EDUCATIONAL COMMENTARY – BLOOD CELL IDENTIFICATION

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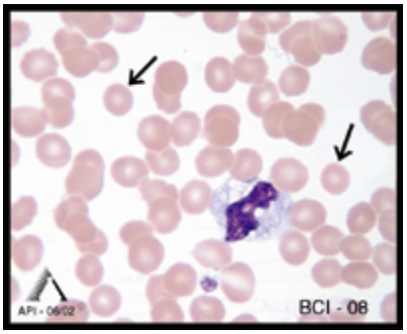
Learning Outcomes

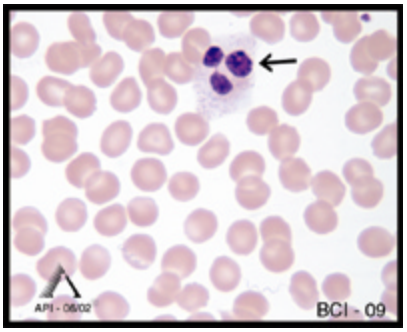
Upon completion of this exercise, the participant will be able to:

- Describe morphologic features of normal peripheral blood erythrocytes and leukocytes.
- Identify characteristic morphologic findings of giant platelets and reactive lymphocytes.
- Distinguish pathogenic spirochetes from contaminants on a Wright's-stained peripheral blood smear.

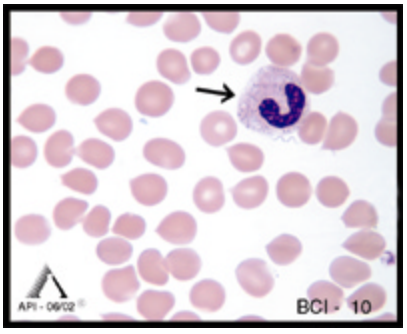
The patient presented in the case study for this testing event has relapsing fever caused by an infection of the bacterium *Borrelia hermsii*. The photographs for review represent both normal and abnormal blood cells and organisms that may be seen in the peripheral blood in this condition.



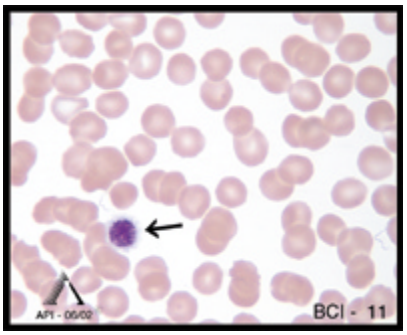
Photograph **BCI-08** shows normal red blood cells or erythrocytes. Mature erythrocytes such as these are classified as cells even though they have no nuclei. They are the most numerous cells in the peripheral blood and are distinctive with their red color, round shape, and area of central pallor. In normal red blood cells, the central pallor approximates 1/3 of the diameter of the cell. Erythrocytes actually circulate as biconcave disks. The thinnest part of the disk corresponds to the area of central pallor when the cell is flattened on a glass slide during smear preparation. Red blood cells contain hemoglobin, which is the oxygen-transporting constituent in erythrocytes and also gives the cells their characteristic red color. Red blood cells are evaluated for size, shape, size of the area of central pallor, distribution on the smear, and the presence or absence of inclusions. The erythrocytes in this photograph are evenly shaped, uniform in size, have an appropriate area of central pallor, are evenly distributed, and contain no inclusions.



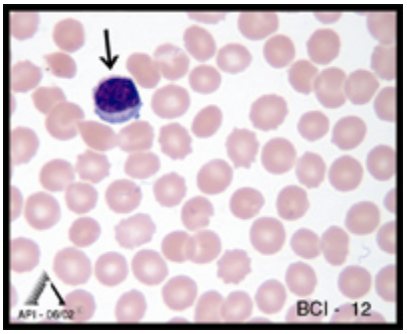
Photograph **BCI-09** shows a normal segmented neutrophil. Note the characteristic nuclear lobes connected only by thin threads of chromatin. Neutrophils usually have 2 to 5 lobes. Also notice the coarsely clumped, dense nuclear chromatin and the absence of any nucleolus. One nuclear lobe has a lighter staining area that should not be confused with an unstained area that represents a true nucleolus. Numerous pink and violet granules are apparent in the cytoplasm.



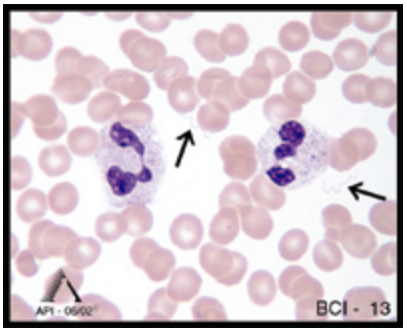
Band neutrophils, as pictured in **BCI-10**, are comparable in size to segmented neutrophils. These cells are the earliest precursors of neutrophil maturation that can normally be seen in the peripheral blood. Bands characteristically have a nucleus that is shaped like a band, a sausage, or the letters "C" or "U". The chromatin, however, is fairly clumped and condensed --indicative of a maturing cell. The cytoplasm contains specific granules and is similar to that seen in segmented neutrophils. Sometimes it can be difficult to distinguish bands from segmented neutrophils, although the band in this picture is a classic example. It can be challenging to classify a cell when the nucleus is twisted or folded. Segmented neutrophils characteristically have at least two of the nuclear lobes separated by a thin filament. The lobes in a band are generally connected by a "bridge" with clear areas of chromatin and parachromatin visible. In cases where the classification of a cell is in doubt, the cell should be identified as the most mature stage.



