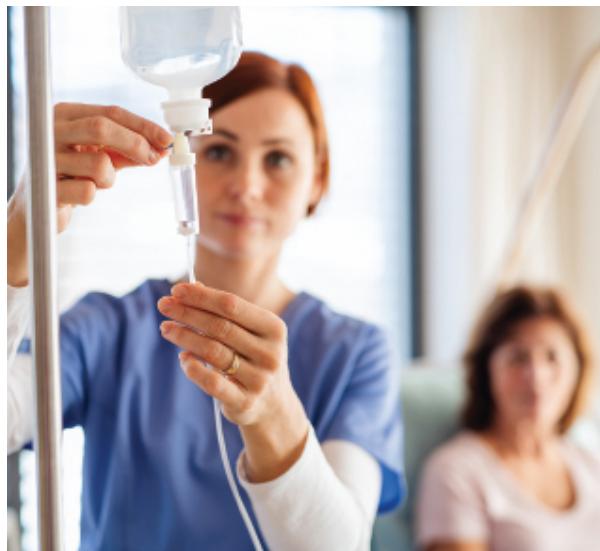


UNIT 6

Hematologic Function

Case Study

EVALUATING COMPLICATIONS OF CHEMOTHERAPY



A 66-year-old woman is receiving a course of chemotherapy for non-Hodgkin lymphoma in the infusion center where you work. You note that upon arrival the patient is short of breath, her SpO₂ is 88% on room air, and her heart rate is regular at 104 bpm. Her chemotherapy infusion is placed on hold and laboratory tests reveal she has anemia. Upon initiation of chemotherapy, all patients receive education about strategies to help avoid complications such as anemia, bleeding, and infection. Earlier in the week another patient had their chemotherapy held due to an infection. You wonder if you should consider a different type of intervention aimed at decreasing complications of chemotherapy.

QSEN Competency Focus: Quality Improvement

The complexities inherent in today's health care system challenge nurses to demonstrate integration of specific interdisciplinary core competencies. These competencies are aimed at ensuring the delivery of safe, quality patient care (Institute of Medicine, 2003). The Quality and Safety Education for Nurses project (Cronenwett, Sherwood, Barnsteiner, et al., 2007; QSEN, 2020) provides a framework for the knowledge, skills, and attitudes (KSAs) required for nurses to demonstrate competency in these key areas, which include ***patient-centered care, interdisciplinary teamwork and collaboration, evidence-based practice, quality improvement, safety, and informatics.***

Quality Improvement Definition: Use data to monitor the outcomes of care processes and use improvement methods to design and test changes to continuously improve the quality and safety of health care systems.

SELECT PRE- LICENSURE KSAs	APPLICATION AND REFLECTION
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Knowledge

Explain the importance of variation and measurement in assessing quality of care

How can you verify the observations made about increased complication rates among patients receiving chemotherapy? Identify the sources of data that could be accessed to demonstrate the need for a change in the processes of care.

Skills

Use quality measures to understand performance

Specify the main objective that you hope to achieve with this population of patients receiving chemotherapy. Specify measurable, time-oriented expected outcomes. Might there be an opportunity for you to do a pilot test of change in the infusion center? If so, how would you go about designing this type of project? Who else from the infusion center team might you need to be involved in this type of project?

Attitudes

Value measurement and its role in good patient care

Reflect on your attitudes toward patients with cancer receiving chemotherapy. Do you tend to think that anemia and infection are unavoidable in patients with cancer receiving treatment?

