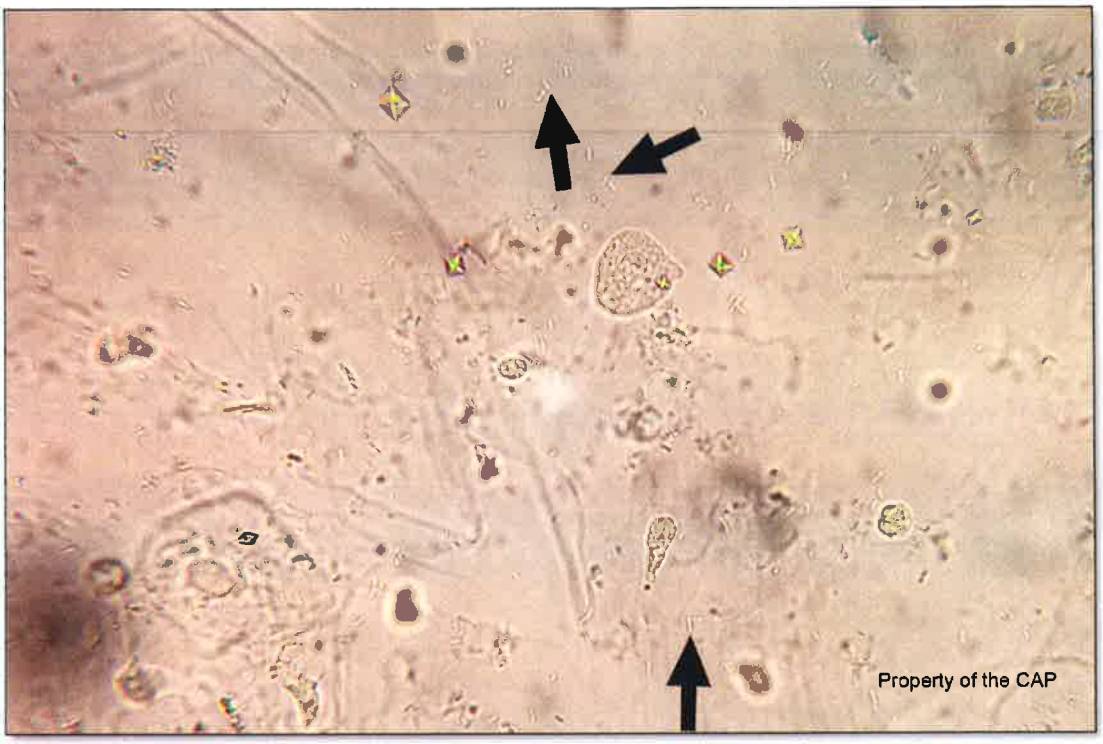
Urine Sediment Photographs

Case History CMP-13 through CMP-15
This urine sample is obtained from a 55-year-old woman after removal of a urine catheter. Laboratory data include: specific gravity = 1.025; pH = 6.0; protein and leukocyte esterase = positive; glucose, ketones, blood, and nitrite = negative. Identify the arrowed object(s) on each image.

(URINE, UNSTAINED, HIGH POWER)

