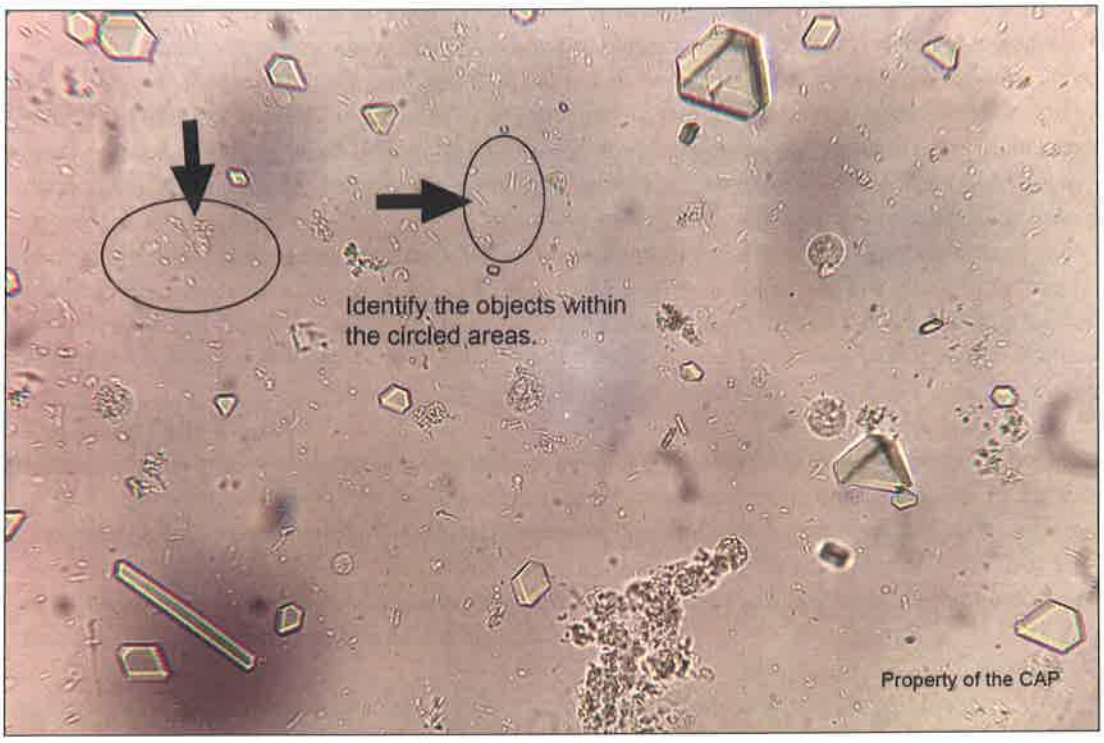
Identification	Participants		Evaluation
	Freq	%	
Ammonium magnesium (triple) phosphate crystals	3616	90.7	Good
Hippuric acid crystals	327	8.2	Unacceptable

The arrowed crystals in this image are triple phosphate crystals. They are identified in this image in a variety of colorless forms including a large long prism (right arrow) and a smaller shorter prism (left arrow). These varied forms are commonly seen. The classic form described as a coffin-lid is not seen but the smaller prism on the left is approximating that shape. Triple phosphate crystals consist of ammonium, magnesium, and phosphate and are also called struvite crystals because they are components of large urinary struvite stones. These crystals are associated with urease-positive bacterial infection and neutral or alkaline urine pH.

8.2% of participants incorrectly identified the arrowed objects as hippuric acid crystals. This type of crystal is found in neutral or acid pH. The clinical history for this image states a pH value of 8.0. Hippuric acid crystals are colorless to pale yellow and, unlike uric acid, may occur as hexagonal prisms, needles, or rhombic plates. They are birefringent when examined with polarized light but lack the interference colors usually seen with uric acid.

Urine Sediment Photographs

USP-03



Identification	Participants		Evaluation
	Freq	%	
Bacteria	3921	98.2	Good

The arrowed circled organisms in this image are bacteria. The medium to long rod-shaped organisms are bacilli that can be seen in urine as the causative agent on of a urinary tract infection. These bacteria can also be seen in the urine as a contaminant due to inadequate urine collection. Urine sample collected for urinalysis and urine culture should be a clean catch urine sample that is collected mid-stream after cleaning the genital area with a towelette. The presence of bacteria with squamous cells and the absence of white blood cells is typical of contaminated collection and will often lead to mixed flora on urine culture. In this image, leukocytes are seen suggesting a clinically-significant urinary tract infection that is more likely to grow pathologic bacteria on urine culture.

eccentrically located toward the basilar regions of these cells. Proximal and distal tubule RTEs can be round, oval or polygonal. Those from the proximal tubule may also have a flat edge where the apical microvillus boarder is located. Collecting duct RTEs are usually columnar but can be cuboidal or polygonal. The cytoplasm is granular. Degenerative changes include fraying of the cytoplasm, leaving indistinct cell borders.