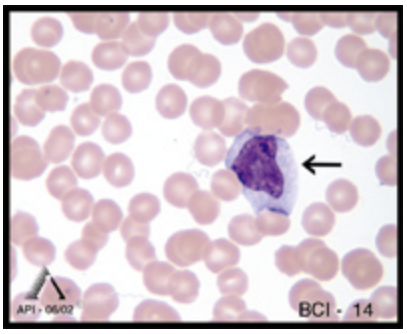
The platelet in photograph **BCI-11** can be described as giant. The term "giant" is used to refer to a platelet that is larger than a normal red blood cell. It is important not to confuse this giant platelet with a nucleated red blood cell or small lymphocyte. Giant platelets may have variable cytoplasmic color, granules, and areas of cytoplasmic zoning. The cell shape in platelets may be irregular with frayed margins or may be smooth and round. Nucleated red blood cells that are similar in size to this platelet will have a cytoplasm that is more pink in color and will be agranular. Small lymphocytes have a nucleus that is about the same size as a normal red blood cell. The cytoplasm will be smooth and contain no granules.



Photograph **BCI-12** shows a normal lymphocyte. Mature lymphocytes are variable in size. This photograph illustrates a smaller lymphocyte. Note the scanty amount of blue cytoplasm. Nuclei in lymphocytes may be round, oval, or slightly indented with clumped, dense chromatin. Nucleoli are sometimes present in lymphocytes, but are often not visible, as is the case with this lymphocyte.



Two spirochetes are visible in photograph **BCI-13**. Visualizing spirochetes on a peripheral blood smear is very important in the diagnosis of this patient's relapsing fever. Relapsing fever may be epidemic and louse-borne, or endemic and tick-borne. *Borrelia recurrentis* is the etiologic agent for epidemic relapsing fever. Numerous other *Borrelia* species, including *Borrelia hermsii,* can cause the endemic form of relapsing fever. Tick-borne relapsing fever is found worldwide, although *Borrelia hermsii* is commonly seen in Canada, the Pacific Northwest, and California. The spirochetes enter the human host through the bite of a tick. They are most often seen in the peripheral blood during febrile periods. The *Borrelia* spirochetes have an affinity for acid dyes, such as Wright's or Giemsa stains, and will therefore appear blue on a smear. Both thick and thin smears should be made when *Borrelia* is suspected in a patient, as sometimes the number of spirochetes is low, especially after multiple febrile relapses. *Borrelia* are bacteria with 4 to 30 loose, helical coils. This uniform shape can help distinguish such spirochetes from contaminants, which are generally more irregular in appearance. It is not possible to identify the specific species of *Borrelia* by reviewing a stained blood smear. Antibody and antigen testing, as was performed on this patient, is necessary to confirm a diagnosis. It should also be mentioned that *Borrelia burgdorferi*, the causative agent of Lyme disease, while also a tick-borne organism, is rarely if ever seen in the peripheral blood.



Photograph **BCI-14** illustrates a reactive or atypical lymphocyte. Another term sometimes used to describe such a cell is "variant." Reactive lymphocytes characteristically demonstrate a wide variety of morphologic appearances on a blood smear. There are no "typical" atypical lymphocytes! This is in contrast to malignant cells, which generally are more uniform and monotonous in morphology. Reactive lymphocytes are most often associated with viral illnesses.

Although reactive lymphocytes display many different features, some generalizations can be made. The cytoplasm in reactive lymphocytes is often abundant and may have vacuoles and/or azurophilic granules. The cytoplasmic margin may be indented by surrounding erythrocytes and may be a darker blue than the remainder of the cytoplasm. The overall staining color of the cytoplasm may be gray, pale blue, or a very deep blue. Nuclei in atypical lymphocytes are also variable in shape. They may be round, oval, indented, have lobes, or be folded. Nucleoli may or may not be present. The nuclear chromatin is often more fine and open than what is normally seen in a lymphocyte, and the parachromatin may be more distinct.

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It sometimes can be difficult to distinguish a reactive lymphocyte from a monocyte. Usually, monocytes are less easily indented by surrounding red blood cells, but may have pseudopodia (extensions of cytoplasm associated with cellular motility). The cytoplasm of monocytes often appears bumpy or uneven while the nuclear chromatin tends to be lacy and loose. Nucleoli are not seen in normal monocytes.

Note that the cell illustrated in BCI-14 has several characteristic features of a reactive lymphocyte, including the indented, darker cytoplasmic edges, an irregularly-shaped nucleus, and more open chromatin and visible parachromatin.