CMP-13

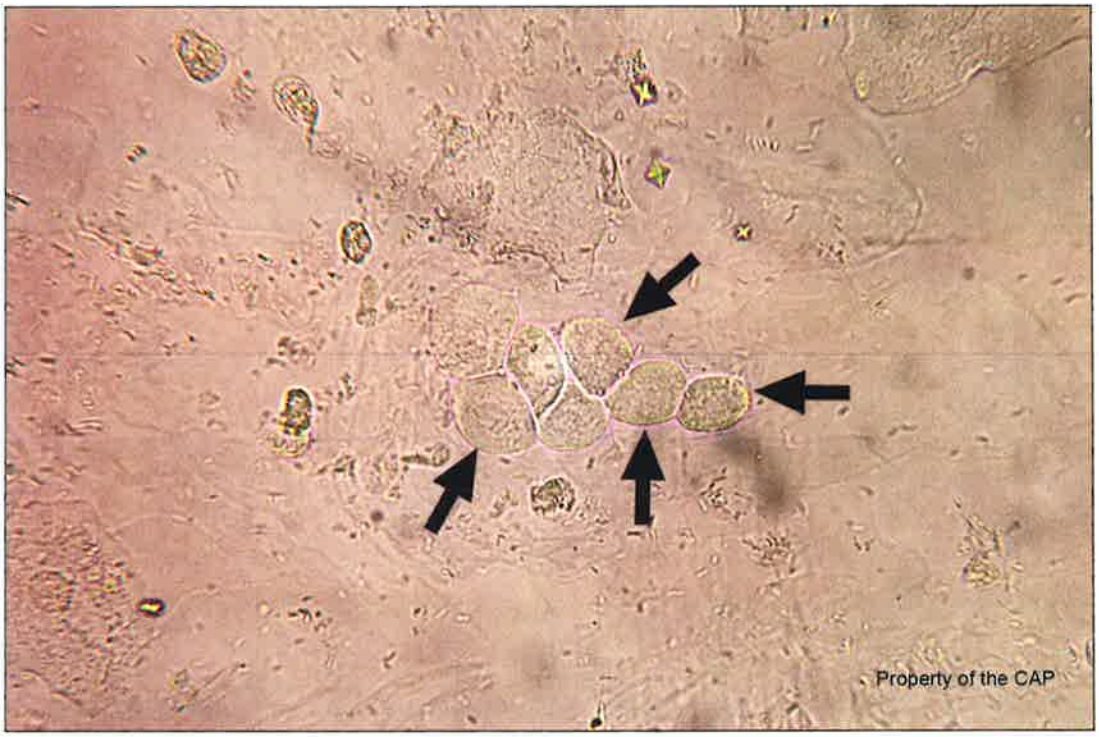


Identification	Participants		Evaluation
	Freq	%	
Bacteria	6133	99.6	Good

The encircled arrowed organisms are bacteria, as correctly identified by 99.6% of participants. The rod shape of the small sized organisms can be seen and are typical of gram-negative enteric bacilli that are the most common cause of urinary tract infections. The concomitant presence of white blood cells and leukocyte-positivity are also consistent with a urinary tract infection and may be used to reflex a urine culture analysis in some laboratories. Although nitrite-positivity is associated with gram negative bacteria, urine samples are often negative for nitrite in patients with clinically significant urinary tract infection with culture-confirmed pathogenic gram-negative bacilli as happened in this case. This is because urine must be in the bladder for a few hours with sufficient nitrate from dietary vegetables for the conversion reaction to nitrites to take place. Therefore, negative nitrates should never be used to exclude a urinary tract infection.

Urine Sediment Photographs

CMP-14



Identification	Referees		Participants		Evaluation
	Freq	%	Freq	%	
Transitional epithelial cell (Urothelial cell)	37	72.5	4585	74.5	Non-consensus
Renal tubular epithelial (RTE) cell	12	23.5	1304	21.2	Non-consensus

This challenge will not be graded as neither referees nor participant responses reached 80% consensus.

The arrowed cluster of cells are transitional epithelial cells, as correctly identified by 74.5% of participants and 72.5% of referees. The cells are identified as medium-sized (20 - 30 µm) round epithelial cells with well-defined cell borders and round well-defined central nuclei. Transitional epithelial cells are also referred to as urothelial cells because they line the urinary tract from the renal pelvis to the distal part of the urethra in the male, and to the base of the bladder in the female. Clusters or sheets of transitional epithelial cells are seen with catheterization, bladder washings, or urinary tract infections.

The arrowed cells were incorrectly identified by 21.2% of participants and 23.5% of the referees as renal tubular epithelial (RTE) cells. Compared to transitional epithelial cells, RTE cells have a higher nuclear-to-cytoplasm ratio, more angular/flat cell borders, more granular cytoplasm, and may have polarized features such as an eccentric nuclei or microvillus border. The cytoplasmic and nuclear borders of RTE cells are less distinctive. Transitional epithelial cells are more likely to cluster, as seen in this image, than RTE cells. Since these features are variable and overlap to some degree, distinguishing RTE from