RTEs can develop distinctive morphologies in certain conditions. In nephrosis or lipiduria, they resorb lipids and become oval fat bodies. These resorbed lipid droplets will exhibit a "Maltese cross" pattern under polarized light. RTEs infected by viruses may have nuclear or cytoplasmic inclusions, best appreciated on stained preparations. RTE cytoplasm can be stained with pigments such as bile and hemosiderin.

Transitional epithelial cells

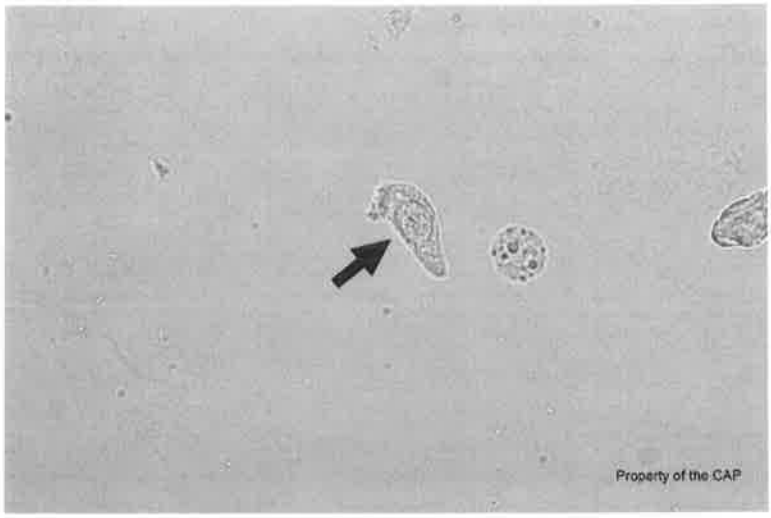
Transitional epithelial cells (TEs) may be larger on average than RTEs, 20 - 40 µm, or 4 - 6x the size of an RBC. They are usually spherical with finely granular or agranular cytoplasm, however they may occasionally have elongated "tails." Their nuclei are round to oval, more often centrally located, and approximately the size of a WBC. TEs may have a slightly lower nuclear:cytoplasmic ratio than RTEs. Despite some RTEs mimicking TEs with elongated tails, a few other features in combination distinguish one from the other. RTEs exhibit fine, somewhat indistinct cell borders with angular or flat sides, whereas TEs have well-defined, almost crisp, cell borders and appear swollen/rounded even when they have a "tadpole" shape (ie, "caudate cell"). Polar cells with eccentrically-placed nuclei and flattened or straight edges along the cell membrane opposite the elongated tail are more likely to represent RTEs than TEs. A visible apical/luminal brush border is a feature seen only in RTEs and not TEs. TEs are often shed during inflammation or due to sloughing during procedures such as catheterization or cystoscopy. TEs may appear as a monolayered cluster or sheet of cells.

Squamous epithelial cells

Squamous epithelial cells are the largest cells in the urine, 30 - 50 µm. They are polygonal and may have curled or folded cell borders. The nucleus is approximately the size of an RBC, leading to a low nuclear:cytoplasmic ratio, and may be centrally or eccentrically placed. The cytoplasm contains keratohyaline granules of varying sizes. With degeneration squamous cells may have frayed cell borders, pyknotic nuclei, and increased cytoplasmic granules.

