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Interpreting Peripheral

Blood Smears Some of the relevant findings in peripheral blood, enlarged lymph nodes, and bone marrow are illustrated in this chapter. Systematic his tologic examination of the bone marrow and lymph nodes is beyond the scope of a general medicine textbook. However, every internist should know how to examine a peripheral blood smear. The examination of a peripheral blood smear is one of the most informative exercises a physician can perform. Although advances in automated technology have made the examination of a peripheral blood smear by a physician seem less important, the technology is not a completely satisfactory replacement for a blood smear interpretation by a trained medical professional who also knows the patient's clinical history, family history, social history, and physical findings. It is useful to ask the laboratory to generate a Wright's-stained peripheral blood smear and examine it. A normal peripheral blood smear is shown in Figure 65-1. The best place to examine blood cell morphology is the feath ered edge of the blood smear where red cells lie in a single layer, side by side, just barely touching one another but not overlapping. The author's approach is to look at the smallest cellular elements, the platelets, first and work his way up in size to red cells and then white cells. Using an oil immersion lens that magnifies the cells 100-fold, one counts the platelets in five to six fields, averages the number per field, and multiplies by 20,000 to get a rough estimate of the platelet count. The platelets are usually 1–2 μm in diameter and have a blue granulated appearance. There is usually 1 platelet for every 20 or so red cells. Of course, the automated counter is much more accurate, but gross disparities between the automated and manual counts should be assessed. Large platelets may be a sign of rapid platelet turnover, as young platelets are often larger than old ones; alternatively, certain rare inherited syndromes can produce large platelets. If the platelet count is low, the absence of large (young) platelets may be an indicator of marrow production problems. Platelet clumping visible on the smear can be associated with falsely low automated platelet counts. Clumping may be caused by the anticoagulant into which the blood is drawn. Similarly, neutrophil fragmentation can be a source of falsely elevated automated platelet counts. The absence of platelet granules may be an artifact of the handling of the blood or may indicate marrow disease or a rare congenital anomaly, gray platelet syndrome. Elevated platelet counts usually signify a myeloproliferative disorder or a reaction to systemic inflammation. Next one examines the red

blood cells. One can gauge their size by comparing the red cell to the nucleus of a small lymphocyte. Both are normally about 8-μm wide. Red cells that are smaller than the small lymphocyte nucleus may be microcytic; those larger than the small lymphocyte nucleus may be macrocytic. Macrocytic cells also tend to be more oval than spherical in shape and are sometimes called mac roovalocytes. The automated mean corpuscular volume (MCV) can assist in making a classification. However, some patients may have both iron and vitamin B12 deficiency, which will produce an MCV in the normal range but wide variation in red cell size. When the red cells vary greatly in size, anisocytosis is said to be present. When the red cells vary greatly in shape, poikilocytosis is said to be present. The electronic cell counter provides an independent assessment of vari ability in red cell size. It measures the range of red cell volumes and reports the results as “red cell distribution width” (RDW). This value is calculated from the MCV; thus, cell width is not being measured

but cell volume is. The term is derived from the curve displaying the frequency of cells at each volume, also called the distribution. The width of red cell volume distribution curve is what determines the RDW. The RDW is calculated as follows: RDW = (standard deviation of MCV ÷ mean MCV) × 100. In the presence of morphologic aniso cytosis, RDW (normally 11–14%) increases to 15–18%. The RDW is useful in at least two clinical settings. In patients with microcytic anemia, the differential diagnosis is generally between iron deficiency and thalassemia. In thalassemia, the small red cells are generally of uniform size with a normal small RDW. In iron deficiency, the size variability and the RDW are large. In addition, a large RDW can sug gest a dimorphic anemia when a chronic atrophic gastritis can pro duce both vitamin B12 malabsorption to produce macrocytic anemia and blood loss to produce iron deficiency. In such settings, RDW is also large. An elevated RDW also has been reported as a risk factor for all-cause mortality in population-based studies, a finding that is unexplained currently.

Interpreting Peripheral Blood Smears CHAPTER 65 After red cell size is assessed, one examines the hemoglobin con tent of the cells. They are either normal in color (normochromic) or pale in color (hypochromic). They are never “hyperchromic.” If more than the normal amount of hemoglobin is made, the cells get larger—they do not become darker. In addition to hemoglobin con tent, the red cells are examined for inclusions. Red cell inclusions are the following:

1. Basophilic stippling—diffuse fine or coarse blue dots in the red cell usually representing RNA residue—especially common in lead poisoning
2. Howell-Jolly bodies—dense blue circular inclusions that repre sent nuclear remnants—their presence implies defective splenic function
3. Nuclei—red cells may be released or pushed out of the marrow pre maturely before nuclear extrusion—often implies a myelophthisic process or a vigorous narrow response to anemia, usually hemolytic anemia
4. Parasites—red cell parasites include malaria and babesia (Chaps. A2 and A6)
5. Polychromatophilia—the red cell cytoplasm has a bluish hue, reflect ing the persistence of ribosomes still actively making hemoglobin in a young red cell Vital stains are necessary to see precipitated hemoglobin called Heinz bodies. Red cells can take on a variety of different shapes. All abnormally shaped red cells are poikilocytes. Small red cells without the central pallor are spherocytes; they can be seen in hereditary spherocytosis, hemolytic anemias of other causes, and clostridial sepsis. Dacrocytes are teardrop-shaped cells that can be seen in hemolytic anemias, severe iron deficiency, thalassemias,

myelofibrosis, and myelodys plastic syndromes. Schistocytes are helmet-shaped cells that reflect microangiopathic hemolytic anemia or fragmentation on an artificial heart valve. Echinocytes are spiculated red cells with the spikes evenly spaced; they can represent an artifact of abnormal drying of the blood smear or reflect changes in stored blood. They also can be seen in renal failure and malnutrition and are often reversible. Acanthocytes are spiculated red cells with the spikes irregularly distributed. This process tends to be irreversible and reflects underlying renal disease, abetalipoproteinemia, or splenectomy. Elliptocytes are ellipticalshaped red cells that can reflect an inherited defect in the red cell membrane, but they also are seen in iron deficiency, myelodysplastic syndromes, megaloblastic anemia, and thalassemias. Stomatocytes are red cells in which the area of central pallor takes on the morphology of a slit instead of the usual round shape. Stomatocytes can indicate an inherited red cell membrane defect and also can be seen in alco holism. Target cells have an area of central pallor that contains a dense center, or bull’s eye. These cells are seen classically in thalassemia, but they are also present in iron deficiency, cholestatic liver disease, and some hemoglobinopathies. They also can be generated artifactually by improper slide making.

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