Cronenwett, L., Sherwood, G., Barnsteiner, J., et al. (2007). Quality and safety education for nurses. *Nursing Outlook*, 55(3), 122–131; Institute of Medicine. (2003). *Health professions education: A bridge to quality*. Washington, DC: National Academies Press; QSEN Institute. (2020). *QSEN competencies: Definitions and pre-licensure KSAs; Quality improvement*. Retrieved on 8/15/2020 at: qsen.org/competencies/pre-licensure-ksas/#quality_improvement

28 Assessment of Hematologic Function and Treatment Modalities

LEARNING OUTCOMES

On completion of this chapter, the learner will be able to:

- 1.** Describe hematopoiesis and the processes involved in maintaining hemostasis.
- 2.** Discuss the significance of the health history to the assessment of hematologic health and specify the appropriate techniques utilized to perform a comprehensive physical assessment of hematologic function.
- 3.** Explain the diagnostic tests and related nursing implications used to evaluate hematologic function.
- 4.** Identify therapies for blood disorders, including nursing implications for the administration of blood components.

NURSING CONCEPTS

Assessment
Clotting

GLOSSARY

anemia: decreased red blood cell (RBC) count

band cell: slightly immature neutrophil

blast cell: primitive white blood cell (WBC)

cytokines: proteins produced by leukocytes that are vital to regulation of hematopoiesis, apoptosis, and immune responses

differentiation: development of functions and characteristics that are different from those of the parent stem cell

erythrocyte: a cellular component of blood involved in the transport of oxygen and carbon dioxide (*synonym:* red blood cell [RBC])

erythropoiesis: process of the formation of RBCs

erythropoietin: hormone produced primarily by the kidney; necessary for erythropoiesis

fibrin: filamentous protein; basis of thrombus and blood clot

fibrinogen: protein converted into fibrin to form thrombus and clot

fibrinolysis: process of breakdown of fibrin clot

granulocyte: granulated WBC (i.e., neutrophil, eosinophil, basophil)

hematocrit: percentage of total blood volume consisting of RBCs

hematopoiesis: complex process of the formation and maturation of blood cells

hemoglobin: iron-containing protein of RBCs; delivers oxygen to tissues

hemostasis: intricate balance between clot formation and clot dissolution

leukocyte: one of several cellular components of blood involved in defense of the body; subtypes include neutrophils, eosinophils, basophils, monocytes, and lymphocytes (*synonym:* white blood cell [WBC])

leukopenia: less-than-normal amount of WBCs in circulation

lymphocyte: form of WBC involved in immune functions

lymphoid: pertaining to lymphocytes

macrophage: reticuloendothelial cells capable of phagocytosis

monocyte: large WBC that becomes a macrophage when it leaves the circulation and moves into body tissues

myeloid: pertaining to nonlymphoid blood cells that differentiate into RBCs, platelets, macrophages, mast cells, and various WBCs

myelopoiesis: formation and maturation of cells derived from myeloid stem cell

natural killer (NK) cells: lymphocytes that defend against microorganisms and malignant cells

neutrophil: fully mature WBC capable of phagocytosis; primary defense against bacterial infection

oxyhemoglobin: combined form of oxygen and hemoglobin; primarily found in arterial blood

phagocytosis: process of cellular ingestion and digestion of foreign bodies

plasma: liquid portion of blood

plasminogen: protein converted to plasmin to dissolve thrombi and clots

platelet: a cellular component of blood involved in blood coagulation (*synonym:* thrombocyte)

red blood cell (RBC): a cellular component of blood involved in the transport of oxygen and carbon dioxide (*synonym:* erythrocyte)

reticulocytes: slightly immature RBCs, usually only 1% of total circulating RBCs

reticuloendothelial system: complex system of cells throughout the body capable of phagocytosis

serum: portion of blood remaining after coagulation occurs

stem cell: primitive cell, capable of self-replication and differentiation into myeloid or lymphoid stem cell

stroma: component of the bone marrow not directly related to hematopoiesis but serves important supportive roles in this process

thrombocyte: a cellular component of blood involved in blood coagulation (*synonym:* platelet)

white blood cell (WBC): one of several cellular components of blood involved in defense of the body; subtypes include neutrophils, eosinophils, basophils, monocytes, and lymphocytes (*synonym:* leukocyte)

Unlike many other body systems, the hematologic system encompasses the entire human body. Patients with hematologic disorders often have significant abnormalities in blood tests but few or no symptoms. Therefore, the nurse must have a good understanding of the pathophysiology of the patient's condition and the ability to make a thorough assessment that relies heavily on the interpretation of laboratory tests. It is equally important for the nurse to anticipate potential patient needs and to target nursing interventions accordingly. Because it is so important to the understanding of most hematologic diseases, a basic appreciation of blood cells and bone marrow function is necessary.

