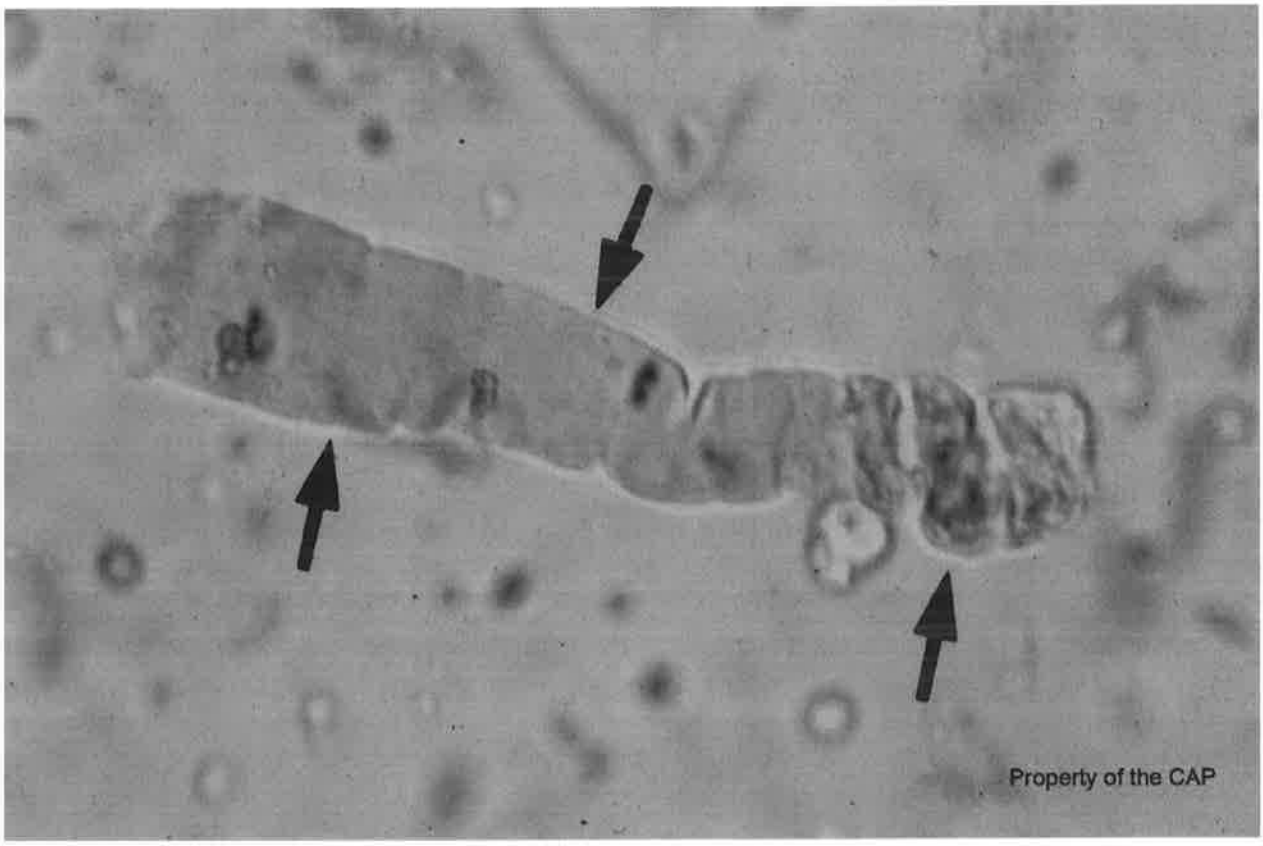
Urine Sediment Photographs
Case History CMP-04 through CMP-06