CMP-14, Cont'd

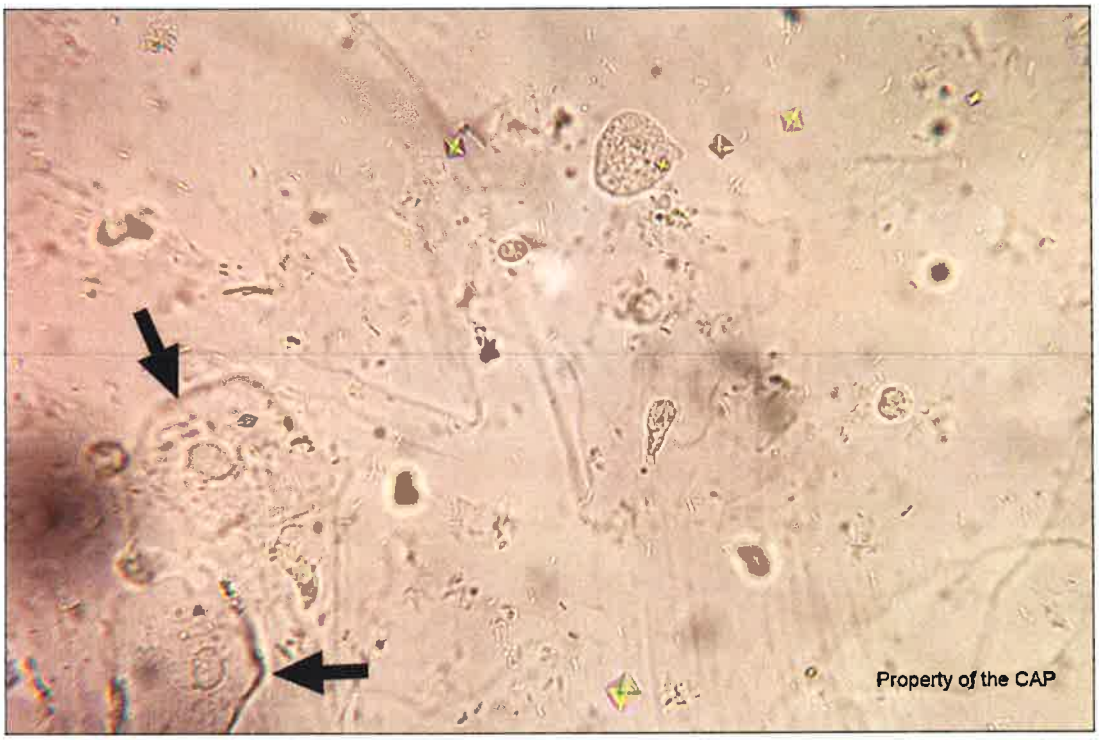
transitional epithelial cells can be challenging as shown by the results of this survey. Since RTE cells are associated with acute tubular necrosis while transitional epithelial cells are not, there is clinical value in learning how to accurately identify these cells in urine.

The arrowed cells were incorrectly identified by 1.7% of participants and 2.0% of the referees as leukocytes. Leukocytes are substantially smaller with a lower nuclear-to-cytoplasm ratio.

Squamous cells (directly above the arrowed cluster and in the lower right corner) can be seen in the image for comparison. The squamous cells are larger, have a small condensed nucleus, cytoplasmic granulation, and have a cell membrane with curled or folded edges.

Urine Sediment Photographs

CMP-15



Identification	Participants		Evaluation
	Freq	%	
Squamous epithelial cell	6061	98.4	Good

The arrowed cells are squamous epithelial cells, as correctly identified by 98.4% of participants. They are identified as being large (50 µm), flat cells with well-defined cell membranes bearing folded edges, cytoplasmic granulation, and a single small, condensed, oval central nucleus about the size of a small lymphocyte. A few squamous cells are seen in most normal urine samples. Their presence has little clinical significance.

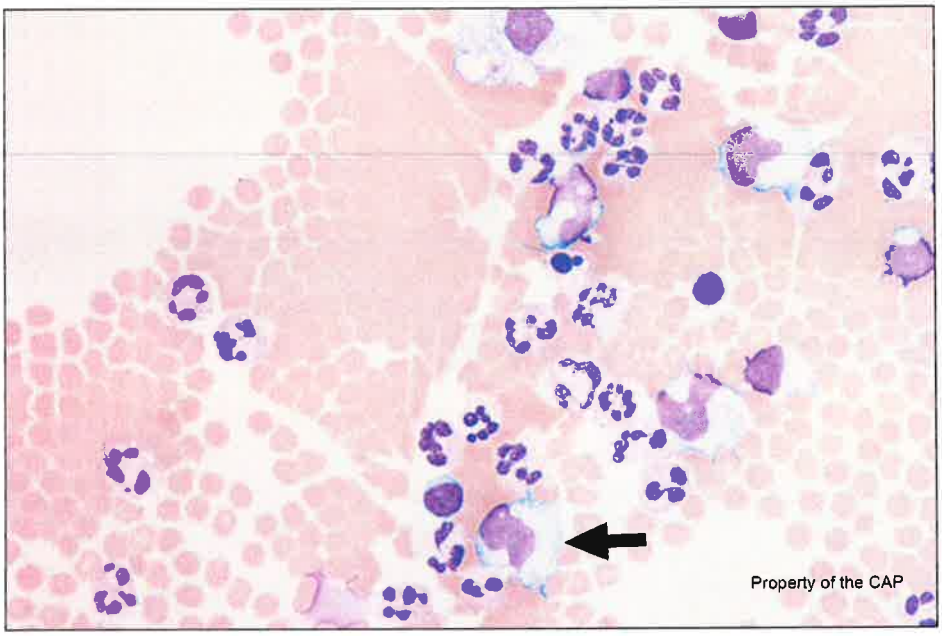
Body Fluid Photographs

Case History CMP-16 through CMP-18

This patient is a 74-year-old woman with abdominal pain and renal mass with ascites. Peritoneal fluid sample laboratory findings include: TNC = 1,371/µL (1.371 x 10E3/µL); RBC = 73,005/µL (73.005 x 10E3/µL). Identify the arrowed object(s) on each image.

