16 HEMATOLOGY: RED AND WHITE BLOOD CELL TESTS

Paul R. Hutson

OBJECTIVES

After completing this chapter, the reader should be able to

- Describe the physiology of blood cell development and bone marrow function
- Discuss the interpretation and alterations of hemoglobin, hematocrit, and various red blood cell indices in the evaluation of macrocytic, microcytic, and normochromic/normocytic anemias
- Describe the significance of abnormal erythrocyte morphology, including sickling, anisocytosis, and nucleated erythrocytes
- Name the different types of leukocytes and describe their primary functions
- Calculate the absolute number of various types of leukocytes from the white blood cell count and differential
- Interpret alterations in the white blood cell count, differential, and CD_4 lymphocyte count in acute bacterial infections, parasitic infections, and human immunodeficiency virus infection
- Identify potential causes of neutrophilia
- Identify how leukocyte phenotypes are used for antitumor drug selection

This chapter reviews the basic functions and expected laboratory values of erythrocytes and leukocytes. It also discusses, in an introductory manner, selected disorders of these two cellular components of blood. It must be remembered that the ability of laboratory medicine to discriminate between leukocytes is increasing, and many methods considered investigational in this edition may become a routine component of blood examination in the future.

PHYSIOLOGY OF BLOOD CELLS AND BONE MARROW

The cellular components of blood are derived from pluripotential stem cells located in the bone marrow that can differentiate into red blood cells (RBCs), white blood cells (WBCs), and platelets (**Figure 16-1**). *Bone marrow* is a highly structured and metabolically active organ, which normally produces 2.5 billion RBCs, 1 billion granulocytes, and 2.5 billion platelets/kg of body weight daily.[1] Production can vary greatly from nearly 0 to 5 to 10 times normal. Usually, however, levels of circulating cells remain in a relatively narrow range (**Table 16-1**).[2]

In the fetus and children, blood cell formation or hematopoiesis occurs in the marrow of virtually all bones, as well as in liver, spleen and other visceral organs. With maturation, the task of hematopoiesis ceases in the liver and shifts to flat bones of the axial skeleton such as the cranium, ribs, pelvis, and vertebrae. The long bones, such as the femur and humerus, do not produce a large amount of blood cells in adulthood because the marrow is gradually replaced by fatty tissue.

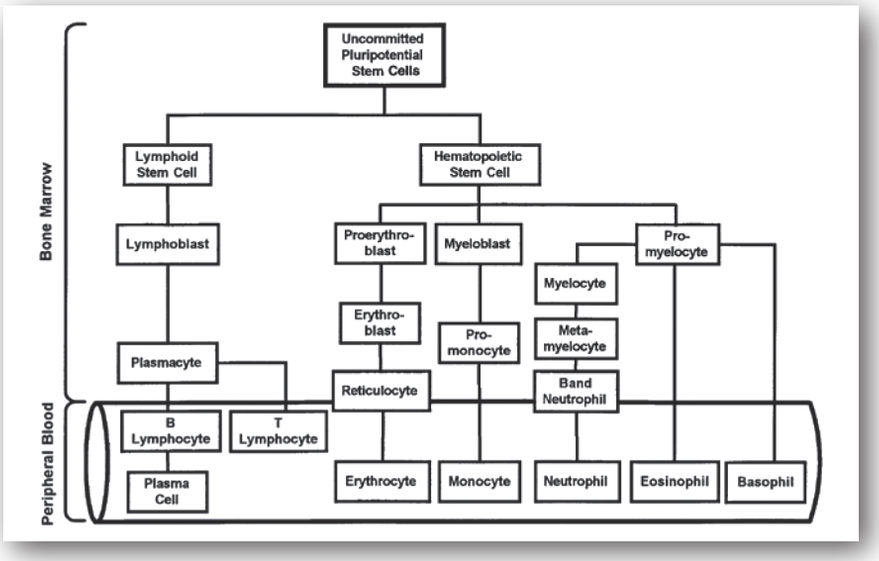

FIGURE 16-1. Schematic diagram of hematopoiesis.

Note: The author wishes to thank Irene Chung for her skilled assistance in the revision of this chapter.