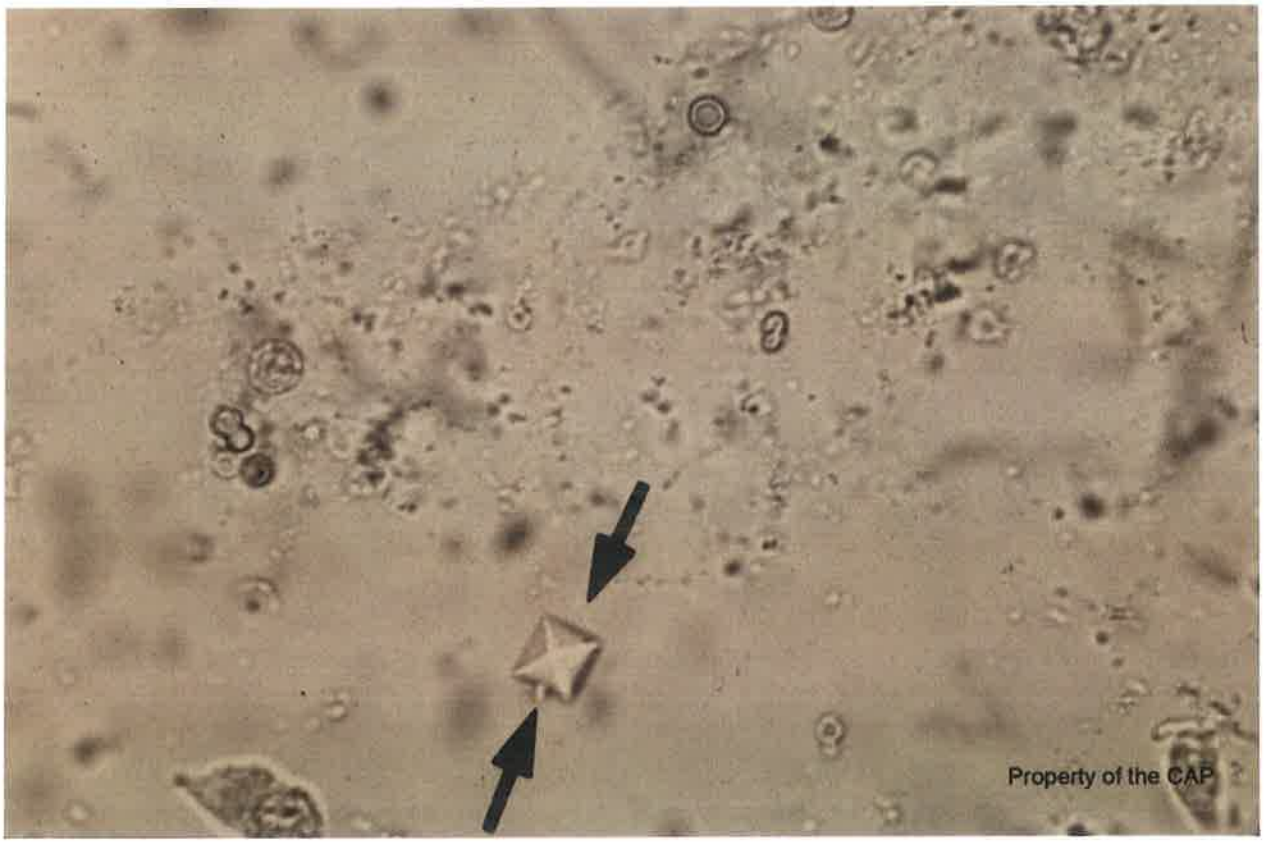
This urine sample is obtained from a 48-year-old homeless man with a 30-year history of diabetes mellitus,edema, and new onset renal failure. Laboratory data includes: BUN = 35 mg/dL (8 - 18 mg/dL); creatinine = 2.8mg/dL (0.35 - 0.93 mg/dL); specific gravity = 1.007; pH = 6.0; blood, glucose, protein, nitrite, and leukocyte esterase = positive; ketones, bilirubin,and urobilinogen=negative.



(URINE, UNSTAINED, HIGH POWER)

	CMP Participants		Performance
Identification	**No.**	**% Evaluation**	
Waxy cast	5890	96.6	Good

The arrowed object is a waxy cast, as correctly identified by 96.6% of participants. Waxy casts are colorless
or pale-yellow acellular casts that are uncommon. Waxy casts are always pathologic and most commonly associated with chronic renal failure. These casts appear flattened, with a smooth dense interior and blunt or
"broken off" ends and sides that may be clefted or notched. The interior of a waxy cast does not polarize. The
matrix of a waxy cast is proteinaceous and appears to be the results of the breakdown of granular and cellular
casts. Cellular and granular casts first form in the proximal convoluted tubules. As a cast ages and degenerates in the distal convoluted tubule it becomes broad and waxy.
Waxy casts may be confused with diaper or other fibers or hyaline casts. Fibers usually have fibrillar ends and internal structure. Hyaline casts are narrow with at least one tapered end and do not appear dense.



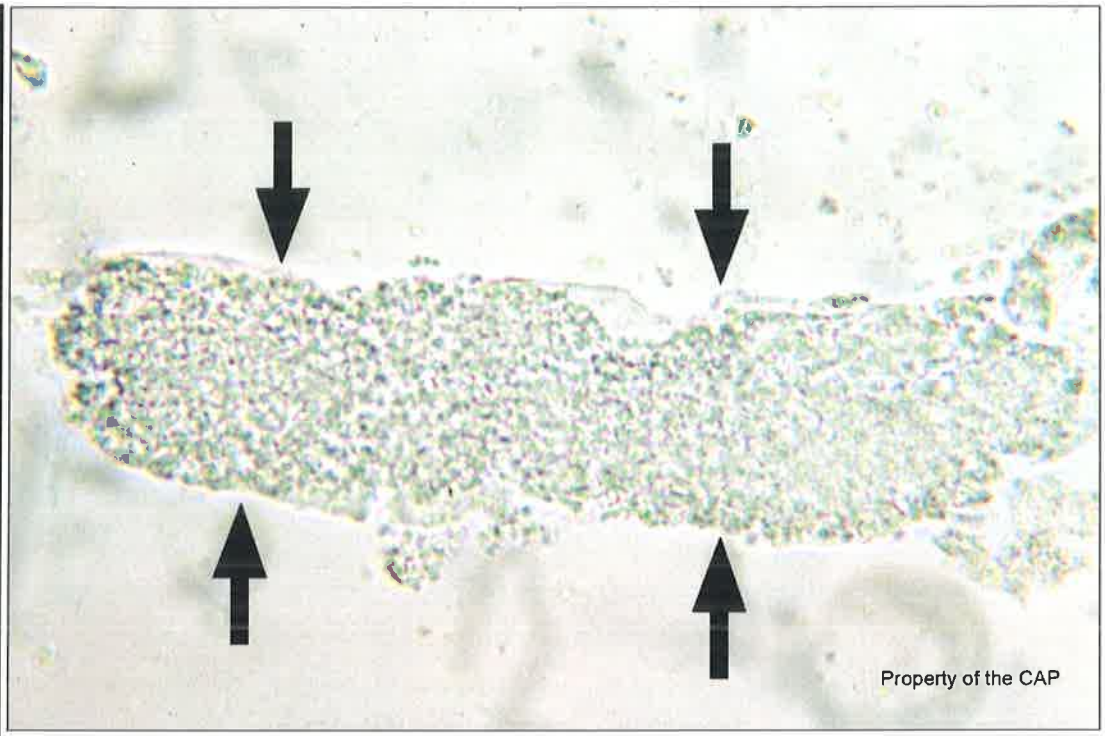
URINE, UNSTAINED, HIGH POWER)