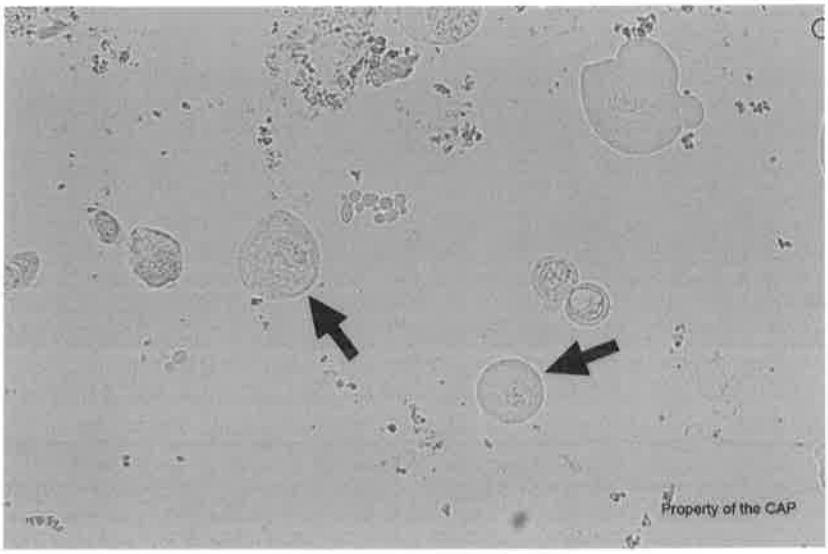
Wildcard challenge cell identifications

WC-01



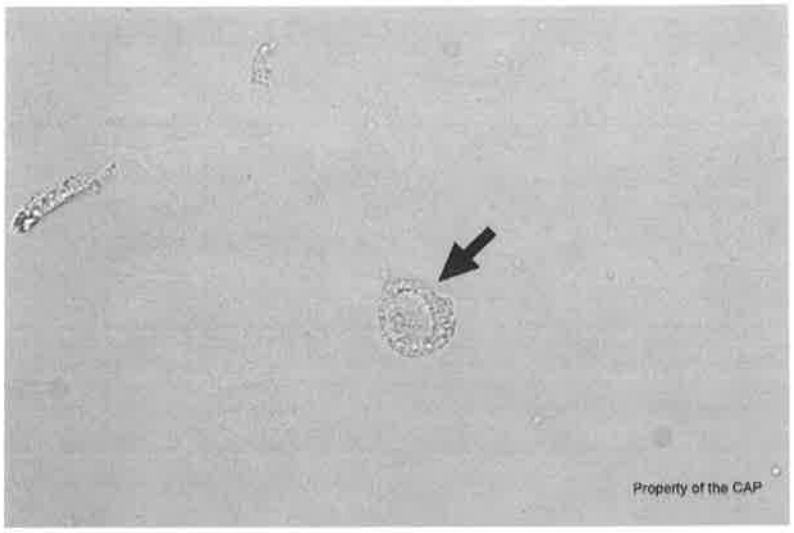
The arrowed cell is a renal tubular epithelial cell (RTE). The cell is elongated, with granular cytoplasm, and the nucleus is slightly eccentrically located.

WC-02



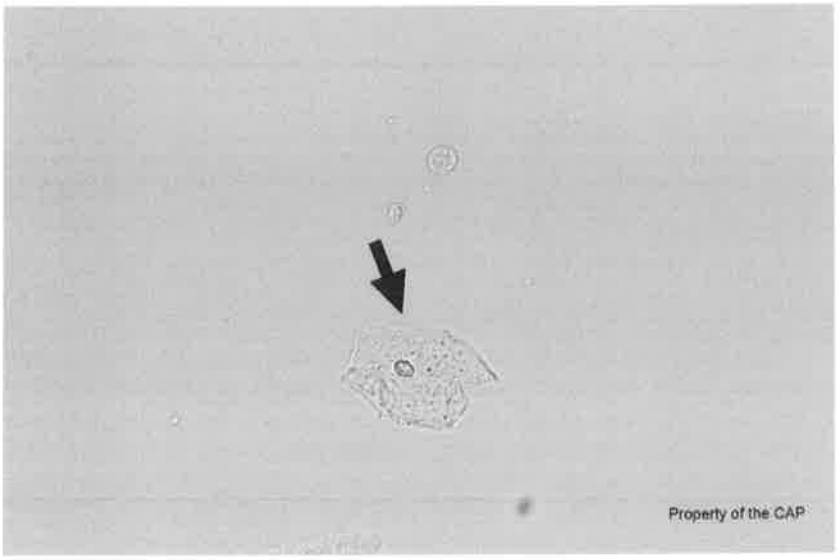
The arrowed cells are transitional epithelial cells (TE). They are identifiable by their round shape, crisp cell borders, centrally located nuclei, and fine to absent cytoplasmic granularity.