Anatomic and Physiologic Overview

The hematologic system consists of the blood and the sites where blood is produced, including the bone marrow and the reticuloendothelial system (RES). Blood is a specialized organ that differs from other organs in that it exists in a fluid state. Blood is composed of plasma and various types of cells which account for 7% to 9% of total blood volume (Jouria, 2018). **Plasma** is the fluid portion of blood; it contains various proteins, such as albumin, globulin, **fibrinogen**, and other factors necessary for clotting, as well as electrolytes, waste products, and nutrients. About 55% of whole blood volume is plasma (American Society of Hematology, 2020).

Bone Marrow

The bone marrow is the site of hematopoiesis, or blood cell formation. In adults, blood cell formation is usually limited to the pelvis, ribs, vertebrae, and sternum. Marrow is one of the largest organs of the body, making up 4% to 5% of total body weight. It consists of islands of cellular components (red marrow) separated by fat (yellow marrow). As people age, the proportion of active marrow is gradually replaced by fat; however, in healthy adults, the fat can again be replaced by active marrow when more blood cell production is required. In adults with disease that causes marrow destruction, fibrosis, or scarring, the liver and spleen can also resume production of blood cells by a process known as extramedullary hematopoiesis.

The marrow is vascular. Within it are primitive cells called **stem cells**. The stem cells have the ability to self-replicate, thereby ensuring a continuous supply of stem cells throughout the life cycle. When stimulated to do so, stem cells can begin a process called **differentiation**, and develop into either **myeloid** or **lymphoid** stem cells (see Fig. 28-1). These stem cells are committed to produce specific types of blood cells. Lymphoid stem cells produce either T or B **lymphocytes**, cells that have specific immune functions that will be described in more detail later. Myeloid stem cells differentiate into three broad cell types: erythrocytes, leukocytes, and platelets. Thus, with the exception of lymphocytes, all blood cells are derived from myeloid stem cells. A defect in a myeloid stem cell can cause problems with erythrocyte, leukocyte, and platelet production. In contrast, a defect in the lymphoid stem cell can cause problems with T or B lymphocytes, plasma cells (a more differentiated form of B lymphocyte), or natural killer (NK) (see Chapter 31 for additional information) (Wimberly, 2019).

The **stroma** of the marrow refers to all tissue within the marrow that is not directly involved in hematopoiesis. However, the stroma is important in an indirect manner, in that it produces the colony-stimulating factors needed for hematopoiesis. The yellow marrow is the largest component of the stroma.

Other cells comprising the stroma include fibroblasts (reticular connective tissue), osteoclasts, osteoblasts (both needed for remodeling of skeletal bone), and endothelial cells.

Blood

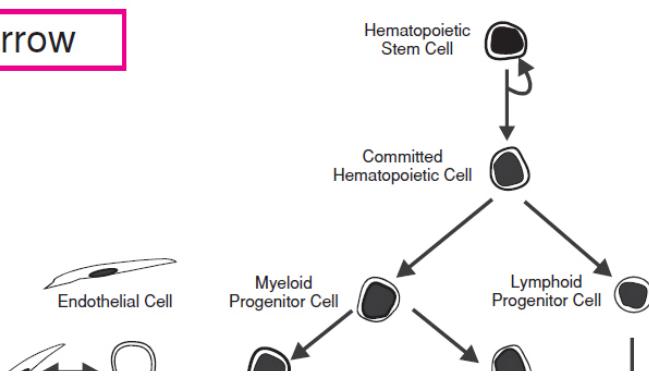
The cellular component of blood consists of three primary cell types (see [Table 28-1](#)): **erythrocytes (red blood cells [RBCs], red cells)**, **leukocytes (white blood cells [WBCs])**, and **thrombocytes (platelets)**. These cellular components of blood normally make up 40% to 45% of the blood volume (American Society of Hematology, 2020). Because most blood cells have a short lifespan, the need for the body to replenish its supply of cells is continuous; this process is termed **hematopoiesis**. The primary site for hematopoiesis is the bone marrow. During embryonic development and in other conditions, the liver and spleen may also be involved.