(PERITONEAL FLUID, CYTOCENTRIFUGE, WRIGHT-GIEMSA, 50X or 100X)

CMP-16

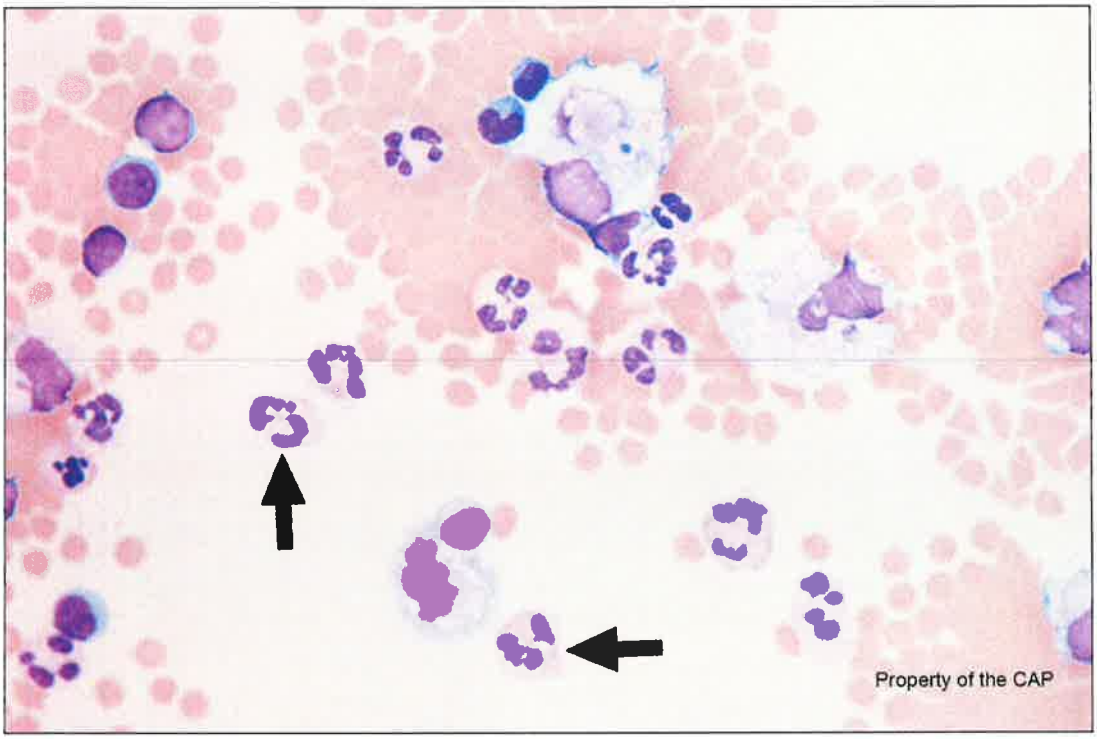


Identification	Participants		Evaluation
	Freq	%	
Monocyte/macrophage	3656	95.3	Good

The arrowed cell is a monocyte/macrophage, as correctly identified by 95.3% of participants. Monocytes arise in the bone marrow and circulate in the peripheral blood. Macrophages differentiate from monocytes after migration into tissues and body fluids. Monocyte/macrophage morphology in fluids is quite variable, ranging from the typical monocyte of the peripheral blood to a vacuolated, activated stage with the morphology of a typical macrophage. Monocytes are usually large (12 to 20 µm) with abundant blue-gray cytoplasm and often contain sparse azurophilic granules. The nucleus is round to oval and may be indented, giving it a kidney bean or horseshoe shape. The chromatin is lacy and small nucleoli may be apparent. Macrophages are larger cells (15 to 80 µm) with abundant cytoplasm showing evidence of active phagocytosis. This includes ingested material such as blood cells, bacteria, hemosiderin, fungi, remnants of digested materials, and post ingestion cytoplasmic vacuoles. One or more round to oval nuclei are present and occasionally prominent nucleoli may be seen. Macrophages can at times be difficult to differentiate from mesothelial cells. Mesothelial cells are usually larger than monocytes/macrophages and usually have biphasic staining cytoplasm and surface microvilli.