WC-03



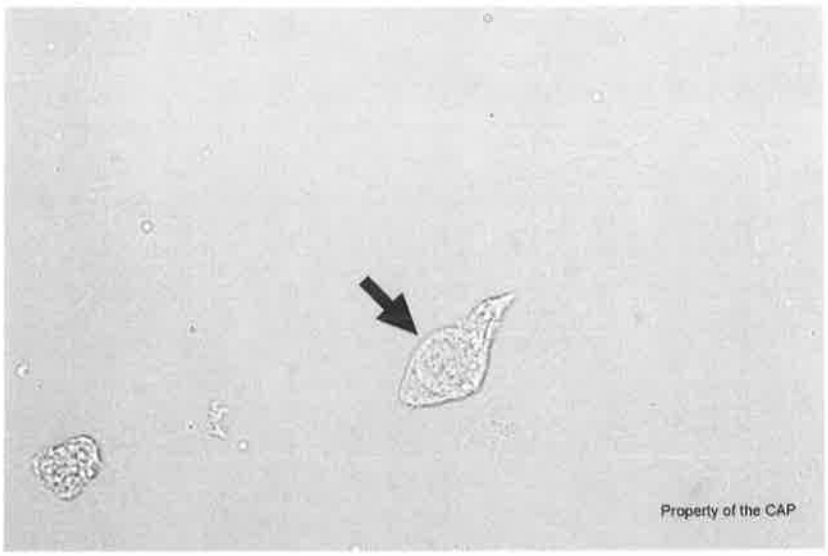
The arrowed cell is an RTE. It has more granular cytoplasm than a TE, with a higher nucleus:cytoplasmic ratio, and an eccentrically located nucleus.

WC-04



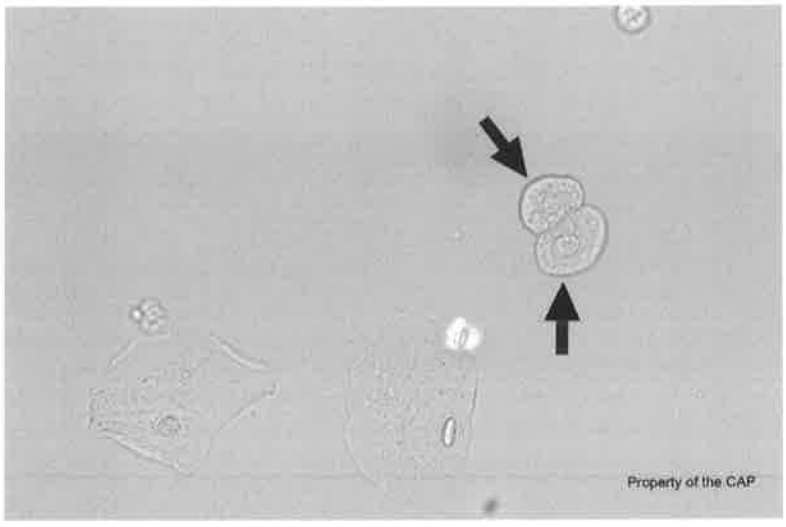
The arrowed cell is a squamous epithelial cell. It is recognizable by its large size relative to the leukocyte in the image, as well as it's polyhedral shape with folded cytoplasmic borders and low nucleus:cytoplasm ratio.

WC-05



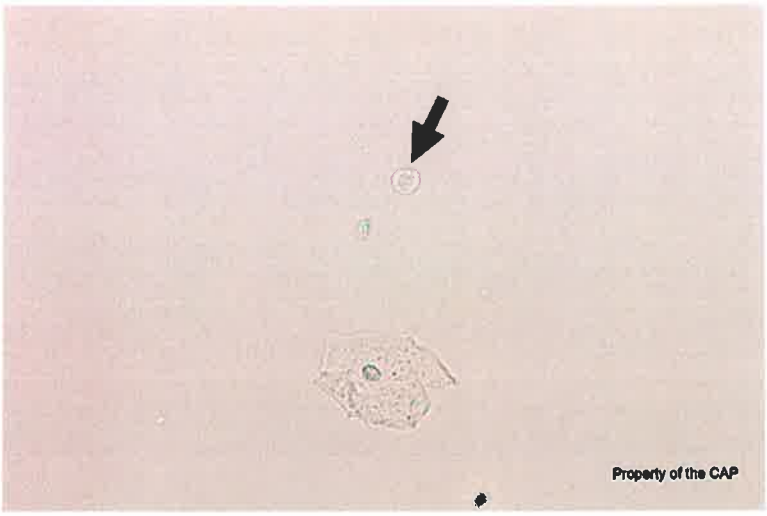
The arrowed cell is an RTE. The most distinctive features in this example are the elongated cell shape and relatively large nucleus.