Identification	CMP Participants No.	% Evaluation	Performance
Calcium oxalate crystal	6025	98.8	Good

The arrowed object(s) are calcium oxalate crystals, as identified correctly by 98.8% of participants. Calcium oxalate crystals may be found in normal urine but are also associated with nephrolithiasis, or kidney stone formation. Calcium oxalate crystals are most often found in acid urine with envelopeshaped/ dipyramidal dihydrate forms being the most common. Monohydrate forms of calcium oxalate are more variable and include ovals, dumbbells and thin hexagons. Calcium oxalate crystals are associated with ethylene glycol poisoning, an oxalate rich diet (eg, tomatoes, apples, asparagus, and rhubarb), medullary sponge kidney, short bowel syndrome, oxalate kidney stones and Crohn disease.
It is difficult to confuse the unique dihydrate envelope forms of calcium oxalate with any other components of urinary sediment. However, the monohydrate forms may be confused with fungi, pinworm ova, and, rarely, hippuric acid. It is common for unusual monohydrate forms to be found mixed with more typical dihydrate forms in the same urine, which aids in identification. Calcium oxalate crystals are colorless and birefringent with polarized light.

Urine Sediment Photographs

CMP-06



(URINE, UNSTAINED, HIGH POWER)

Identification	CMP Participants No.	%	Performance Evaluation
Granular cast	5989	98.3	Good

The arrowed object is a granular cast, as correctly identified by 98.3% of participants. Granular casts vary in length, are rarely bent or folded and have rounded ends and smooth margins. The matrix of a granular cast contains few to many fine or coarse spherical granules scattered throughout. The granules in a granular cast are the breakdown products of pre-existent cells, such as erythrocytes or leukocytes. Small numbers of granular casts may be seen in normal urine, with increased numbers seen in stress, following strenuous exercise, systemic disease (eg, heart failure) or renal disease.

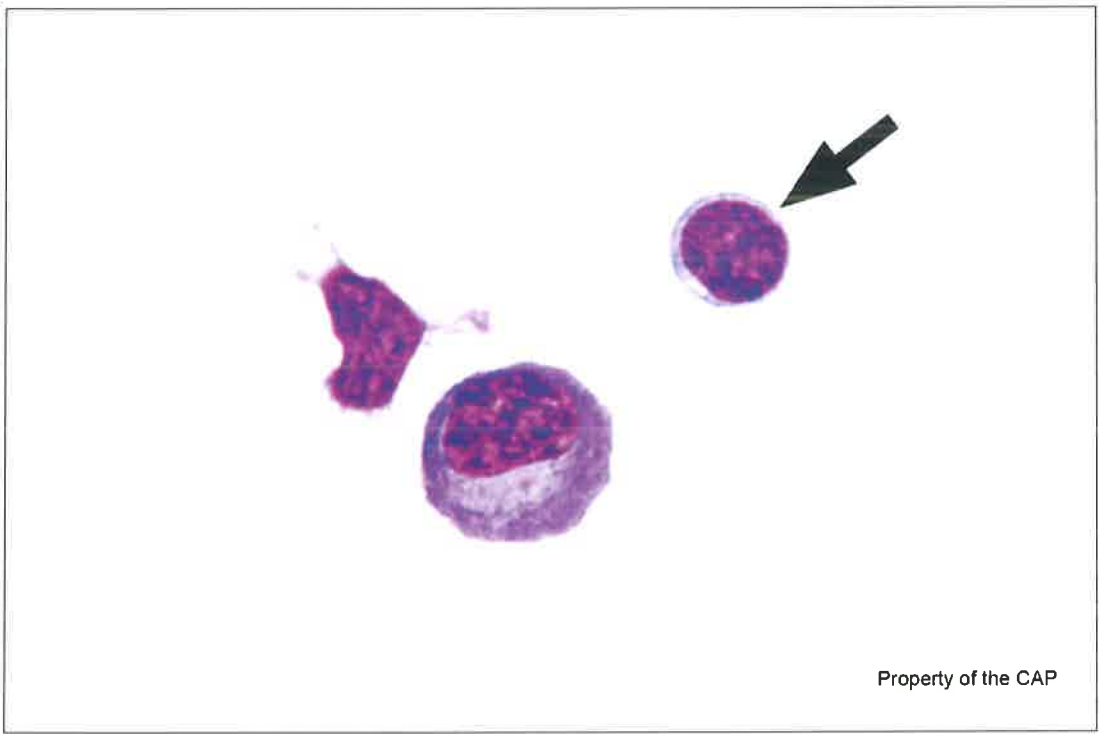
Hyaline casts with occasional granules should not be confused with granular casts. Casts with identifiable cellular elements should be identified accordingly as red cell or white cell casts. Fatty casts contain highly refractile globules of fat with a "Maltese cross" pattern on polarization. They may also contain granules, but are most accurately identified as fatty casts.

Body Fluid Photographs

Case History CMP-07 through CMP-09

This patient is a 42-year-old man admitted through the emergency department because of unusual and bizarre behavior over the past 1.5 months. Laboratory data shows: Total nucleated cells = 14 cells/µL (0.014 x 10E3/µL); RBC = 290 cells/µL (0.290 x 10E3/µL); CSF chemistries: glucose = normal; protein = elevated. CBC, urinalysis, and comprehensive chemistry profile were all within normal range. A VDRL test was positive and confirmed by a positive *Treponena pallidum* antibody test.