Under normal conditions, the adult bone marrow produces about 175 billion erythrocytes, 70 billion **neutrophils** (a mature type of WBC), and 175 billion platelets each day. When the body needs more blood cells, as in infection (when neutrophils are needed to fight the invading pathogen) or in bleeding (when more RBCs are required), the marrow increases its production of the cells required. Thus, under normal conditions, the marrow responds to increased demand and releases adequate numbers of cells into the circulation.

Blood makes up approximately 7% to 9% of the normal body weight and amounts to 5 to 6 L of volume for men and 4 to 5 L of volume for women (Nair, 2017). Circulating through the vascular system and serving as a link between body organs, blood carries oxygen absorbed from the lungs and nutrients absorbed from the gastrointestinal (GI) tract to the body cells for cellular metabolism. Blood also carries hormones, antibodies, and other substances to their sites of action or use. In addition, blood carries waste products produced by cellular metabolism to the lungs, skin, liver, and kidneys, where they are transformed and eliminated from the body.

Physiology/Pathophysiology

Bone Marrow



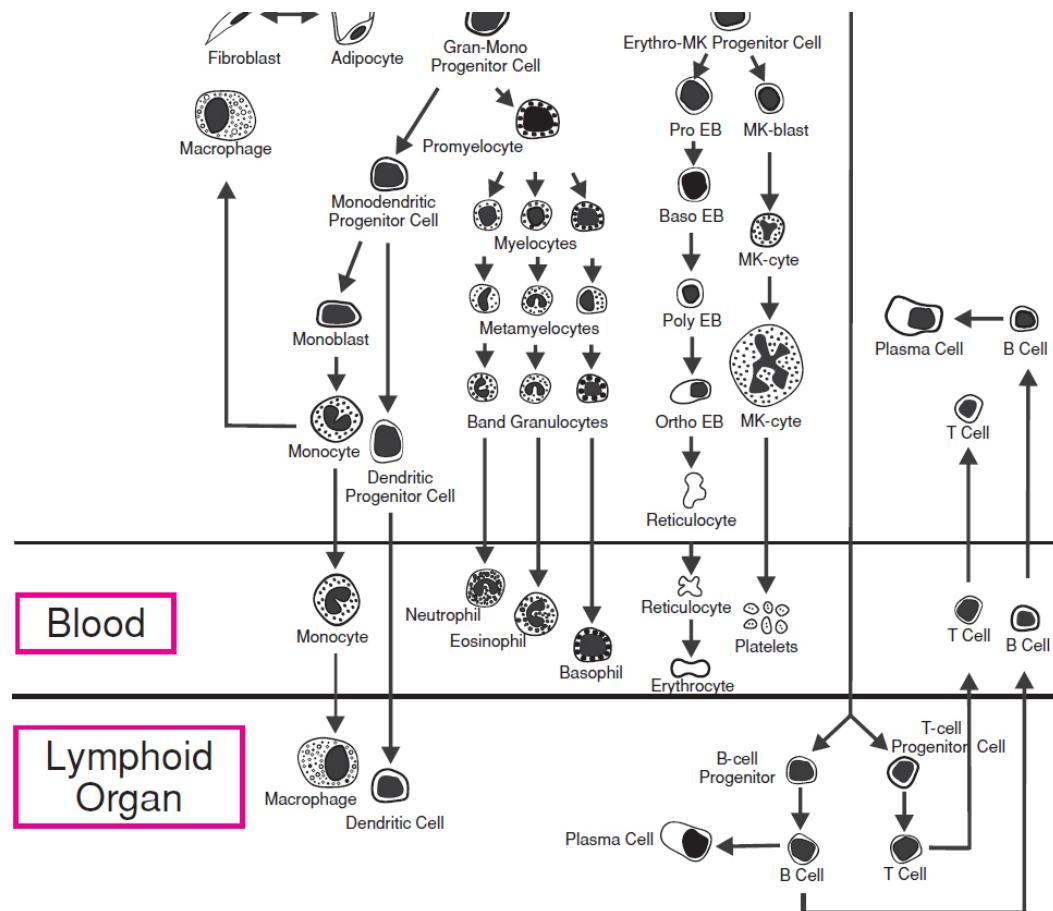


Figure 28-1 • Hematopoiesis and stromal stem cell differentiation.

Uncommitted (pluripotent) stem cells can differentiate into myeloid or lymphoid stem cells. These stem cells then undergo a complex process of differentiation and maturation into normal cells that are released into the circulation. The myeloid stem cell is responsible not only for all nonlymphoid white blood cells but also for the production of red blood cells (RBCs) and platelets. Each step of the differentiation process depends in part on the presence of specific growth factors for each cell type. When the stem cells are dysfunctional, they may respond inadequately to the need for more cells, or they may respond excessively, and sometimes uncontrollably, as in leukemia. Reprinted with permission from Koury, M., Mahmud, N., & Rhodes, M. (2009). Origin and development of blood cells. In J. P. Greer, J. Foerster, G. M. Rodgers (Eds.). *Wintrobe's clinical hematology* (12th ed.). Philadelphia, PA: Lippincott Williams & Wilkins.

