Fig. 2.1. Differentiation of pluripotential stem cells to the committed cell lines of the hematopoietic system. Major features of the hematopoietic system include the following: (1) Proliferation of myeloid and lymphoid cells classically occurs in marrow and other lymphoid tissues, respectively. (2) Seven nonlymphoid cell types and three major types of lymphoid cells are produced by the system. In this figure, all cells are part of the leukon except those of the erythrocyte and platelet lineage.

CFU-GEMM, colony-forming unit–granulocyte, erythrocyte, monocyte, megakaryocyte.

Fig. 2.2. Neutrophil kinetics in health. Marrow has three major neutrophil pools: (1) self-renewal stem cells (CFU-G); (2) ProNP, or mitotic pool, that contains myeloblasts (Mb), progranulocytes (Pg), and myelocytes (Mc); and (3) MatNP, or postmitotic pool, that contains metamyelocytes (Mmc), band neutrophils (B), and segmented neutrophils (S). A SNP is within the MatNP and contains segmented neutrophils. When neutrophils leave the marrow and enter blood, they distribute between the MNP and CNP. After neutrophils bind to adhesion proteins on endothelial cells, they migrate into tissues to form the TNP. In the TNP, the neutrophils perform their protective functions and die.

Fig. 2.3. Lymphocyte kinetics in health. Lymph nodes and other primary lymphoid tissues are sites of lymphocyte production but also potential destinations of blood lymphocytes. Blood lymphocytes are distributed between marginal and circulating pools and may enter lymphoid organs or nonlymphoid tissues. Lymphocytes that enter nonlymphoid tissue may remain or may enter the afferent lymphatic vessels and be transported to regional lymph nodes and then perhaps to blood via the thoracic duct.

Fig. 2.4. Hemocytometer. The hemocytometer has two components: the thicker glass with special grids on each side and a cover glass. Each grid has nine 1 mm^2 squares used for leukocyte counting, and each central square is divided into 25 smaller squares that are used for erythrocyte and platelet counting. The distance between the grid surface and the coverslip is 0.1 mm; thus, the volume of the space above the grid is 0.9 mm^3 (0.9 μL).

Fig. 2.5. Schematic representation of cell counting principles.

Left: Impedance principle: Blood cells (*solid circles*) suspended in an isotonic diluent enter a bath, pass through a small aperture (about 100 μm diameter), and then leave the bath (flow shown by *dotted arrows*). Concurrently, electrons (e^-) are moving from a cathode, through the aperture, to an anode. When a cell passes through the aperture, it displaces electrons and interrupts the current briefly, thus creating a voltage peak than can be viewed via an oscilloscope (*top*). Each voltage peak represents a cell (a particle) passing through the aperture; the height of the peak corresponds primarily to the volume of the cell. Particles within a certain impedance range are considered erythrocytes, particles in a lower range are considered platelets, and other particles are not recognized as cells (if the instrument has a "voting out" program). The mean cell volume represents the average volume detected within the erythrocyte range. The erythrocyte concentration represents the number of particles (within the erythrocyte range) per volume. Another bath is used for determining leukocyte concentration. After addition of lysing agent to remove erythrocytes and platelets, the leukocyte nuclei and fluid pass through an aperture and the instrument considers those particles to be leukocytes.

Right: Flow cytometry principle: Blood cells suspended in an isotonic diluent are injected into a special flowing fluid. The fluid dynamics in the system create a sheath around the diluent to form a sample stream. Cells in the sample stream pass through a laser beam, mostly one at a time. Each cell scatters the light in different directions, depending on the cell's size and contents. Sensors detect the scattered light at various locations. Computer programs analyze the data from the sensors to determine which cell has passed through the laser beam.

Fig. 2.6. Schematic representation of IDEXX QBC VetTube after centrifugation of whole blood. Centrifugal forces separate the components of blood into five layers (plasma, platelets, agranulocytes, granulocytes, and erythrocytes) based on their relative densities. The buffy coat (composed of platelets and leukocytes) is expanded by a float that has a density similar to buffy coat cells. Layers are recognized by use of fluorescence markers for DNA, RNA, and lipoprotein, and the thickness of each cell layer is used to derive cell concentrations (see the text).