Body Fluid Photographs

CMP-17

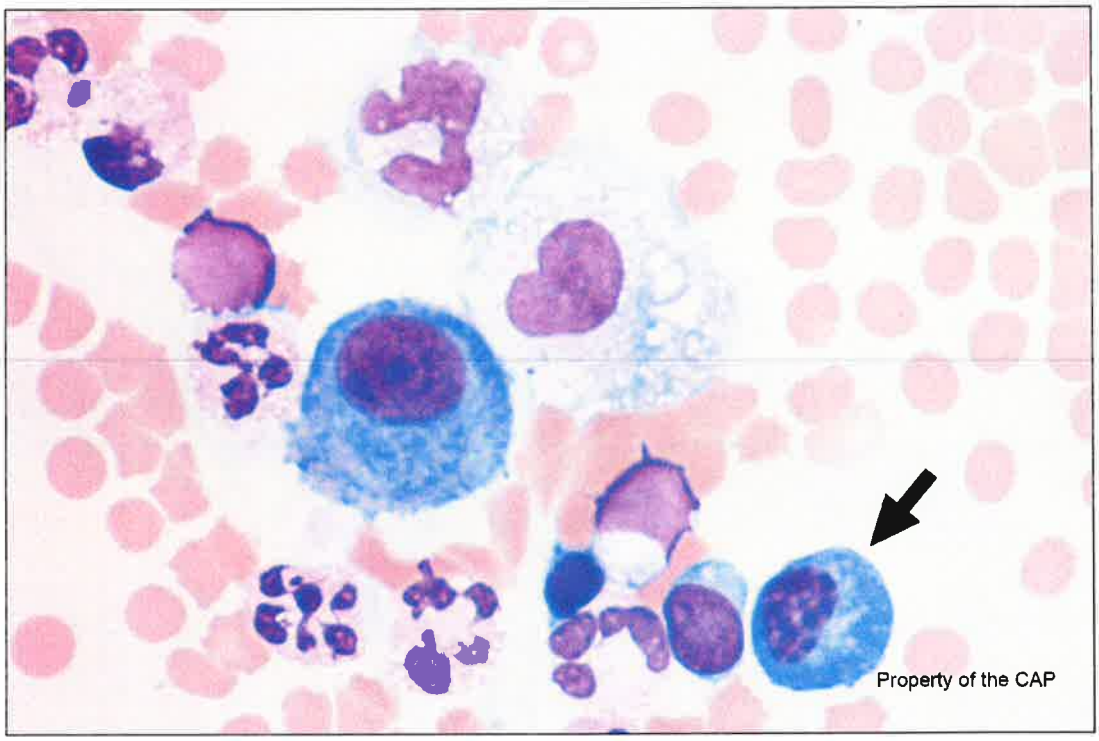


Identification	Participants		Evaluation
	Freq	%	
Neutrophil, segmented or band	3770	98.3	Good

The arrowed cell is a neutrophil, as correctly identified by 98.3% of participants. Usually, a segmented or band neutrophil is easily recognized. Often, the nuclear lobes appear eccentric in cytocentrifuge preparations. The cytoplasm may contain toxic granules or vacuoles. Intracellular bacteria, crystals, or debris may be seen in pathologic conditions. If inclusions are present, the more specific choice such as "neutrophil/macrophage with phagocytized bacteria" or "neutrophil/macrophage containing crystal" should be used. Neutrophils in body fluids can show morphologic change due to autolysis, including nuclear pyknosis and fragmentation, making recognition of cell type difficult. These autolytic neutrophils can be mistaken for nucleated red blood cells; however, the presence of a few azurophilic granules in the cytoplasm provides a clue to their neutrophilic origin.

Body Fluid Photographs

CMP-18



Identification	Referees		Participants		Evaluation
	Freq	%	Freq	%	
Plasma cell, normal/abnormal	36	76.6	2764	72.2	Non-consensus
Mesothelial cell	7	14.9	777	20.3	Non-consensus

This challenge will not be graded as neither referees nor participant responses reached 80% consensus.

The arrowed cell is a plasma cell, as correctly identified by 76.6% of referees and 72.2% of participants. Plasma cells are terminally differentiated forms of B lymphocytes and can be seen in all body fluids but are not normally present. They may be seen in infectious, inflammatory, or neoplastic processes. Plasma cells have round to oval, eccentrically placed nuclei with condensed, clumped chromatin. The cytoplasm is deeply basophilic, often with a perinuclear clear zone or "hof" in the region of Golgi apparatus. Occasionally, the cytoplasm may contain immunoglobulin-filled vacuoles that may appear clear. Binucleated plasma cells occasionally can be seen. The eccentric nuclear location and paranuclear clear zone are helpful in differing plasma cells from plasmacytoid lymphocytes. Mesothelial cells may resemble plasma cells, but they are usually larger in size, have more centrally placed nuclei with smooth rather than ropey chromatin, and usually lack the perinuclear clear zone.

Clinical Presentation:
This patient is a 74-year-old woman with abdominal pain and renal mass with ascites. Peritoneal fluid sample laboratory findings include: TNC = 1,371/µL (1.371 x 10E3/µL); RBC = 73,005/µL (73.005 x 10E3/µL). Identify the arrowed object(s) on each image.

