EDUCATIONAL COMMENTARY – BLOOD CELL ID: NORMAL PERIPHERAL BLOOD LEUKOCYTES AND MORPHOLOGIC VARIATIONS IN ERYTHROCYTES

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To view the blood cell images in more detail, click on the sample identification numbers underlined in the paragraphs below. This will open a new browser tab or window containing a virtual image of the selected cell and the surrounding fields. You will need Adobe Flash or the Microsoft Edge browser (included with Windows 10) to use this feature. Click on this link for the API ImageViewer™ Instructions.

Learning Outcomes
On completion of this activity, the participant should be able to:

- identify morphologic characteristics of normal peripheral blood leukocytes;
- describe morphologic features and the etiology of Howell-Jolly bodies; and
- discuss distinguishing morphologic characteristics of echinocytes and schistocytes.

Case Study
A CBC with differential was ordered for a 62 year old female who recently underwent a splenectomy. Her CBC results are as follows: WBC=6.5 x 10⁹/L, RBC=2.67 x 10¹²/L, Hgb=9.7 g/dL, Hct=29.6%, MCV=110.9 fL, MCH=36.5, MCHC=32.9 g/dL, RDW =18.0%, Platelet=220 x 10⁹/L.

Educational Commentary
The images presented in this exercise represent both normal leukocytes and abnormalities in erythrocytes that may be seen in the peripheral blood.

**Image BCI-08** shows an eosinophil. Eosinophils are medium-sized cells with characteristic bright, red-orange cytoplasmic granules. These granules are typically numerous, large, and uniform in shape. Nuclei in eosinophils are often bilobed. The chromatin is dense and clumped.
Monocytes are the largest cells that can normally be seen in the peripheral blood. The cytoplasm may be abundant and frequently has vacuoles. Faint lilac or purple granules may be present. The cytoplasm often appears bumpy, uneven, rough, or “sandy.” Nuclear shape is variable in monocytes. Nuclei may be indented and lobed, as in this example, or kidney-shaped, oval, or round. The chromatin is not as clumped as may be seen in other normal peripheral blood leukocytes, and stains lighter colors of purple.

Lymphocytes vary in size. Small lymphocytes, such as this cell, do not have much cytoplasm, and the cytoplasm is generally blue. The nucleus occupies almost the entire cell. Nuclei in small lymphocytes are typically round, oval, or only slightly indented. The chromatin is dense and clumped.

The arrow in Image BCI-11 identifies a Howell-Jolly body. Red blood cells (RBCs) are evaluated on a stained peripheral blood smear to assess size, shape, area of chromaticity or central pallor, distribution (dispersed, clumped, or with rouleaux formation), and whether or not inclusions are present. Normal erythrocytes have no inclusions. The appearance of Howell-Jolly bodies indicates the patient has some type of anemia or has had a splenectomy. The laboratory results provided for this testing event show decreased values for both hemoglobin and hematocrit.

Howell-Jolly bodies are typically small inclusions, although they may vary in size. They are usually round and stain purple or purple-blue. Howell-Jolly bodies are most often present as single inclusions near the periphery of the cell, but are sometimes found as two or more inclusions, especially when the anemia is severe. They represent nuclear remnants and form by one of two possible mechanisms. In one
mechanism, a chromosome becomes separated from the mitotic spindle during cell division and is retained in the cell after the nucleus is expelled. In the other process, abnormal fragmentation of the nucleus causes small amounts of DNA to remain in the cell. Again, as the larger nuclear mass is extruded, separated fragments are retained. Usually the spleen pits Howell-Jolly bodies from red blood cells. However, if the anemia is severe the spleen may not be able to remove all inclusions. Likewise, if the spleen is dysfunctional or, as in the patient in this exercise, removed completely, Howell-Jolly bodies will be readily apparent. Numerous conditions are associated with the formation of Howell-Jolly bodies including severe hemolytic anemias, megaloblastic anemias, some cases of leukemia, congenital dyserythropoietic anemia, myelodysplastic syndromes, and hemoglobinopathies.

Image BCI-12 shows a band neutrophil. Bands are medium-sized cells. Their cytoplasm contains numerous small, specific granules that appear tan, pink, or violet. Note the overall pinkish color of the cytoplasm in this band versus the bright orange cytoplasm of the eosinophil in Image BCI-08. Bands are characterized by their nucleus, which is shaped like the letter C or U. The chromatin is dense and clumped.

Image BCI-13 identifies an echinocyte. Echinocytes are red blood cells with short blunt or slightly pointed projections evenly spaced around the cell surface. For this reason, echinocytes are sometimes called “burr” or “crenated” cells. Echinocytes generally have 10-30 spicules as well as an area of central pallor. These cells are usually the same size as normal erythrocytes, but may also be microcytic, as in this example. Echinocytes are most commonly seen on a peripheral blood slide as an artifact of smear preparation or sample condition. If the blood smear dries too slowly, if the slide is prepared with too much blood and is spread too thickly, or if the blood specimen is too old, echinocyte formation may occur. Variations in pH can also cause echinocytes. If basic substances on the glass slide diffuse into the medium surrounding the red blood cells, the pH increases and may result in the formation of echinocytes. Although not often seen, clinical conditions, including severe renal disease and burns, have also been associated with the presence of echinocytes. The mechanisms of shape change in these situations are not completely
understood, but may be a result of accumulation of lipids on the RBC surface or loss of intracellular adenosine triphosphate (ATP) such that the cell can no longer be maintained as a discocyte.

**Editor’s notes:** Some participants incorrectly classified this cell as an acanthocyte. Acanthocytes, in contrast to echinocytes, have no area of central pallor. Likewise, acanthocytes have fewer irregularly spaced surface projections than the number seen in echinocytes. Spicules in acanthocytes also vary in length and may be pointed or rounded at the ends. Echinocyte projections sometimes are sharp and pointed, but often are more blunt.

The final image in this testing event, Image BCI-14, shows a schistocyte. Schistocytes are fragmented red blood cells of various sizes and shapes, although most are small. They generally are irregularly shaped cells and have no area of central pallor. Physiologic changes associated with many disease states and clinical conditions can cause the formation of schistocytes. Most notable are the microangiopathic hemolytic anemias, which result in the deposition of fibrin within the lumen of small blood vessels. The obstructed vessels impair the usual flow of RBCs, which then shear on the fibrin strands. The cells may re-seal their membranes, but are nevertheless fragmented. Other situations such as heat and malignant high blood pressure can also damage erythrocytes and result in schistocytes. Regardless of the cause, the presence of schistocytes on a peripheral blood smear is a significant and reportable finding.

**Editor’s notes:** Image BCI-14 could be classified as an acanthocyte and many participants did make this result choice. The morphologic distinction between schistocytes and acanthocytes is not always clearly recognizable. Both cells generally have no area of central pallor. While schistocytes are fragmented erythrocytes and tend to be triangular, their shape is variable. Schistocytes are also usually defined by having two or more points or projections. Acanthocytes often have more numerous, needle-like or rounded projections spaced irregularly around the cell’s surface. The cell in this image has some features suggestive of an acanthocyte.

**Summary**

A careful review of a peripheral blood smear is important in the evaluation of any patient with anemia. The patient presented in this testing event had recently undergone a splenectomy. Therefore, the
appearance of RBC inclusions and abnormal erythrocyte shape changes is not unexpected. These peripheral blood findings can provide several clues to the possible cause of the anemia.

References


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