Fig. 2.7. Neutrophilia kinetics.

A. Neutrophil kinetics in health (a reduced version of Fig. 2.2).

B. Acute inflammatory neutrophilia: Neutrophilia occurs because the release of neutrophils from the marrow exceeds the migration of neutrophils to the inflamed tissue. A left shift is created by the release of band neutrophils from the MatNP.

C. Chronic inflammatory neutrophilia: Neutrophilia occurs because the release of neutrophils from the marrow exceeds the migration of neutrophils to the inflamed tissue. A left shift may not be present because granulocytic hyperplasia maintains the SNP.

D. Steroid neutrophilia: Neutrophilia occurs because of a shift of neutrophils from the MNP to the CNP, decreased migration of neutrophils to tissue, and release of neutrophils from the SNP and sometimes the MatNP.

E. Physiologic (shift) neutrophilia: Neutrophilia occurs because of the shift of neutrophils from the MNP to the CNP.

F. Chronic myeloid leukemia: Neutrophilia occurs because of an uncontrolled proliferation of a clone of neoplastic neutrophil precursors. Acute myelogenous leukemia may create a leukocytosis, but the neoplastic cells may not be easily recognized as being of neutrophil lineage.

Fig. 2.8. Neutropenia kinetics.

A. Neutrophil kinetics in health (a reduced version of Fig. 2.2).

B. Inflammatory neutropenia (overwhelming tissue demand): Neutropenia occurs because the margination and migration of neutrophils into the inflamed tissues exceed the release of neutrophils from marrow.

C. Endotoxin neutropenia: Neutropenia occurs because endotoxins stimulate the margination of neutrophils (sequestration of neutrophils in the MNP). With the concurrent inflammatory response, a variety of changes in neutrophil kinetics are possible. Endotoxins may also affect marrow cells to cause increased release of neutrophils (see the text).

D. Peripheral destruction neutropenia: Neutropenia occurs because neutrophils are being destroyed by macrophages, perhaps because of antineutrophil antibodies. If persistent, granulocytic hyperplasia will develop.

E. Granulocytic hypoplasia neutropenia: Neutropenia occurs because neutrophil production is decreased.

F. Ineffective production neutropenia: Neutropenia occurs because a disorder prevents an orderly maturation of neutrophil precursors in the marrow and thus neutrophil production is decreased. This may occur at different stages of neutrophil maturation. It may be caused by immune-mediated cell destruction in some cases.

Fig. 2.9. Lymphocytosis kinetics.

A. Lymphocyte kinetics in health (a reduced version of Fig. 2.3).

B. Chronic inflammatory lymphocytosis: Lymphocytosis occurs because of increased lymphopoiesis associated with the immune response to the inflammatory agent. The lymphocytosis is a part of lymphoid hyperplasia.

C. Physiologic (shift) lymphocytosis: Lymphocytosis occurs because of the shift of lymphocytes from the MLP to the CLP.

D. Lymphoproliferative neoplasia: A lymphoid leukemia results from an uncontrolled proliferation of a lymphoid cell clone. This figure illustrates the leukemic manifestation of lymphoma; see the text for other lymphoid leukemias.

Fig. 2.10. Lymphopenia kinetics.

A. Acute inflammatory lymphopenia: Lymphopenia occurs because of (1) increased migration of lymphocytes to inflamed tissue, (2) homing of lymphocytes to lymphoid tissues, and (3) decreased movement of lymphocytes from lymph nodes back to blood.

B. Steroid lymphopenia: Soon after administration of glucocorticoids, lymphopenia occurs because of the movement of lymphocytes to lymphoid tissues and decreased efflux of lymphocytes from lymph nodes. With persistent administration, glucocorticoids can become lymphotoxic and thus destroy lymphocytes in lymph nodes and other tissues.

C. Depletion lymphopenia: Lymphopenia occurs because lymphocytes are lost from the vascular system with a loss of lymph or lymph-rich fluid.

D. Lymphopenia of lymphoid hypoplasia or aplasia: Lymphopenia occurs because of decreased lymphocyte production.