(PERITONEAL FLUID, CYTOCENTRIFUGE, WRIGHT-GIEMSA, 50X or 100X)

CASE DISCUSSION: Renal cell carcinoma in peritoneal fluid

Identification of malignant epithelial cells in body fluids is crucial because their presence has an important impact on the prognosis. Recognition of the specific source of malignancy can guide targeted chemotherapy. A variety of malignant cells can be found in body fluids and their morphology is related to the primary underlying neoplasm. Malignant cells may be numerous in the peritoneal fluid, but in some instances, only rare cells are present and therefore, it is essential to evaluate the entire slide carefully for detection of tumor cells.

The neoplastic cells can resemble macrophages and mesothelial cells in the Wright-Giemsa stained cytocentrifuge preparations, making their recognition difficult. Reactive changes can mimic malignant features, making identification challenging. Some of the helpful cytologic features for accurate identification of tumor cells include high nuclear-to-cytoplasmic ratio, irregularly shaped nuclei, increased cell and nuclear size, atypical nuclear chromatin patterns, large nucleoli, abundant mitoses, and a tendency to form large clusters. Sometimes pseudo-gland formation can be noted in involvement of body fluids by adenocarcinoma.

Peritoneal involvement is uncommon in renal cell carcinoma. On rare occasions, malignant ascites is the initial presentation of cancer. The incidence of ascites appears to be higher in papillary renal cell carcinoma in comparison to other histological subtypes. Recognition of peritoneal carcinomatosis in renal cell carcinoma is crucial as it may indicate poor prognosis. The involvement of peritoneum might be through hematogenous spread, direct tumor extension, or tumor seeding from prior surgical resection. Malignant ascites in patients with renal cell carcinoma can be difficult to diagnose due to the bland morphology of the tumor cells and therefore their cytological appearance can easily be confused with reactive mesothelial cells and macrophages. However, there are features that can be helpful for the correct diagnosis. The carcinoma might present with single cells or clusters of cells with clear to granular and vacuolated cytoplasm, large nuclei with round to markedly irregular nuclear outlines, vesicular or clumped chromatin, and prominent nucleoli. The neoplastic cells may have papillary configuration or form acinar groups.

In conclusion, in the absence of typical symptoms or prior history of renal cell carcinoma, the diagnosis of peritoneal involvement by neoplastic cells can be easily overlooked in patients presenting with ascites. Although rare, renal cell carcinoma should be considered as a possible cause of malignant ascites.

Sahar Nozad, MD
Hematology and Clinical Microscopy Committee

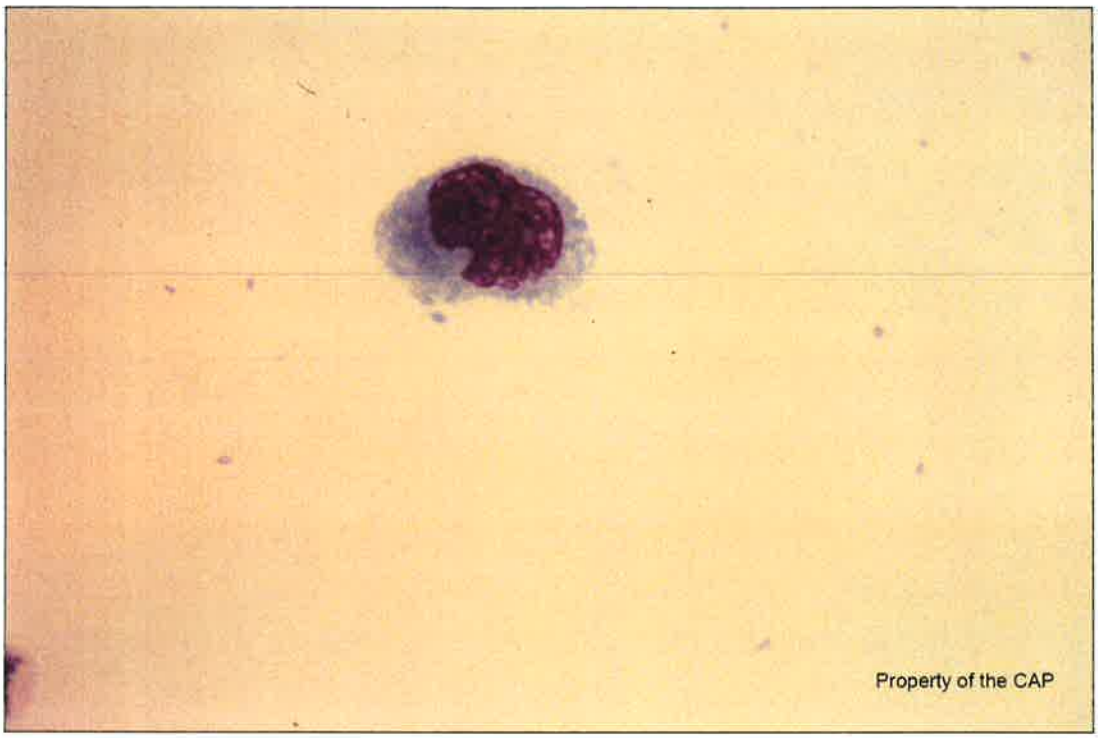
REFERENCES:

