EDUCATIONAL COMMENTARY – MORPHOLOGIC CHANGES IN PERIPHERAL BLOOD CELLS

Educational commentary is provided through our affiliation with the American Society for Clinical Pathology (ASCP). To obtain FREE CME/CMLE credits click on Earn CE Credits under Continuing Education on the left side of the screen.

Learning Outcomes
After completion of this testing event, participants will be able to

- describe the morphologic characteristics of normal peripheral blood cells.
- identify abnormalities in erythrocyte morphology associated with some types of thalassemias and hemoglobinopathies.
- compare the morphologic features of a segmented neutrophil with those of a hypersegmented neutrophil.

Case History
A 16 year old female was seen by her physician as a follow up to treatment for pneumonia. Laboratory findings included: WBC= 17.4 x 10^9/L, RBC= 6.11 x 10^{12}/L, Hgb= 10.6 g/dL, Hct= 35%, MCV= 57.0 fl, MCH= 17.3 pg, MCHC= 30.3 g/dL, RDW= 19.8%, Platelets= 902 x 10^9/L, and NRBCs= 11. The patient has a diagnosed abnormality in the production of hemoglobin. The images for review represent normal leukocytes, but several abnormalities in erythrocytes are also seen in the peripheral blood in this condition.

The cell shown in Image BCI-15 is a normal basophil. Basophils feature deep or blue-black cytoplasmic granules. As in this example, the granules are often large, round, numerous, and obscure the nucleus. Basophilic granules are also water soluble and may be washed away during the staining process. In such cases, clear or light areas will be seen in the cytoplasm.
EDUCATIONAL COMMENTARY – MORPHOLOGIC CHANGES IN PERIPHERAL BLOOD CELLS (cont.)

Image BCI-16 is an eosinophil. Just as basophils are readily distinguished by the very dark specific granules, eosinophils feature red-orange granules that fill the cytoplasm. Eosinophilic granules are frequently large, uniform in size, and numerous. The nucleus in this image appears to be bilobed. This is a common characteristic of eosinophils.

The cells identified in Image BCI-17 are codocytes, or target cells. Note the central, dense area of hemoglobin surrounded by a white rim and then a final area of more hemoglobin. The actual circulating shape of the codocyte is that of a bell or a Mexican hat. The cell assumes the target appearance when flattened and dried on a glass slide. Target cells form when the erythrocyte membrane surface is increased relative to the hemoglobin content. Disorders such as liver disease can cause excess cholesterol and phospholipid to accumulate on the red blood cell membrane. Conditions such as iron deficiency anemia, thalassemias, and hemoglobinopathies that are associated with decreased hemoglobin content may also result in target cell formation. Finally, codocytes can be seen artifically on stained peripheral blood smears. If a wet slide is blown dry rather than air dried during the process of smear preparation, codocytes may form.
EDUCATIONAL COMMENTARY – MORPHOLOGIC CHANGES IN PERIPHERAL BLOOD CELLS (cont.)

Image BCI-18 is a nice example of a small, normal lymphocyte. Lymphocytes vary in size. The nuclear chromatin in smaller lymphocytes is dense and clumped, with a nuclear shape that is usually slightly indented, round, or oval. Nucleoli are generally not visible. The cytoplasm is typically scanty and blue. An additional interesting observation can be made with this image. The nuclei of small lymphocytes should be about the same size as erythrocytes. Note that the majority of the red blood cells are smaller than the nucleus of this lymphocyte. This comparison is a useful guide in determining the size of erythrocytes and in this case indicates microcytosis.

Image BCI-19 shows a normal segmented neutrophil. Neutrophils are easily identified by several morphologic features. They typically have 2 to 5 nuclear lobes connected by thin threads of chromatin. The chromatin is dense and clumped. The cytoplasm in neutrophils is filled with small granules that generally appear pink, tan, or violet.