WC-06



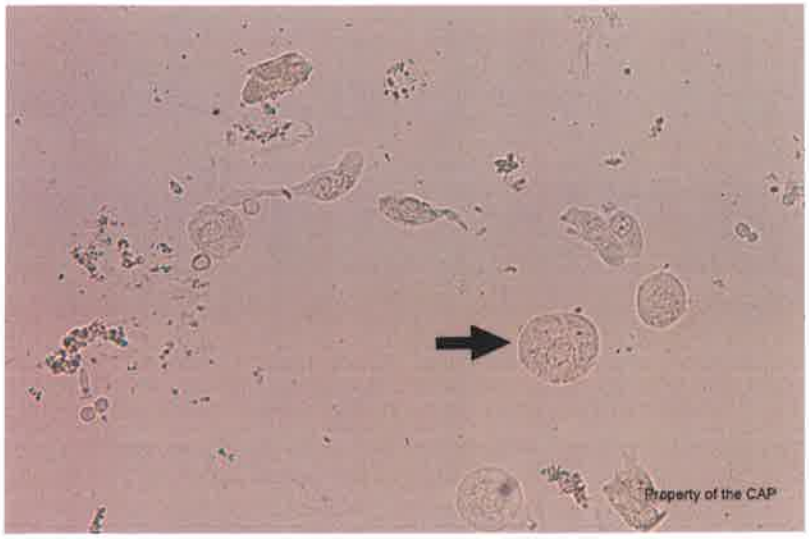
The arrowed cells are TEs. These examples show a typical rounded shape with very distinct cell borders. As in this image TE may be shed it pairs or groups. The nuclei are centrally located. The nucleus:cytoplasmic ratio is lower than in an RTE, but higher than the squamous epithelial cells in the image.

WC-07



The arrowed cell is a leukocyte, specifically a granulocyte as identified by the nuclear lobes. It is significantly smaller than the squamous epithelial cell in the image, and slightly larger than the squamous epithelial cell nucleus, and has a round cell border.

WC-08



The arrowed cell is a TE. It is large compared to the RBCs in the field. The cell is round with a crisp cytoplasmic border, finely granular cytoplasm, and centrally located round nucleus. There are also partially degenerated RTE in the image, which are smaller, have an elongated cell shape, and higher nucleus:cytoplasmic ratio compared to the TE.

Megan Nakashima, MD
Hematology and Clinical Microscopy Committee

References:

1. College of American Pathologists. *Hematology and Clinical Microscopy Glossary*. 2021.
2. Haber MH, Blomberg, D, Galagan KA, Glassy EF, Ward PCJ, eds. *Color Atlas of the Urinary Sediment*. College of American Pathologists. 2010.

COLLEGE of AMERICAN PATHOLOGISTS

Attestation of Participation of Self-Reported Training*

We the participants below have completed the review of the CM-A 2022 CAP Program
Product Mailing, Year
Participant Summary/Final Critique report and can self-report this activity towards fulfilling education and maintenance of certification (MOC) requirements. Time spent on activity* _____.

Participant	Date	Participant	Date
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____

_____ _____

Director (or Designee) Signature - I have verified that the individuals listed above have successfully participated in this activity. Date

Retain this page for record-keeping and auditing purposes.

1. Go to www.cap.org
2. Click **Login** and enter your User ID and Password.
   - If you are unsure whether you have an *individual* web account with the CAP, or do not remember your user ID and password, click on **PASSWORD HINT**.
   - If you do not have an *individual* web account, click **CREATE AN ACCOUNT**. Complete and submit the account request form. You will be notified within one business day that your individual account has been activated.
3. Click **Learning** from the top menu bar
4. Click **Transcript** from the menu bar
5. Click **+ Add my own activity**
6. Follow prompts to enter 'Self-Reported Training Activities' including upload of this supporting documentation*.

For assistance, call our Customer Contact Center at 800-323-4040 or 847-832-7000 option 1.

**** CAP Self-Reported Training activities do not offer CE credit but can be used towards fulfilling requirements for maintenance of certification by agencies such as the American Society of Clinical Pathology (ASCP). Please verify with your certifying agency to determine your education requirements. Individuals should report the actual time spent completing the activity.***