TABLE 28-1 Blood Cells

Cell Type	Major Function
WBC (Leukocyte)	Fights infection
Neutrophil	Essential in preventing or limiting bacterial infection via phagocytosis
Monocyte	Enters tissue as macrophage; highly phagocytic, especially against fungus; immune surveillance
Eosinophil	Involved in allergic reactions (neutralizes histamine); digests foreign proteins
Basophil	Contains histamine; integral part of hypersensitivity reactions
Lymphocyte	Integral component of immune system
T lymphocyte	Responsible for cell-mediated immunity; recognizes material as “foreign” (surveillance system)
B lymphocyte	Responsible for humoral immunity; many mature into plasma cells to form antibodies
Plasma cell	Secretes immunoglobulin (antibody); most mature form of B lymphocyte
RBC (Erythrocyte)	Carries hemoglobin to provide oxygen to tissues; average lifespan is 120 days
Platelet (Thrombocyte)	Fragment of megakaryocyte; provides basis for coagulation to occur; maintains hemostasis; average lifespan is 10 days

WBC, white blood cell; RBC, red blood cell.

Adapted from Norris, T. L. (2019). *Porth's pathophysiology: Concepts of altered health state* (10th ed.). Philadelphia, PA: Wolters Kluwer.

The danger that trauma can lead to excess blood loss always exists. To prevent this, an intricate clotting mechanism is activated when necessary to seal any leak in the blood vessels. Excessive clotting is equally dangerous, because it can obstruct blood flow to vital tissues. To prevent this, the body has a fibrinolytic mechanism that eventually dissolves clots (thrombi) formed within blood vessels. The balance between these two systems—clot (thrombus) formation and clot dissolution or **fibrinolysis**—is called **hemostasis**.