1. Galagan KA, Blomberg D, Cornbleet PJ, Glassy EF. *Color Atlas of Body Fluids*. College of American Pathologists 2006.
2. Jennison E, Wathuge GW, Gorard DA. Renal cell carcinoma presenting with malignant ascites. *JRSM Open*. 2015;6(4):2054270415585087.
3. Soputro NA, Kapoor J, Zargar H, Dias BH. Malignant ascites following radical nephrectomy for cystic renal cell carcinoma. *BMJ Case Rep*. 2021;14(7):e243103.
4. Renshaw AA, Comiter CV, Nappi D, Granter SR. Effusion cytology of renal cell carcinoma. *Cancer*. 1998;84(3):148-152.
5. Sidana A, Kadakia M, Friend JC, et al. Determinants and prognostic implications of malignant ascites in metastatic papillary renal cancer. *Urol Oncol*. 2017;35:114.e9–114.e14.

CMMP – Clinical Microscopy Miscellaneous Photographs

(NASAL, WRIGHT-GIEMSA)

CMMP-32



Identification	Participants		Evaluation
	Freq	%	
Eosinophils are absent	1841	95.7	Good

This is a nasal smear is absent for eosinophils. The leukocyte in this Wright-Giemsa stain lacks the large intense eosin-staining granules and bi-lobed nucleus seen in eosinophils. Nasal smears showing eosinophils are often caused by allergic disease like asthma or seasonal allergies.

Urine Sediment Color Photographs

Case History USP-04 through USP-06

This urine sample is obtained from an 88-year-old man with fever and altered mental status. Urinalysis data include: specific gravity = 1.023; pH = 6.0; protein, blood, leukocyte esterase, and nitrite = positive; glucose and ketones = negative. Identify the arrowed object(s) on each image.

(URINE, UNSTAINED, HIGH POWER)