CMP-07



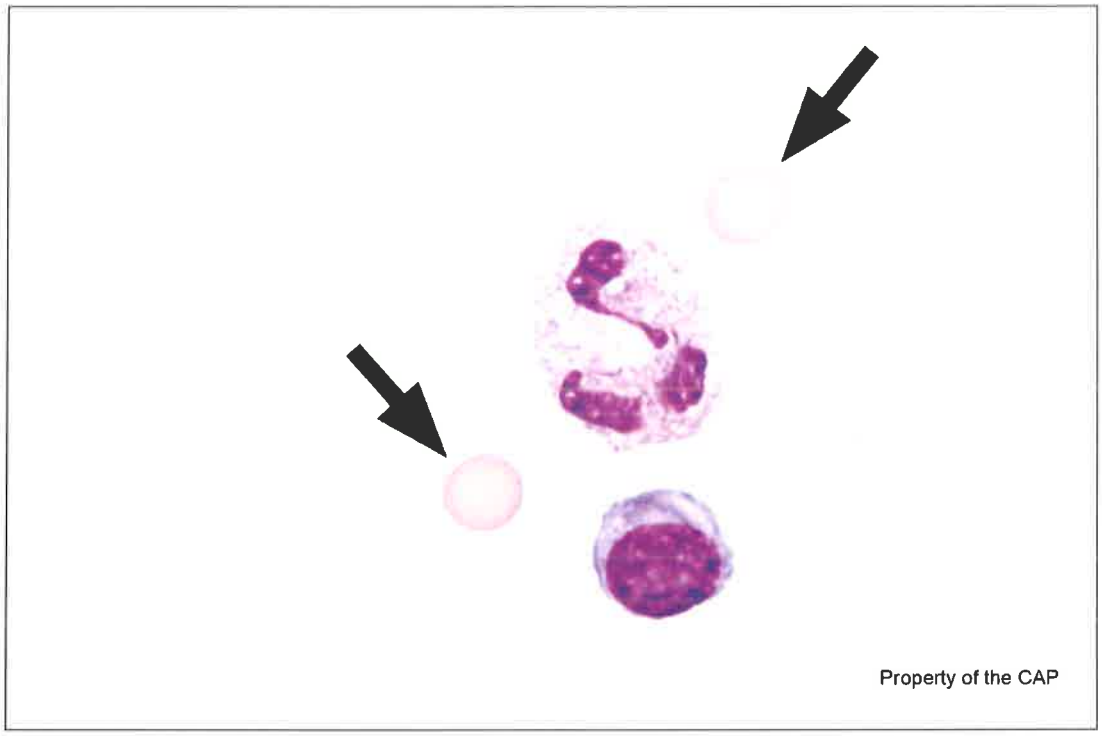
(CSF, CYTOCENTRIFUGE, WRIGHT-GIEMSA, 100X)

Identification	CMP Participants No.	%	Performance Evaluation
Lymphocyte	3822	99.3	Good

The arrowed object is a lymphocyte, as correctly identified by 99.3% of participants. The cytologic features of lymphocytes from body fluids prepared by cytocentrifugation may differ from those in blood smears. Changes induced by cytocentrifugation may include cytoplasmic spreading, nuclear convolutions, and nucleolar prominence. The mature or quiescent lymphocyte appears slightly larger than its counterpart on blood smears, often with more abundant cytoplasm but usually smaller than neutrophils and monocytes. Because of the high speed used in cytocentrifugation, a small nucleolus may be seen, and this should not be interpreted as indicative of lymphoma or immaturity. The lymphocyte arrowed in this image is without morphologic abnormality.

Body Fluid Photographs

CMP-08



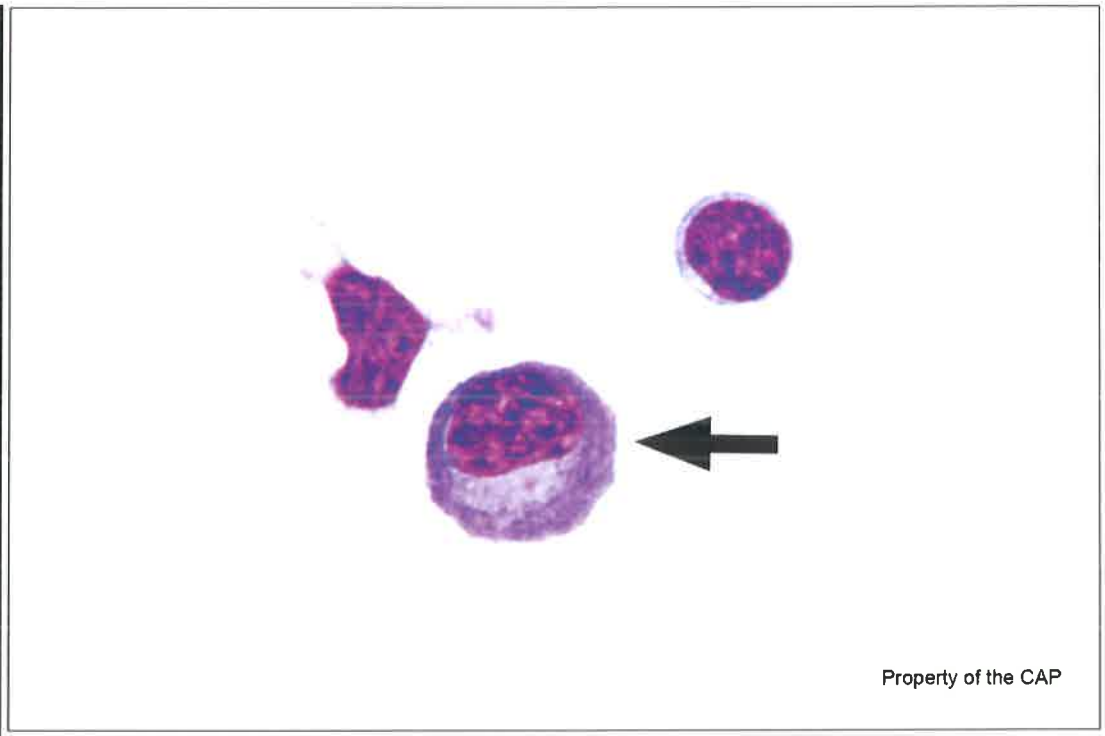
(CSF, CYTOCENTRIFUGE, WRIGHT-GIEMSA, 100X)

