Erythrocytes in urine are similar to those seen in other sites. They generally retain their uniform size and biconcave disk shape and usually contain hemoglobin. In older specimens or hypertonic specimens where analysis is delayed, the cells may become crenated and resemble foreign objects such as pollen grains. In hypotonic specimens, hemoglobin pigment is variably lost and cells may be reduced to colorless spherical membranes (“ghost cells”) and resemble fat, oil droplets, or yeast. In situations where identification is ambiguous, use of special imaging techniques such as polarization can be helpful. Nucleated red cells or sickle cells can rarely be found in patients with sickle cell disease. Macrophages containing ingested red cells or hemosiderin may be observed in any patient with chronic hematuria.

SYNONYMS
RBC, red cell

VITAL STATISTICS
size ......................... diameter 7-8 μm
shape ....................... round to slightly oval biconcave disk, crenated in hypertonic specimens with irregular edges and surfaces; spherical “ghost” cells in hypotonic specimens
nuclear shape ............... not applicable
chromatin ................. not applicable
cytoplasm .................. pale yellow-orange, may be colorless; shades of red to purple in stained specimens

KEY DIFFERENTIATING FEATURES
uniform size and general shape
variable amounts of hemoglobin pigment present

POTENTIAL LOOK-ALIKES
yeast cells
pollen grains
starch granule
sperm heads
free fat droplets
air bubbles
small granulocytes (crenated specimens)
calcium oxalate crystals (monohydrate form)

ASSOCIATED DISEASE STATES/CONDITIONS
normal in small numbers (<5 per hpf)
glomerular diseases
trauma
neoplasms
urinary tract calculi
urinary infection
systemic coagulopathies
anitocoagulants, some chemotherapeutic agents, other medications
PNH or other intrinsic red cell disorders
contaminated specimen (vaginal, etc.)
This urine specimen was obtained from a 77-year-old female who was a resident of a long-term care facility, with diagnoses of severe osteoporosis and dementia. She had recently become confused and her urine was cloudy and foul smelling. Urinalysis showed: pH=6.5; specific gravity=1.014; leukocyte esterase, blood, glucose, protein=positive; blood, protein, nitrite, glucose, ketones=negative.

Three red cells are clearly seen in this image and show typical orientations of on edge (clearly demonstrating the biconcave shape), en face, and slightly rotated with an eccentric pale zone. All are uniformly round, contain hemoglobin, and should not be confused with any of the potential look-alikes.

In hypertonic urine, the red cells shrink and wrinkle, becoming crenated.

This urine specimen is from an 80-year-old male complaining of right flank pain. Urinalysis showed: pH=6.5; specific gravity=1.020; protein=2+; blood=2+.

Scattered throughout the field are numerous red cells containing almost no hemoglobin (ghost cells). Others have an irregular shape with a suggestion of spike-like projections and could represent early examples of crenated red cells. The empty cells can be identified as red cells by their uniform size, lack of a thick refractile membrane, and absence of buds. Finally, occasional cells scattered throughout the field exhibit internal cytoplasmic folds or creases that could be confused with starch except for their coloration. If identification of these cells was of particular concern, this could be resolved using special imaging techniques such as polarized light or interference contrast microscopy. Ultimately this patient was found to have a urinary calculus.
This urine sample was obtained from a 34-year-old parturient patient who subsequently delivered a normal male child. Her pregnancy was complicated by hypertension, and she developed renal failure in the immediate postpartum period.

Both arrowed objects are erythrocytes. None have any of the features of casts or crystals and should not be confused with them. All of the red cells in this field contain abundant hemoglobin. Isolated cells near the center and at the bottom of the field are smaller with small spike-like projections consistent with crenated forms. The large object near the center is a neutrophil, identifiable by the folded nucleus and granular cytoplasm.

Unexplained hematuria in the absence of casts or crystals can be seen in patients with urinary tract neoplasms.