Image BCI-20 illustrates a red blood cell with a specific inclusion called a hemoglobin C crystal. These crystals stain very densely and are variable in shape, although the rod or rhomboid configuration shown is typical. A clear or colorless area often surrounds the crystal. Sometimes a faint outline of the remaining erythrocyte membrane can be seen. Note that hemoglobin C crystals are also present in Images BCI-16, BCI-18, and BCI-19.
Although the diagnosis for this patient is thalassemia trait (or beta thalassemia minor), it is likely the patient also has another abnormal hemoglobin disorder called hemoglobin C disease. The appearance of hemoglobin C crystals is a characteristic morphologic finding in this disorder. The abnormal hemoglobin C crystallizes when dehydrated and precipitates within the cell. These crystals are more often seen in patients who have been splenectomized because the red blood cells with hemoglobin C crystals are less deformable and become trapped and destroyed in the spleen.

Some participants reported “bacteria, extracellular” for Sample BCI-20. An important distinction between bacteria and this Hemoglobin C crystal is that bacteria stain pale blue or purplish black with Wright stain and not red or pink. Only a Gram stain will give classic gram positive (purple) or gram negative (red or pink) reactions. Bacteria will also be smaller than this crystal, usually the size of platelets or smaller.

Another response was “ovalocyte (elliptocyte)” or “pencil cell.” Elliptocytes have an area of central pallor and the inclusion shown has none. A pencil cell is a descriptive term to refer to an ovalocyte or elliptocyte that is characteristically associated with iron deficiency anemia. This inclusion is not only much smaller, but again it lacks the characteristic central pallor.

Image BCI-21 is a hypersegmented neutrophil. These cells have increased segmentations in the nucleus. True hypersegmented neutrophils have at least 6 or more distinct lobes. However, if more than 10% of the neutrophils have 5 nuclear lobes, hypersegmentation may be considered. The cell in this image appears to have at least 6 lobes. The overall cell size and shape resembles normal segmented neutrophils, though sometimes hypersegmented neutrophils are slightly larger. The nuclear chromatin is also usually clumped, but it may appear less dense than that of a normal neutrophil.

Cytoplasmic features parallel normal cells as well, the cytoplasm in both types of cells contains numerous light pink or lilac granules.
Characteristics of normal segmented neutrophils and hypersegmented cells are compared in the Table.

### Table: Comparison of Segmented and Hypersegmented Neutrophils

<table>
<thead>
<tr>
<th>Type</th>
<th>Size</th>
<th>Nucleus</th>
<th>Cytoplasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Segmented neutrophil</td>
<td>Medium</td>
<td>2-5 lobes; clumped chromatin</td>
<td>Pink, tan, or violet granules</td>
</tr>
<tr>
<td>Hypersegmented neutrophil</td>
<td>Large</td>
<td>&gt;6 lobes; chromatin less clumped</td>
<td>Pink, tan, or violet granules</td>
</tr>
</tbody>
</table>

Hypersegmented neutrophils are most often associated with megaloblastic anemias like vitamin B₁₂ and folic acid deficiencies. These cells are rarely seen in the peripheral blood of a patient with a hemoglobin disorder. However, in this particular patient who probably has a mixed hemoglobinopathy, a secondary folic acid deficiency may develop over time as a result of the hemolytic process associated with hemoglobin disorders. If folic acid is depleted, hypersegmentation of neutrophils may be seen in the peripheral blood.

### Summary

This patient has an inherited condition that affects the production of hemoglobin (hemoglobinopathy). Such disorders can impair the structure or quantity of hemoglobin and, in some cases, both types of abnormalities can be seen in the same person. Several morphologic changes may be visible in the peripheral blood when patients have defects related to hemoglobin synthesis. Target cells are a common finding in these conditions. Microcytosis is also evident in the images presented for review and is an important finding in many hemoglobin abnormalities. The low mean corpuscular volume reaffirms the microcytosis. Other morphologic changes evident in this patient are not characteristic for the diagnosis, but underscore the significance of a careful and systematic review of the peripheral blood smear.

### Reference


© ASCP 2010