Identification	CMP Participants No.	%	Performance Evaluation
Erythrocyte	3821	99.2	Good

The arrowed objects are erythrocytes, as correctly identified by 99.2% of participants. These are typical mature erythrocytes without nuclei and are similar to those present in the peripheral blood. Erythrocytes are not typically found in normal body fluid samples and may reflect hemorrhage or traumatic contamination. They may also be seen in association with many disease states, such as malignancy or inflammation. Erythrocytes may appear crenated in certain fluids, but that finding is not clinically significant.

Body Fluid Photographs

CMP-09



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

Identification	CMP Referees No.	CMP Referees %	CMP Participants No.	CMP Participants %	Performance Evaluation
Plasma cell, normal/abnormal	49	80.3	3049	79.2	Good
Lymphocyte, reactive	4	6.6	343	8.9	Unacceptable
Neutrophil, immature (metamyelocyte, myelocyte, promyelocyte)	2	3.3	168	4.4	Unacceptable
Monocyte/macrophage	4	6.6	165	4.3	Unacceptable
Immature or abnormal cell, would refer information for identification	2	3.3	35	0.9	Good

This challenge is being graded based on referee consensus. The arrowed object is a plasma cell, as correctly identified by 80.3% of referees and 79.2% of participants. Immature, would refer is an acceptable answer. Plasma cells are terminally differentiated B-cells. They can be seen in body fluids but are not normally present. They may be seen in infectious, inflammatory, or neoplastic processes. They have round to oval, eccentrically placed nuclei with condensed, clumped chromatin. The cytoplasm is deeply basophilic, with a paranuclear clear zone or Golgi region. Occasionally, the cytoplasm may contain immunoglobulin-filled vacuoles that may appear clear. Mesothelial cells may resemble plasma cells, but they are usually larger in size, have more centrally placed nuclei with smooth rather than condensed, clumped chromatin, and usually lack the perinuclear clear zone.

8.9% of participants called the arrowed cell a reactive lymphocyte. Reactive lymphocytes tend to be larger than lymphocytes, with increases in volume of both nucleus and cytoplasm. Included within the spectrum of

reactive lymphocytes are plasmacytoid lymphocytes. Plasmacytoid lymphocytes are medium-sized cells with irregular, densely clumped chromatin, absent to indistinct nucleoli, abundant basophilic cytoplasm, and often a paranuclear clear zone (hof). However, plasmacytoid lymphocytes do not typically have all the described characteristics of a true plasma cell and are therefore characterized as reactive lymphocytes. Moreover, when reactive lymphocytes are present within a sample, they often are seen in a morphologic spectrum and include other reactive forms such as immunoblasts. Immunoblasts are large cells with round to oval nuclei, fine, delicate chromatin, prominent nucleoli, and moderate amounts of deeply basophilic cytoplasm. The arrowed cell has all the hallmark characteristics of a plasma cell, making plasma cell the more appropriate choice.

4.4% of participants called the arrowed cell an immature neutrophil. Immature stages of the myeloid series are infrequently found in body fluids, unless there is an accompanying increase in those same cells in the peripheral blood or bone marrow contamination occurs. Immature myeloid cells have the same morphology as in the marrow and peripheral blood. Specifically, each stage, other than a blast, would have cytoplasmic granules, either primary or secondary depending on the stage of maturation. These granules are not seen in the arrowed cell making immature neutrophil an incorrect choice. Moreover, the chromatin of the arrowed cell is too coarse and cytoplasm too basophilic for a typical immature neutrophil.

4.3% of participants called the arrowed cell a monocyte/macrophage. 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 containing sparse azurophilic granules. The nucleus is round to oval and may show indentation, 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 other blood cells or bacteria, hemosiderin, fungi, and remnants of digested materials as well as cytoplasmic vacuoles post ingestion. One or more round to oval nuclei are present and occasionally prominent nucleoli may be seen. The arrowed cell has more basophilic cytoplasm than seen in a monocyte/macrophage and has much coarser chromatin than a monocyte/macrophage making monocyte/macrophage an in correct choice.

Case Presentation:

This patient is a 42-year-old man admitted through the emergency department because of unusual and bizarre behavior over the past 1½ months. Laboratory data shows: Total nucleated cells = 14 cells/µL (0.014 x 10E3/µL); RBC = 290 cells/µL (0.290 x 10E3/µL); CSF chemistries: glucose = normal; protein = elevated. CBC, urinalysis, and comprehensive chemistry profile were all within normal range. A VDRL test was positive and confirmed by a positive *Treponema pallidum* antibody test.

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

Case Discussion: Neurosyphilis

After reaching a nadir at the turn of the century, syphilis rates in the United States have been increasing since 2000.[1] *Treponema pallidum*, a spirochete bacterium and the causative agent of syphilis, may disseminate to the central nervous system (CNS) within hours to days after inoculation. Neurosyphilis refers to the infection of the CNS in a patient with syphilis and can occur at any stage. Many patients with neurosyphilis are co-infected with HIV.

