EDUCATIONAL COMMENTARY – BLOOD CELL ID: MORPHOLOGIC FEATURES THAT AID IN DISTINGUISHING COMMON PERIPHERAL BLOOD LEUKOCYTES

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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 virtual image of the selected cell and the surrounding fields. If the image opens in the same window as the commentary, saving the commentary PDF and opening it outside your browser will allow you to switch between the commentary and the images more easily. You will need Adobe Flash to use this feature. Click on this link for the API ImageViewer™ Instructions.

LEARNING OUTCOMES

On completion of this exercise, the participant should be able to:

- identify characteristic morphologic findings in segmented neutrophils and neutrophilic band cells.
- describe morphologic hallmarks associated with reactive lymphocytes.
- compare and contrast morphologic features seen in normal lymphocytes, reactive lymphocytes, and monocytes.

Case Study

A 13 year old male was seen by his physician for a fever and sore throat. The CBC results are as follows: WBC=8.9 x 10^9/L, RBC=4.13 x 10^12/L, Hgb=13.4 g/dL, Hct=37.2%, MCV=90.1 fL, MCH=32.4 pg, MCHC=36.0 g/dL, RDW=13.7 %, Platelet=208 x 10^9/L.

Educational Commentary

The patient presented in the case study for this testing event has infectious mononucleosis. The images for review represent several types of cells that may be seen in the peripheral blood in this condition.

Image **BCI-08** shows a normal segmented neutrophil. The nuclear lobes, connected only by thin threads of chromatin, are a classic feature of these cells. Usually these cells have from two to five lobes. Also, the nuclear chromatin is dense and clumped. Numerous light pink granules fill the cytoplasm.
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Image **BCI-09** is a normal lymphocyte. These cells are variable in size and often have a scanty rim of blue cytoplasm. The nuclei are relatively large in contrast to the cytoplasm and are generally oval, round, or slightly indented. The dark purple chromatin is dense and clumped.

In contrast, the cell depicted in **Image BCI-10** is a reactive (also called *atypical* or *variant*) lymphocyte. Although there are no "typical" atypical lymphocytes, certain morphologic features are often associated with these cells. The overall cell size is large when compared with normal lymphocytes. The nuclear shape may be round, oval, indented, or folded. The nuclear chromatin is purple, frequently open and fine, with more distinct parachromatin than that seen in a normal lymphocyte. Sometimes, as in this example, the cell may show lighter staining areas of the nucleus that resemble nucleoli. The presence of nucleoli does not indicate the cell is immature as occurs in a pathologic condition, but that the cell has been stimulated by an antigen and is reacting appropriately.

The cytoplasm in reactive lymphocytes is generally abundant and may be gray, pale blue, or an intense deep blue; areas of clearing may also be seen. It is not unusual to see the cytoplasmic margins sprawl and form contours around adjacent red blood cells. Sometimes this interface with red blood cells is a darker blue than the remainder of the cytoplasm. Occasionally, vacuoles and azurophilic granules are present in the cytoplasm.

A small percent of reactive lymphocytes may be seen in the peripheral blood of healthy persons. However, increased numbers of these cells are associated with many clinical conditions, including viral illnesses such as infectious mononucleosis.

**Editor’s note:** Additional examples of reactive lymphocytes can be seen by scanning the virtual image using the ImageViewer™. To see one of these examples, click “Additional reactive lymph 1” or “Additional reactive lymph 2”.

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Image **BCI-11** shows a monocyte. Monocytes are the largest cells that can normally be seen in the peripheral blood. Nuclei in these cells may be round, oval, indented, or lobulated. The chromatin stains a slightly lighter shade of purple when compared with normal lymphocytes or segmented neutrophils and is generally more open, with less clumping. At times, the nucleus may have numerous folds or convolutions, but that is not apparent in this example. The cytoplasm of monocytes is abundant, blue-gray, and may appear unevenly stained. There are often vacuoles and sometimes a dusting of purple-red azurophilic granules. Sometimes cytoplasmic projections may be seen. Using the API ImageViewer™, it is possible to see many other examples of monocytes.

