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Clinical Disorders of Neutrophils

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INTRODUCTION

Leukocytes provide the main defense against bacterial infection. Monocytes and granulocytes are phagocytic cells that can kill ingested bacteria through the generation of reactive intermediates. Monocytes also release inflammatory mediators that increase the activity of lymphocytes. Lymphocyte function is discussed in Chapter 49.

NORMAL GRANULOCYTE DEVELOPMENT, STRUCTURE, AND FUNCTION

Neutrophils

Neutrophils (i.e., polymorphonuclear leukocytes) are the predominant white blood cell in the peripheral blood. They are morphologically recognizable by their characteristic segmented nucleus. Neutrophils also contain cytoplasmic granules that give them a characteristic appearance and are functionally important (Fig. 48-1).

Neutrophils achieve intracellular killing of bacteria through chemotaxis, adhesion, and phagocytosis (Fig. 48-2). *Chemotaxis* is the ordered movement of the cell toward an attracting stimulus, such as bacterial formyl peptides or complement fragments (i.e., C3b and C5a). Neutrophils adhere to endothelial cells by interaction of neutrophil surface glycoproteins (i.e., CD11b/CD18) with endothelial adhesion molecules (i.e., intracellular adhesion molecule 1 and endothelial leukocyte adhesion molecule 1), a process called *margination*. In response to a chemotactic stimulus, the adherent neutrophils move toward the target along the endothelial surface.

The syndrome of leukocyte adhesion deficiency underscores the importance of neutrophil adhesion as the first step in bacterial killing. This rare congenital disease is caused by the absence of surface expression of the CD11b/CD18 complex on neutrophils. Neutrophils fail to adhere to endothelium, are unable to undergo chemotaxis, and do not phagocytose or kill bacteria. Patients have severe, life-threatening bacterial infections despite high levels of circulating neutrophils.

Phagocytosis requires recognition of target bacteria or debris by the neutrophil. Targets are opsonized by the surface binding of immunoglobulin or complement factor C3b. The neutrophil has surface receptors for C3b and the Fc portion of immunoglobulin G, which allows recognition and binding to the opsonized target. The target then becomes engulfed in a phagocytic vacuole, which fuses with neutrophil granules inside the cell.

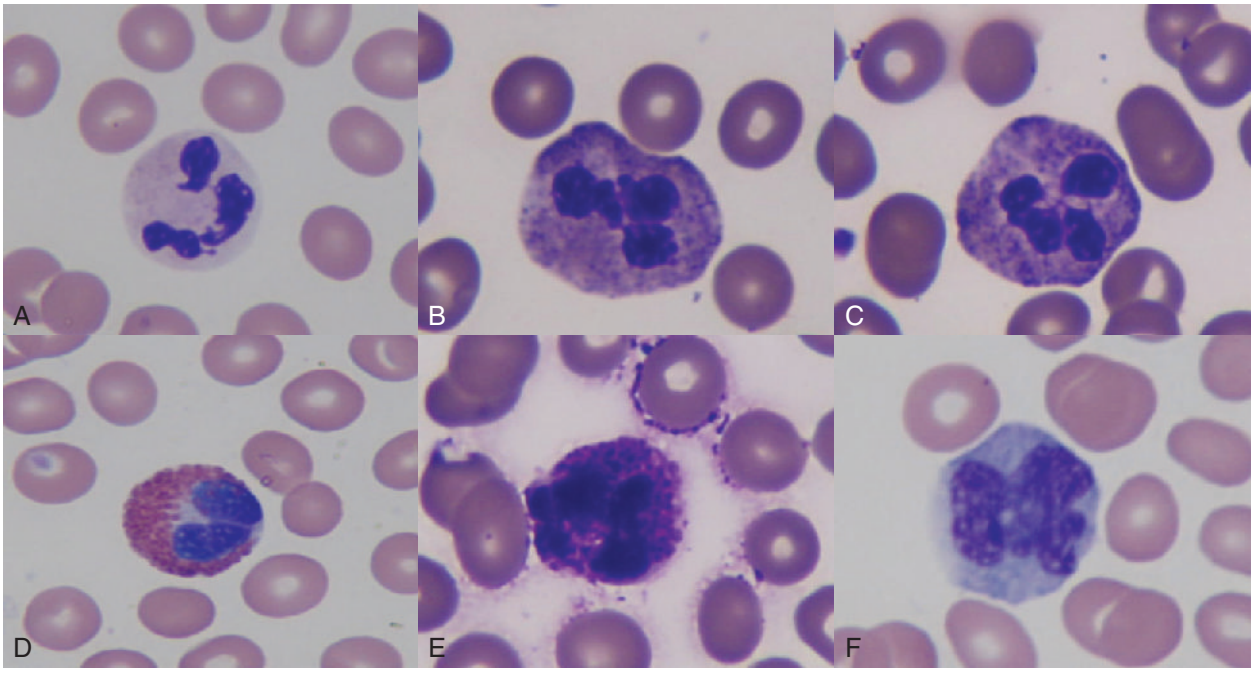

FIGURE 48-1 Normal granulocytes and monocytes in peripheral blood. **A** to **C,** Neutrophils (i.e., polymorphonuclear cells). **D,** Eosinophils. **E,** Basophils. **F,** Monocytes. (Courtesy Robert J. Homer, MD, PhD, Yale School of Medicine, New Haven, Conn.)