Signs of Sepsis

**Tips for evaluating a peripheral blood smear for possible sepsis**

By Scott Warner, MLT(ASCP)

In an era of point of care testing and increasing automation, it's nice to be needed. Laboratory testing is critical in cases of sepsis. **There's no substitute for a set of human eyes examining a peripheral blood smear under a microscope.** Understanding the urgency of sepsis and what to look for can make your skills shine.

**Sepsis**

Sepsis is typically the presence of bacteria, toxins or other infectious organisms in the blood. Also called blood poisoning and septicemia, sepsis can spread rapidly throughout organ systems and is associated with fever, chills, malaise, low blood pressure and mental status changes. Rapid laboratory testing is often needed to confirm this life threatening illness.

Sepsis can be deadly if not treated quickly. In 1990, Jim Henson, the creator of the Muppets, died from toxic shock syndrome caused by Group A streptococcus at age 53. The physician heading the care team at New York Hospital where Henson was admitted said at the time that antibiotics might have saved Henson's life had he come to the hospital a few hours earlier.

More recently, in 2009, Brazilian model Mariana Bridi da Costa died from sepsis after being diagnosed with a urinary tract infection. Physician efforts to save her included amputating her feet, hands, and removing part of her stomach and both kidneys. She was 20. While rare in young, healthy people like da Costa, death can happen in a matter of hours once an infection reaches a certain stage.

According to the Merck Manual website, there are 900,000 cases of sepsis of various severity in the United States annually causing 210,000 deaths. Greater severity predicts increased mortality. **Laboratory indicators of acute sepsis include an elevated white count and greater than 10% immature forms; at onset white counts and absolute neutrophil counts may be decreased.** Other markers include electrolytes, lactate levels, and arterial blood gases. The stages are summarized in the Table.

<table>
<thead>
<tr>
<th>Category</th>
<th>Signs &amp; Symptoms</th>
<th>Annual Cases</th>
<th>Deaths</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sepsis</strong></td>
<td>At least 2 of the following:</td>
<td>400,000</td>
<td>60,000</td>
<td>15%</td>
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<td>- Temp &gt;30 °C or &lt;36°C</td>
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<td>- Heart rate &gt; 90 beats per minute</td>
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<td></td>
<td>- Resp rate &gt; 20 breaths per minute or PaCO2 &lt;32 mmHg</td>
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<tr>
<td></td>
<td>- WBC &gt; 12000 / μL or &lt; 4000 / μL or &gt;10% immature forms</td>
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<tr>
<td><strong>Severe Sepsis</strong></td>
<td>Sepsis with failure of at least one organ</td>
<td>300,000</td>
<td>60,000</td>
<td>20%</td>
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<tr>
<td><strong>Septic Shock</strong></td>
<td>Severe sepsis with organ hypoperfusion and hypotension that respond poorly to initial fluid resuscitation</td>
<td>200,000</td>
<td>90,000</td>
<td>45%</td>
</tr>
</tbody>
</table>
In 1992 the term "sepsis" was broadened to systemic inflammatory response syndrome (SIRS), to describe infectious and noninfectious causes of critical illnesses, including burns, trauma and pancreatitis. The Cleveland Clinic website reports similar numbers to the above, citing SIRS as the tenth leading cause of death in the United States. The incidence of sepsis is also rising annually by 8%.

Septic patients can present in the urgent care setting with a number of serious but nonspecific signs and symptoms, such as a fever and rapid heart rate. Your alertness and skill in recognizing key neutrophil characteristics under the microscope can add a critical piece to the puzzle.

**Under the Microscope**

To evaluate a peripheral blood smear for possible sepsis, it's important to visually examine neutrophils in a cell differential. Since their primary function is phagocytosis of microbes and other infectious agents, they are most likely to be affected by sepsis. Here are the most common neutrophil types to look for:

**Bands.** Bands (sometimes called "stabs") comprise 10-15% of the cells in the bone marrow and are normally present in small numbers in the peripheral circulation. The nuclear chromatin is clumped and the nucleus indented to more than half the distance from the farthest nuclear margin, i.e., indented more than a metamyelocyte but less than segmented forms. Typically it is non-segmented in an S, C, or U shape. The literature has at least three different definitions.

Your lab may or may not enumerate band counts for a number of reasons: lack of consistency, precision, and specificity. Bands have traditionally indicated a so-called "left shift" to more immature neutrophil forms as precursors are released from the bone marrow during stress. Despite physician use of bandemia as a clinical marker, there is little support in textbooks.

**Toxic changes, by contrast, are more specific than increased band counts, resulting from the activation of increased cytokines during infection, burns or trauma. They consist of the following:**

**Toxic granulation.** Toxic granulation (see Figure 1) is the presence of large granules in the cytoplasm of neutrophils that are purplish-blue, dark blue or red in appearance. These are azurophilic granules present in myeloid forms not normally seen in later stages.

**Döhle bodies.** Döhle bodies (see Figure 1), which are remnants of endoplasmic reticulum, are single or multiple cytoplasmic inclusion bodies of variable size and shape. Typically they are blue or gray-blue in color and on the periphery of the cell, often at the membrane. They may be difficult to see if toxic granulation is also present or may be confused with May-Hegglin anomaly.

**Vacuoles.** Cytoplasmic vacuoles (see Figure 2) are clear spaces that indicate recent phagocytic activity, often variable in size and sometimes distorting the appearance of the cell. EDTA storage, however, can also produce these changes; storage conditions and age of the specimen should be considered when vacuolization is the only toxic change seen.

Rarely, phagocytized bacteria, bacteria, or other microorganisms are seen on peripheral blood smears and usually indicate an overwhelming infection. Stain precipitate can be confused with bacteria, note.

**Part of the Team**

Toxic changes that include an increased white count (the patient in the Figures has a white count of 32,000), increase absolute neutrophil count with or without band forms, and cytoplasmic elements listed above are an opportunity for you as a technologist to jump in and help the team caring for the patient. Considering patient presentation, including a telephone call to the physician, is always a good idea when
toxic changes are seen. Mislabeling, improper storage and poor staining can lead to errors. Any toxic changes should be considered carefully before reporting. If, for example, a patient presents with chest pain but toxic changes are seen, it's a good idea to double check your work.

The laboratory role in emergency medicine is critical, even more so under the microscope. In cases of sepsis and other severe conditions, rapid and accurate identification of toxic changes gives the physician useful information needed to confirm a diagnosis. Awareness of the patient condition and the importance of these changes is one more step in providing better patient care.

Scott Warner is lab manager at Penobscot Valley Hospital, Lincoln, Maine.

References