Meningitis, or inflammation of the meninges, is the most common neurologic presentation of neurosyphilis. However, other presentations are possible and include meningovascular syphilis, general paresis, or tabes dorsalis, which is associated with poor balance and lightning pains in the lower extremities. The vast majority of patients with meningitis present with a combination of two or more conditions: headache, fever, neck stiffness, and/or altered level of consciousness.[2] Given the altered mental status seen in our patient, evaluation for meningitis is prudent.

Sampling of the cerebrospinal fluid (CSF) is crucial in the evaluation of patients with suspected meningitis. CSF should be sent for cell count and differential, cytology, glucose, total protein, and cultures. Additional CSF sample should be collected for other potential studies based on the results of the initial work-up. In our patient, the total nucleated cell count (normal: 0 - 5 cells/µL in adults) and total protein (normal: 15 - 45 mg/dL in adults < 60 years of age) are elevated. The elevated total nucleated cell count and total protein raises the possibility of meningitis.

Plasma cells, as seen in the images, are not normal constitutes of CSF. They may be seen in cases of meningitis caused by Lyme disease, neurosyphilis, tuberculosis, a variety of viruses including herpes, and cysticercosis. They may also be seen in the setting of neurologic disorders such as multiple sclerosis and also in a variety of other disorders such as sarcoidosis. Finally, in rare cases, they can be seen in patients with CNS involvement by plasma cell myeloma. In our patient, the VDRL and *Treponema pallidum* antibody tests were positive, confirming syphilis.

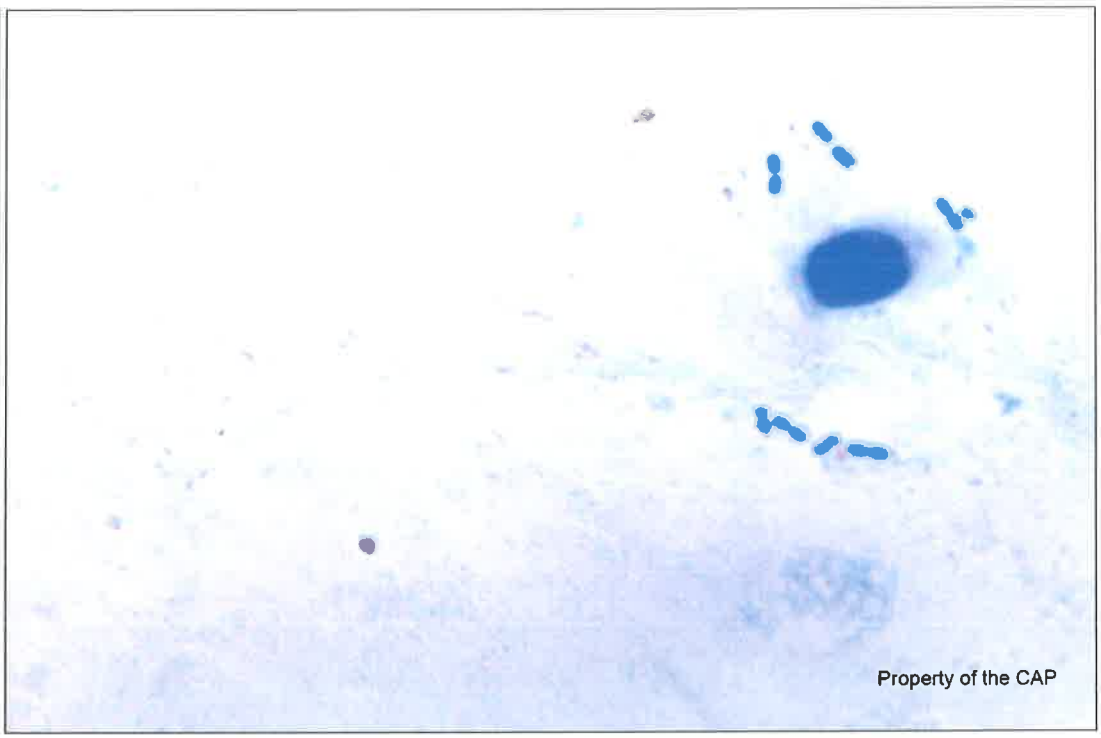
Natasha M. Savage, MD, FCAP
Hematology and Clinical Microscopy Committee

References:

1. Tuddenham S, Ghanem KG. Neurosyphilis: Knowledge Gaps and Controversies. *Sex Transm Dis.* 2018;45(3):147-151.
2. McGill F, Heyderman RS, Panagiotou S, Tunkel AR, Solomon T. Acute bacterial meningitis in adults. *Lancet.* 2016;388(10063):3036-3047.

CMMP – Clinical Microscopy Miscellaneous Photographs

CMMP-22



(NASAL, WRIGHT-GIEMSA) High power magnification

Identification	CMMP Participants No.	%	Performance Evaluation
Eosinophils are absent	2062	99.1	Good

