**EDUCATIONAL COMMENTARY – BLOOD CELL IDENTIFICATION**

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**Learning Outcomes**

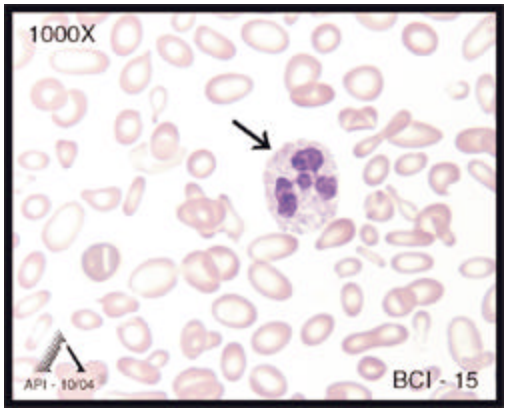
Upon completion of this exercise, the participant will be able to:

- Discuss morphologic characteristics of normal peripheral blood leukocytes.
- Identify morphologic abnormalities in erythrocytes associated with hereditary elliptocytosis.
- Discuss the pathophysiology of hereditary elliptocytosis.

The patient presented in the case study for this testing event has been diagnosed with hereditary elliptocytosis. The photographs show both normal leukocytes and abnormal shape changes in erythrocytes that may be seen in the peripheral blood of patients with this condition.

This 48 year old African-American patient has had a second kidney transplant. The CBC data was as follows: WBC=7.3 x $10^9$/L, RBC=6.30 x $10^{12}$/L, Hgb=9.1 g/dL, Hct=31%, MCV=48.6 fL, MCH=14.5 pg, MCHC=29.9 g/dL, RDW=25.1%, Platelets=832 x $10^9$/L. There was an instrument flag for "RBC morphology" and the histogram for the platelet count indicates it may be falsely elevated. WBC Differential: Neutrophils=71%, Lymphocytes=20%, Monocytes=6%, Eosinophils=1%, Basophils=2%.

**BCI-15** illustrates a normal segmented neutrophil. Neutrophils characteristically have a nucleus with 2-5 lobes connected by threads of chromatin. The chromatin is dense and coarsely clumped. In addition, segmented neutrophils have numerous, small cytoplasmic granules that stain violet, pink, or tan.



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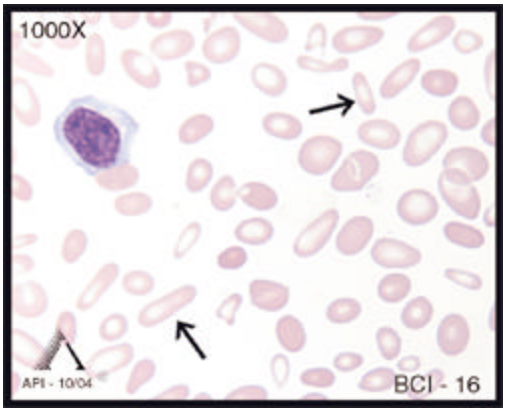
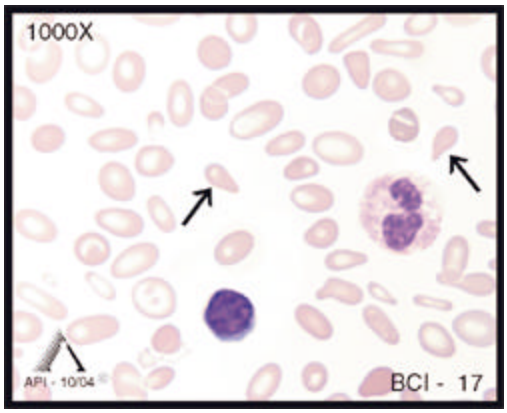



Photograph **BCI-16** shows 2 elliptocytes, but note that there are several more similar cells in the picture. These cells are also called ovalocytes. These elongated cells vary in morphology from ovals to cigar, rodlike structures. Classic elliptocytes have sides that are almost parallel, hemoglobin that is concentrated at both ends, ends that are blunt, and a prominent area of central pallor.

Hereditary elliptocytosis is a subtype of a heterogeneous group of RBC disorders associated with intrinsic defects in membrane proteins. The major defects affect skeletal proteins in the RBC and their ability to interact with each other in supporting the membrane. The defects may actually be deficiencies of certain proteins or molecular abnormalities that affect association or binding mechanisms. These conditions variously result in different degrees of hemolytic anemia. Immature, nucleated erythrocytes as well as reticulocytes are known to be round in shape. Therefore, the ovalocytic form of these cells is acquired as they circulate. Elliptocytes may also be seen in other disorders and are rarely seen (<1%) in normal individuals. In other disease conditions, the ovalocytes represent <25% of the RBCs. In general, 10% ovalocytes present on a blood smear suggests hereditary elliptocytosis, while >25% may be considered diagnostic of hereditary elliptocytosis.