This urine was obtained from a 67-year-old male complaining of “smoky” urine and weight loss. Urinalysis showed: pH=5.0; specific gravity=1.012; protein=trace; blood=positive.

The arrowed objects are erythrocytes. None have any of the features of casts or crystals and should not be confused with them. All of the red cells in this field contain abundant hemoglobin. Isolated cells near the center and at the bottom of the field are smaller with small spike-like projections consistent with crenated forms. The large object near the center is a neutrophil, identifiable by the folded nucleus and granular cytoplasm.

Unexplained hematuria in the absence of casts or crystals can be seen in patients with urinary tract neoplasms.
Additional Examples of Red Blood Cells

This field contains a large mass of erythrocytes, as seen in the urinary sediment. Erythrocyte clumps in the urinary sediment can be an artifact of specimen preparation or can represent a blood clot. Individual cells are small and frequently have an orange tint due to the hemoglobin they contain. If trapped WBCs can be identified, the possibility of a blood clot should be considered. It is important to not mistake clumps of red cells for a red cell cast. In this example, there is no evidence of a protein matrix.

This image is a photomicrograph of the urinary sediment using interference contrast microscopy. This technique imparts a three-dimensional appearance to the image and allows visualization of inclusions or other internal structural details. These cells are of uniform size, and the prominent spicules represent infoldings of the membrane due to loss of intracellular water when the cells are present in hypertonic urine. Crenated red cells can be confused with pollen grains or white cells, especially lymphocytes, but the lack of internal structural details establishes the origin in this case.

This interference contrast photomicrograph illustrates several normal red cells. Some cells clearly have a central indentation representing a biconcave disk. Two mucous strands adherent to an unidentified cell can be seen at the bottom of the photomicrograph.
Additional Examples of Red Blood Cells

This is a bright-field image of the urinary sediment from a case of trauma. Several normal erythrocytes are present, easily recognized by their red-orange color and biconcave disk shape. A short red cell cast is present in the center of the image.

This is a bright-field image of the urinary sediment. Numerous normal erythrocytes are present, many appearing as biconcave disks with central pallor. Normal granulocytes with discrete nuclear lobation are present; the one at the lower left edge of the image appears to have an overlying erythrocyte.

This interference contrast photomicrograph illustrates several normal red cells. Some cells clearly have a central indentation representing a biconcave disk. Budding yeast would have a capsule and, often, some internal structure. Fat droplets vary in size and, when viewed with polarized light, would be birefringent with “Maltese cross” formation.

Abnormal red cells could have some similarities. Dysmorphic red cells often form buds and could be similar to the overlapping normal cells seen to the left of center. However, dysmorphic red cells vary in size and, when viewed with ordinary bright-field illumination, would clearly not be normal cells. Another consideration would be the rare instance where red cells containing inclusions (Howell-Jolly bodies, parasites such as malaria or babesia) were present in the urinary sediment. These cells would all demonstrate some internal structure when viewed with interference contrast microscopy and would likely vary in size. Examination of a stained specimen could also resolve the issue if required.
Yeast
Both round and oval forms are found, but these can vary in size and can show “budding.”

Sperm
Heads of spermatozoa may become separated from the tails and mimic budding dysmorphic RBCs. They are generally smaller than RBCs.

Air Bubbles
Bubbles are round, variable in size, and demonstrate dark refractile periphery.

Fat Droplets
Free lipid droplets have a uniform round appearance but vary in size. Variability in size distinguishes fat droplets from RBCs.

Neutrophils
Necrobiotic granulocytes may be small with an irregular surface mimicking crenated RBCs. In concentrated urine, WBCs can also shrink and resemble RBCs; granules and nuclei are usually visible, however.

Starch
Starch granules are small, slightly larger than a RBC, and often have a central indented or slit-like area.

Pollen
Grains of pollen can be round or oval but are much larger than RBCs, typically 20 µm or more in diameter.

Calcium Oxalate
Monohydrate form may contain oval and round refractile elements. Finding dihydrate forms in adjacent fields will help to distinguish the crystals from RBCs.