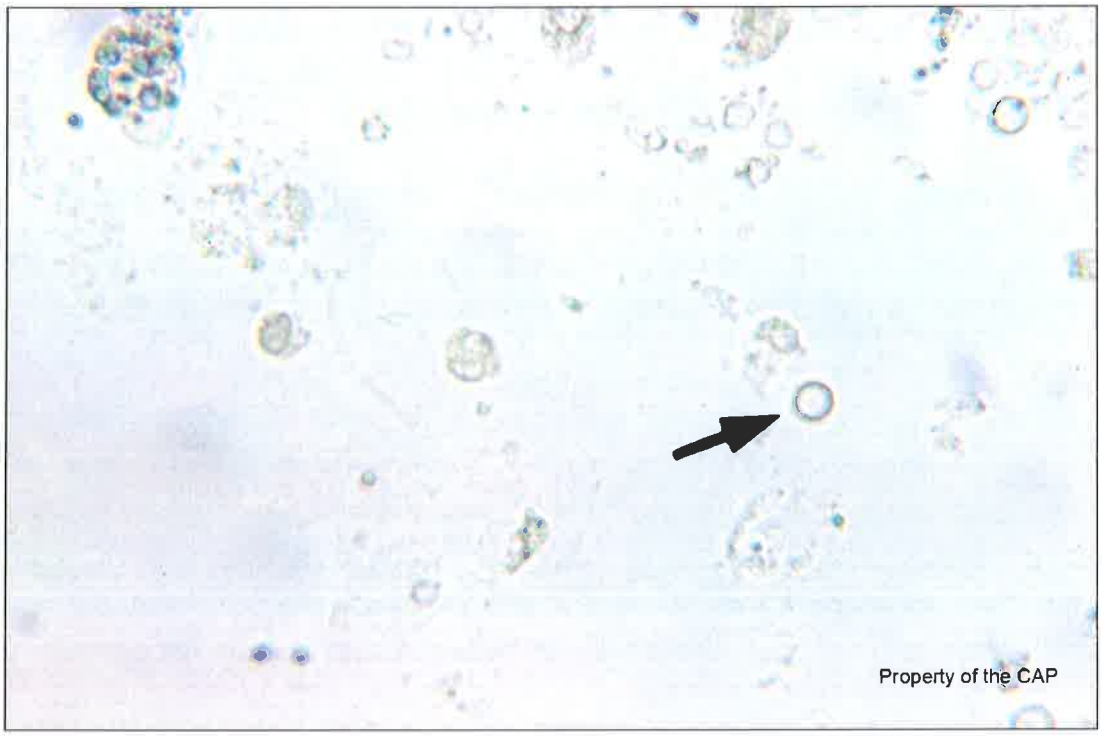
This nasal smear is negative for eosinophils. Nasal smears for eosinophils are prepared by having the patient blow his/her nose in a nonabsorbent material (wax paper, plastic wrap). A thin smear of the mucus is transferred to a glass slide and allowed to air dry. The slide is usually stained using a Wright-Giemsa stain, although some labs may perform the less common Hansel stain. Eosinophils are recognized microscopically by their typically bilobed nuclei and characteristic eosinophilic granules. Nasal eosinophils are seen in patients with clinical allergic rhinitis. In nonallergic causes of nasal discharge, either acellular mucus or neutrophils will be present on the nasal smear.

CMMP – Urine Sediment Color Photographs

Case History USP-01 and USP-03

This urine sample is from a 14-year-old girl who is asymptomatic. Laboratory data include: specific gravity = 1.012; pH = 5.5; ketones, glucose, protein, nitrite, bilirubin, and urobilinogen = negative; blood and leukocyte esterase = positive.

USP-01



(URINE, UNSTAINED, HIGH POWER) High power magnification

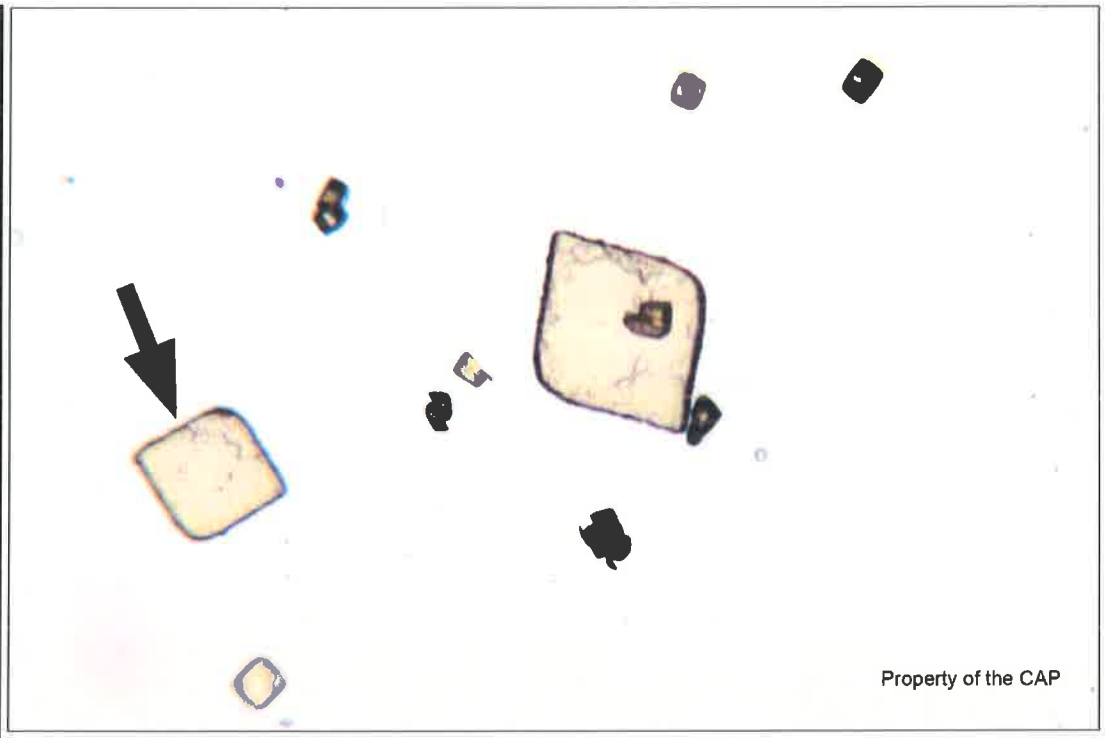
Identification	CMMP Participants No.	%	Performance Evaluation
Erythrocyte	3991	95.9	Good

The arrowed objects are erythrocytes, as correctly identified by 95.9% of participants. Erythrocytes, or red blood cells, are round with no nucleus and 7 to 8 µm in diameter. In unstained specimens they appear as pale yellow-orange discs in, however the cells may be colorless or fainter if the sample is old or hypotonic. In hypertonic urine red blood cells may become crenated.