TABLE 16-1. Reference Ranges and Interpretative Comments for Common Hematological Tests (Typical CBC)[a]

TEST NAME	RANGE[a] REFERENCE	SI UNITS	COMMENTS
RBC	Males: 4.5–5.9 × 10^6 cells/µl Females: 4.1–5.1 × 10^6 cells/µl	4.5–5.9 × 10^{12} cells/L 4.1–5.1 × 10^{12} cells/L	
Hgb	Males: 14–17.5 g/dL Females: 12.3–15.3 g/dL	140–175 g/L or 8.68–10.85 mmol/L 123–153 g/L or 7.63–9.49 mmol/L	Amount of Hgb in given volume of whole blood; indication of oxygen-transport capacity of blood; elevated in hyperlipidemia
Hct	Males: 42–50% Females: 36–45%	0.42–0.5 0.36–0.45	Percentage volume of blood comprised of erythrocytes; usually approximately three times Hgb
RBC indices MCV	80–96 fL/cell	80–96 fL/cell	Hct/RBC: average size of RBCs in a specimen; increased in vitamin B_{12} and folate deficiency, cold agglutinins, reticulocytosis, hyperglycemia, and leukemic cells; decreased in iron deficiency
MCH	27–33 pg/cell	27–33 pg/cell	Hgb/RBC: average amount of hemoglobin in RBCs in a specimen; increased in vitamin B_{12} and folate deficiency; decreased in iron deficiency
MCHC	33.4–35.5 g/dL	334–355 g/L	Hgb/Hct: average concentration of Hgb in RBCs in a specimen; increased in hyperlipidemia and cold agglutinins; decreased in iron deficiency
Reticulocyte count	0.5–2.5% of RBCs	0.005–0.025	Immature RBCs; increased in acute blood loss and hemolysis; decreased in untreated iron, vitamin B_{12}, and folate deficiency
RDW	11.5–14.5%	0.115–0.145	Measure of variation in RBC volumes (anisocytosis): the larger the width percent, the greater the variation in size of RBCs; increased in early iron deficiency anemia and mixed anemias
WBC count	4.4–11.3 × 10^3 cells/µL	4.4–11.3 × 10^9 cells/L	Elevated by neutrophil demargination with exercise, glucocorticoids, epinephrine; decreased with cold agglutinins
Platelet count	150,000–450,000 cells/µL	150–450 × 10^9 cells/L	Elevated in presence of RBC fragments and microcytic erythrocytes; decreased in presence of large numbers of giant platelets and platelet clumps
MPV	6.8–10 fL	6.8–10 fL	

Hct = hematocrit; Hgb = hemoglobin; RBC/s = red blood cell/s; RDW = RBC distribution width; MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; MCV = mean corpuscular volume; MPV = mean platelet volume; SI = International System of Units; WBC = white blood cell.
[a]Modified from references 8 and 9.

Radiation directed to large portions of hematopoietic bones can lead to deficient hematopoiesis in patients treated for cancerous lesions such as bony metastases. Similarly, preparation for a bone marrow transplant will often include total body irradiation to destroy the hematopoietic cells of the recipient in the bone, spleen, and other sites so that the grafted cells will not be destroyed by residual host defenses.

Although the majority of hematopoiesis occurs in the marrow, modern methods of identifying cellular characteristics have demonstrated that pluripotential cells—identified by a cellular expression of the surface marker CD34—also normally circulate in the blood.[3,4]

Although the majority of this chapter discusses laboratory analysis of blood obtained from the vein (peripheral venipuncture), an analysis of the bone marrow itself may be needed to diagnose or monitor various disease states, most commonly the leukemias discussed later in the chapter. Bone marrow specimens are usually obtained from the posterior iliac crest of the pelvis or, less commonly because of increased risk, from the sternum. Bone marrow sampling can involve an aspirate, a core biopsy, or both. After penetrating the bone cortex with the bone marrow needle and entering the medullary cavity inside the bone containing the marrow, a heparinized syringe is attached to the needle and 1 to 2 mL of bone marrow is aspirated. The contents of the syringe are smeared on a series of slides that are stained and examined microscopically. If special studies such as flow cytometry or cytogenetics are requested, additional heparinized syringes are aspirated and submitted to the laboratory. The bone marrow biopsy is obtained with the same needle by advancing it further past the site of aspiration through the bone marrow to cut a sample of the bone marrow matrix for removal and examination. The biopsy provides the advantage of examining the structure of the marrow stroma, as well as the spatial relationship of the various hematopoietic cells.[5]

Blood pluripotential (stem) cells become increasingly differentiated in the bone marrow until they are committed to develop further into erythrocytes, platelets, or various leukocytes (Figure 16-1). Many regulatory proteins including colony-stimulating factors are involved in the differentiation and proliferation phases of hematopoiesis, but their functions and interrelationships are not yet fully understood. In addition to the colony-stimulating factors mentioned above, proteins that stimulate hematopoiesis include erythropoietin,