Monocytes should not be confused with reactive lymphocytes. Although both cells may be large with abundant cytoplasm, nuclear and cytoplasmic differences can help distinguish these two cells. The nuclei in lymphocytes vary in shape and are often more irregular than those seen in monocytes. However, monocyte nuclei may show variations in shape as well. Parachromatin in lymphocytes tends to be fine, evident, and white, whereas it is lacy and more “brainlike” in monocytes. Nucleoli may be prominent in reactive lymphocytes but not visible in monocytes. The cytoplasm in reactive lymphocytes is often a deep blue, with darker edges at the contact point with other cells. In contrast, the cytoplasm in monocytes is a light bluish gray and stains unevenly. The following table summarizes the characteristics of small lymphocytes, reactive lymphocytes, and monocytes.

**Table. Characteristics of Lymphocytes and Monocytes**

<table>
<thead>
<tr>
<th></th>
<th>Small Lymphocyte</th>
<th>Reactive Lymphocyte</th>
<th>Monocyte</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Size</strong></td>
<td>8-12 µm</td>
<td>9-30 µm</td>
<td>15-18 µm</td>
</tr>
<tr>
<td><strong>Nucleus</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shape</td>
<td>Round</td>
<td>Irregular, lobulated, oval, notched</td>
<td>Horseshoe, round, folded</td>
</tr>
<tr>
<td>Chromatin</td>
<td>Clumped; parachromatin not evident; lavender</td>
<td>Fine (but not like a blast); parachromatin evident and white</td>
<td>Lacy, loose strands; “brainlike”</td>
</tr>
<tr>
<td>Nucleoli</td>
<td>Usually absent</td>
<td>May be prominent</td>
<td>Absent</td>
</tr>
<tr>
<td><strong>Cytoplasm</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amount</td>
<td>Scant</td>
<td>Abundant</td>
<td>Abundant</td>
</tr>
<tr>
<td>Color</td>
<td>Blue</td>
<td>Often deep, intense blue, with darker edges at contact points with other cells</td>
<td>Light bluish gray</td>
</tr>
</tbody>
</table>
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**Image BCI-12** is a band neutrophil. This cell is similar in size to the segmented neutrophil illustrated in image BCI-08. Band neutrophils feature a nucleus shaped like a band, the letters C or U, or a sausage, and the nuclear lobes are not separated by filaments. The chromatin is generally condensed and clumped. As with the segmented neutrophil, the band’s successor in maturation, the cytoplasm of the band is filled with pink, tan, or violet granules.

**Image BCI-13** is a smudge or basket cell. These cellular remnants represent a white cell that has been damaged during smear preparation. This process often occurs with cells that are fragile, typically lymphocytes. It is not uncommon to see these fragments in chronic lymphocytic leukemia or in infectious mononucleosis, as in this case study. The distorted cell appears either as a smear of chromatin (smudge) or with chromatin strands that spread out from a nuclear mass, such as a basket. The cytoplasm has been stripped away. Therefore, it is not possible to specifically identify the cell. Significant smudging should be reported, but it can be prevented by adding bovine serum albumin, 22%, to a few drops of blood before making the smear.

**Image BCI-14** shows another normal monocyte. There are similarities to the cell in image BCI-11. This monocyte has fewer vacuoles and is more uniform in shape, but the nuclear shape, chromatin pattern, and cytoplasmic staining characteristics are nearly identical in both cells. It is helpful to contrast this monocyte with the reactive lymphocyte in image BCI-10 as well as with other reactive lymphocytes and monocytes that can be observed by scanning with the ImageViewer™.
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Summary

The patient in the case study for this testing event was diagnosed as having infectious mononucleosis. It is not surprising to see reactive lymphocytes in the peripheral blood of this adolescent: an increase in reactive lymphocytes is characteristic of this viral illness. Although this condition is benign, complications can arise. Laboratory professionals play an important role in identifying this infection and ensuring appropriate treatment is initiated.

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