While small numbers of erythrocytes may be found in the urine sediment of otherwise normal patients, larger numbers are suggestive of disease in the kidney or urinary tract. Hematuria can also be seen in patients who have undergone trauma or have bleeding disorders or iatrogenic anticoagulation. Contamination by menstrual blood frequently causes falsely positive test results.

CMMP – Urine Sediment Color Photographs

USP-02



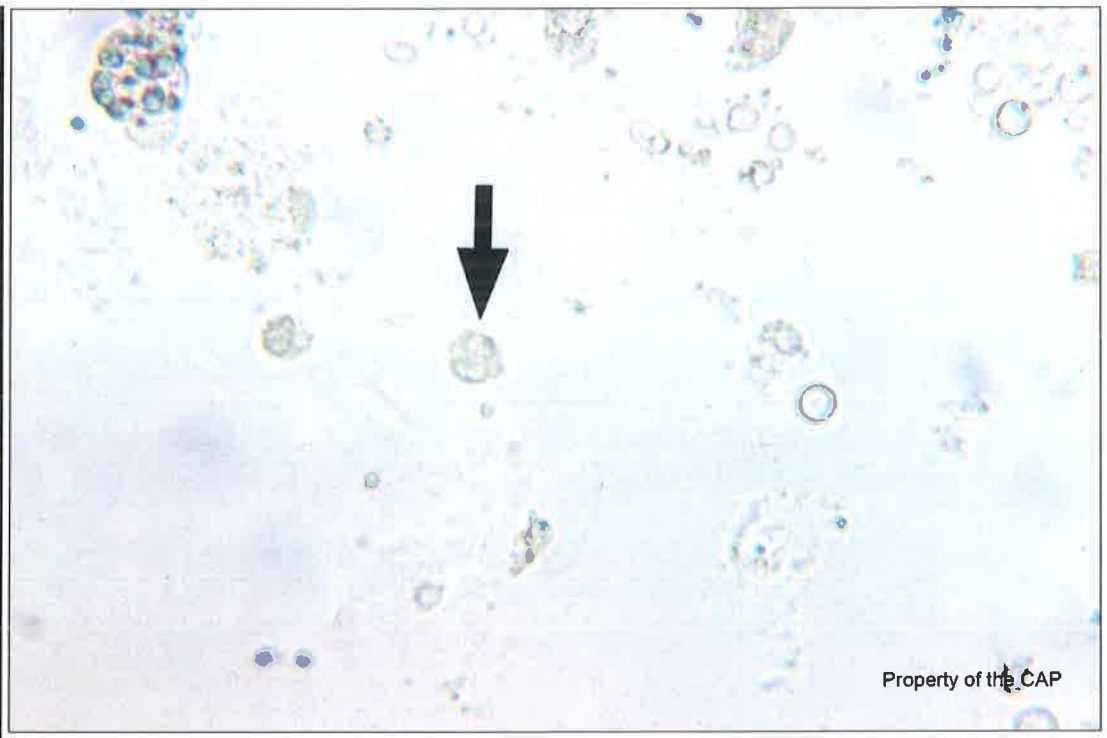
(URINE, UNSTAINED, HIGH POWER)

Identification	CMMP Participants No.	%	Performance Evaluation
Uric acid	4049	97.2	Good

The arrowed object is a uric acid crystal, as correctly identified by 97.2% of participants. Uric acid crystals are found in urine specimens with low pH. The crystals are yellow to brown in color and birefringent. Uric acid crystals can form in a wide variety of sizes and shapes, including needles, rosettes, clubs, barrels, lemons, and occasionally hexagonal plates. The common forms are four-sided and flat, either rhomboids or slightly elongated with round sides and tapered ends described as resembling traditional whetstones. Uric acid crystals are often seen in low numbers in normal urine. However, the presence of a large number in freshly voided urine, or in conjunction with erythrocytes and casts could suggest hyperuricemia (uric acid nephrolithiasis, tumor lysis syndrome) or gouty nephropathy, respectively.

CMMP – Urine Sediment Color Photographs

USP-03



(URINE, UNSTAINED, HIGH POWER)

Identification	CMMP Participants No.	%	Performance Evaluation
Leukocyte	4004	96.2	Good

The arrowed object is a leukocyte, as correctly identified by 96.2% of participants. The most common leukocyte found in urine is the neutrophil; other leukocytes which may be present are eosinophils and lymphocytes. Neutrophils in urine are 10 - 12 µm in diameter, round, oval or amoeboid, with a segmented, lobulated or fused (in degenerated specimens) nucleus. The chromatin is coarsely granular or clumped and the cytoplasm is granular. Small numbers of leukocytes (up to 5) are normal. The presence of larger numbers of neutrophils indicate inflammation, and the presence of many or clumped neutrophils is strongly suggestive of acute infection.

COLLEGE of AMERICAN PATHOLOGISTS

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We the participants below have completed the review of the CAP CM-A 2019 (Product Mailing, Year) Participant Summary/Final Critique report and can self-report the recommended 0.5 (Education Hours) hours towards fulfilling education and certification of maintenance requirements.

Participant	Date	Participant	Date

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

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