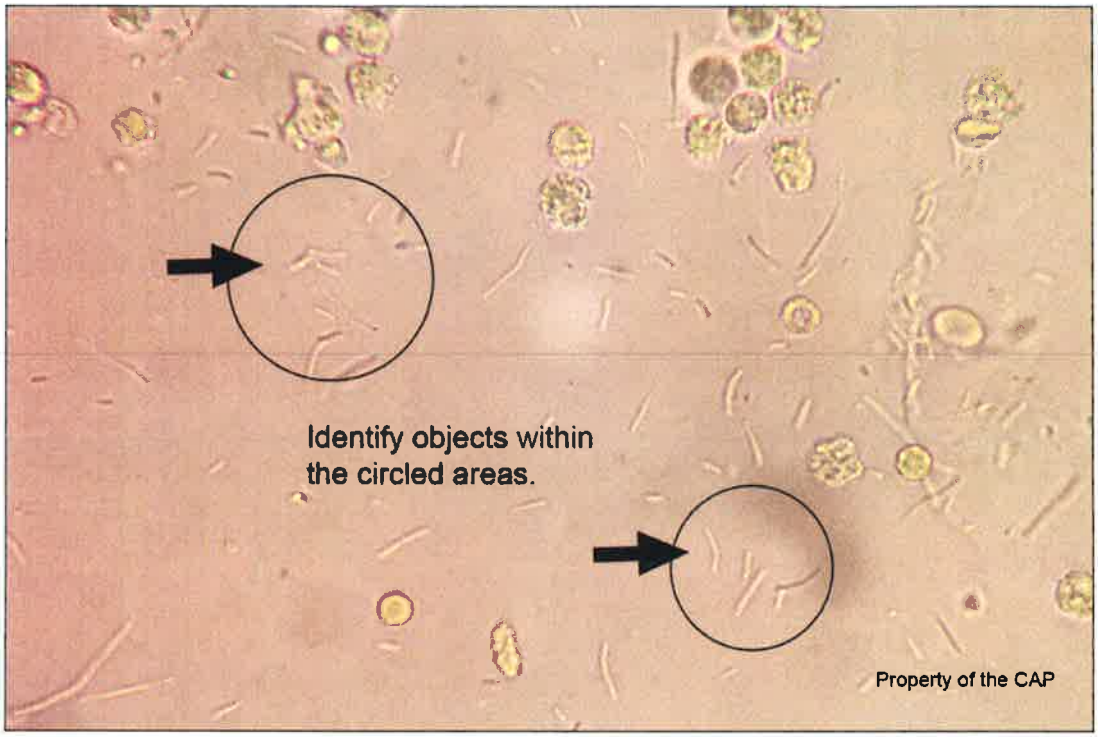
USP-04

Identification	Participants		Evaluation
	Freq	%	
Erythrocyte	3954	99.4	Good

The arrowed cell in this image is an erythrocyte. The cell's classic biconcave shape is manifest by its central pallor that occupies one-third of the cell diameter. The cell lacks a nucleus and is approximately 7 µm in diameter distinguishing it from the many leukocytes seen in this image which are twice the size and nucleated. The erythrocyte is non-granular in contrast to the surrounding leukocytes. The presence of red cells in the urine, termed hematuria, is an important early indicator of disease, such as bladder cancer, stones, infection, or inflammatory kidney disease.

Urine Sediment Photographs

USP-05



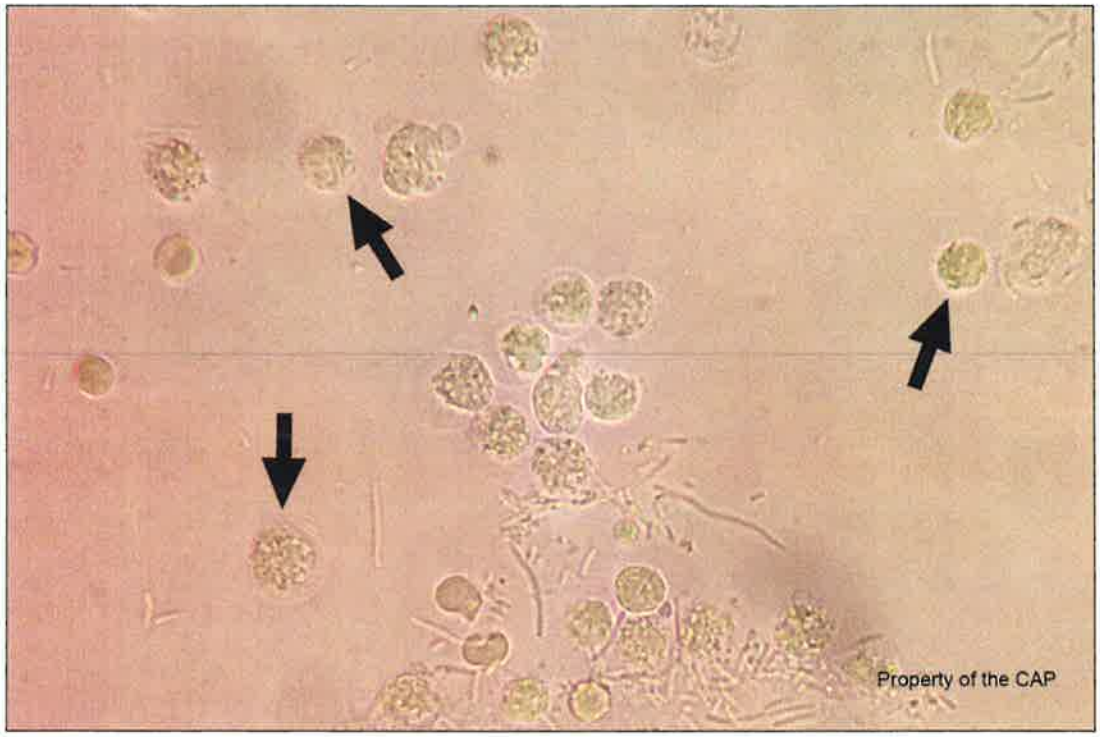
Identification	Participants		Evaluation
	Freq	%	
Bacteria	3927	98.7	Good

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, numerous surrounding leukocytes are seen, suggesting a clinically significant urinary tract infection that is more likely to grown pathologic bacteria on urine culture.

Urine Sediment Photographs

USP-06



Identification	Participants		Evaluation
	Freq	%	
Leukocyte (neutrophil, eosinophil, lymphocyte)	3948	99.3	Good

The arrowed cells in this image are leukocytes. The cells are round nucleated cells with granular appearance approximately 10 – 12 µm in diameter. The lobular nuclear contours and marked granular cytoplasm suggest that the white blood cell may be a neutrophil. However, in routine urinalysis using unstained brightfield microscopy the differential type of leukocyte cannot be readily determined and cells are simply reported as white blood cells. An increased number of leukocytes is associated with both infectious and non-infectious kidney and urinary tract disease.

COLLEGE of AMERICAN PATHOLOGISTS

Attestation of Participation of Self-Reported Training*

We the participants below have completed the review of the CM-B 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.***