The cells identified in **BCI-17** are called dacryocytes, or teardrop cells. Teardrops classically are elongated at one end and may or may not retain an area of central pallor. The elongated end may be long and tapered, short and blunt, or barely visible. It is not surprising to see dacryocytes in this patient; different hemolytic subtypes of hereditary elliptocytosis may be associated with the presence of dacryocytes. In anemias in which inclusions form, these pear-shaped cells appear when splenic macrophages retard the passage of the cell causing the cell to stretch into an abnormal shape. The teardrop cell cannot return to a normal biconcave shape either because it was deformed beyond the limits of the membrane or because it has been a dacryocyte for too long. However, the mechanism resulting in teardrop erythrocytes in hereditary elliptocytosis and certain other conditions has not been defined.

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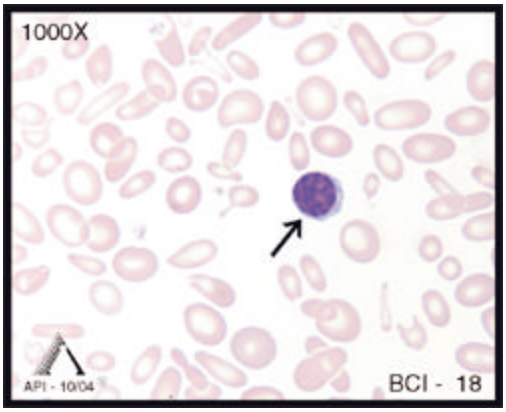
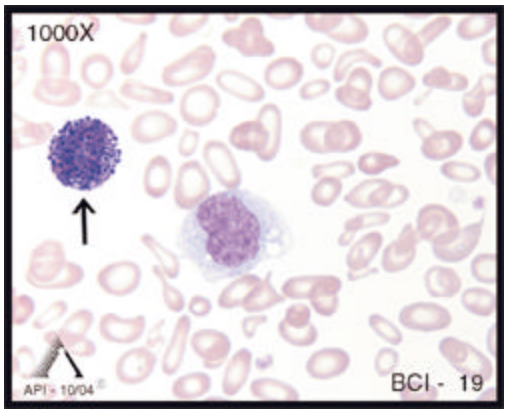
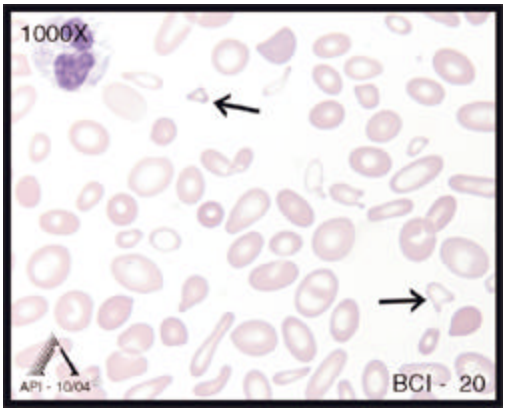



A normal lymphocyte is depicted in **BCI-18**. Lymphocytes are variable in size, but the one shown here is a nice example of a small lymphocyte. In small lymphocytes the cytoplasm is blue and often scanty. The nuclei are round, oval, or may be slightly indented. The chromatin is clumped, condensed, and stains a dark purple. Nucleoli are sometimes present but often are not visible. The pink areas seen in this nucleus demonstrate lighter-staining areas of chromatin and are not nucleoli.




The cell shown in **BCI-19** is a normal basophil. Basophils are characterized by numerous blue-black or deep purple cytoplasmic granules. Note how the granules obscure the nucleus.




The arrows in photograph **BCI-20** point to schistocytes or fragmented RBCs. These cells are usually caused by some type of mechanical damage. However, hereditary elliptocytosis is classified into 3 broad groups based on clinical severity and RBC morphology. These groups are common hereditary elliptocytosis, spherocytic hereditary elliptocytosis, and stomatocytic hereditary elliptocytosis. Common hereditary elliptocytosis further includes several subtypes. Some of these subgroups are associated with varying degrees of erythrocyte fragmentation.

The helmet cell or keratocyte is a specific type of schistocyte. Helmet cells have 2 projections on either end that are tapered and hornlike. The cell on the right in this photograph represents a keratocyte. Sometimes the protrusions are longer than in the cell shown here. This cell also has an area of central pallor, but some helmet cells will lack such pallor. The cell identified in the upper left field is more of a

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nonspecific fragmented cell. Fragmented cells may appear in a variety of shapes. Schistocytes are often microcytic because they are fragments of cells. In fact, the increase in this patient's platelet count is most likely a result of the increased number of peripheral blood microcytes.

Stomatocytes are shown in **BCI-21**. In contrast to normal biconcave-shaped erythrocytes, these cells are uniconcave. Therefore, when the cells are flattened on a glass slide during smear preparation, the area of central pallor appears as a slit, or "mouth" ("stoma" is Greek for mouth). It is not clear whether the presence of these cells in this patient might represent a subgroup of hereditary elliptocytosis.