Erythrocytes (Red Blood Cells)

The normal erythrocyte is a biconcave disc that resembles a soft ball compressed between two fingers (see Fig. 28-2). It has a diameter of about 8 μm and is so flexible that it can pass easily through capillaries that may be as small as 2.8 μm in diameter. The membrane of the red cell is very thin so that gases, such as oxygen and carbon dioxide, can easily diffuse across it; the disc

shape provides a large surface area that facilitates the absorption and release of oxygen molecules.

Mature erythrocytes consist primarily of **hemoglobin**, which contains iron and protein and makes up 95% of the cell mass. Mature erythrocytes have no nuclei, and they have many fewer metabolic enzymes than do most other cells. The presence of a large amount of hemoglobin enables the red cell to perform its principal function, which is the transport of oxygen between the lungs and tissues. Occasionally, the marrow releases slightly immature forms of erythrocytes, called **reticulocytes**, into the circulation. This occurs as a normal response to an increased demand for erythrocytes (as in bleeding) or in some disease states.

The oxygen-carrying hemoglobin molecule is made up of four subunits, each containing a heme portion attached to a globin chain. Iron is present in the heme component of the molecule. An important property of heme is its ability to bind to oxygen loosely and reversibly. Oxygen readily binds to hemoglobin in the lungs and is carried as **oxyhemoglobin** in arterial blood. Oxyhemoglobin is a brighter red than hemoglobin that does not contain oxygen (reduced hemoglobin); thus, arterial blood is a brighter red than venous blood. The oxygen readily dissociates (detaches) from hemoglobin in the tissues, where the oxygen is needed for cellular metabolism. In venous blood, hemoglobin combines with hydrogen ions produced by cellular metabolism and thus buffers excessive acid. Whole blood normally contains about 15 g of hemoglobin per 100 mL of blood (Fischbach & Fischbach, 2018).

Erythropoiesis

Erythroblasts arise from the primitive myeloid stem cells in bone marrow. The erythroblast is an immature nucleated cell that gradually loses its nucleus. At this stage, the cell is known as a reticulocyte. Further maturation into an erythrocyte entails the loss of the dark-staining material within the cell and slight shrinkage. The mature erythrocyte is then released into the circulation. Under conditions of rapid **erythropoiesis** (i.e., erythrocyte production), reticulocytes and other immature cells may be released prematurely into the circulation. This is often seen when the liver or spleen takes over as the site of erythropoiesis and more nucleated red cells appear within the circulation.

Differentiation of the primitive myeloid stem cell into an erythroblast is stimulated by **erythropoietin**, a hormone produced primarily by the kidney. If the kidney detects low levels of oxygen, as occurs when fewer red cells are available to bind oxygen (i.e., **anemia**), or with people living at high altitudes with lower atmospheric oxygen concentrations, erythropoietin levels increase. The increased erythropoietin then stimulates the marrow to increase the production of erythrocytes. The entire process of erythropoiesis occurs over 1 week (Wimberly, 2019). For normal erythrocyte production, the bone marrow also requires iron, vitamin B₁₂, folate, pyridoxine (vitamin B₆), protein, and

other factors. A deficiency of these factors during erythropoiesis can result in decreased red cell production and anemia.

Iron Stores and Metabolism

The rate of iron absorption is regulated by the amount of iron already stored in the body and by the rate of erythrocyte production. Daily dietary iron requirements vary based on age, gender, and health status. For example, pregnant women require up to 30 mg of iron daily, while adult men require up to 12 mg and children up to 10 mg of iron daily (Trevithick, 2019). Additional amounts of iron, up to 2 mg daily, must be absorbed by women of childbearing age to replace that lost during menstruation. Total body iron content in the average adult is approximately 3 g, most of which is present in hemoglobin or in one of its breakdown products. Iron is stored as ferritin and when required, the iron is released into the plasma, binds to transferrin, and is transported into the membranes of the normoblasts (erythrocyte precursor cells) within the marrow, where it is incorporated into hemoglobin. Iron is lost in the feces, either in bile, blood, or mucosal cells from the intestine.

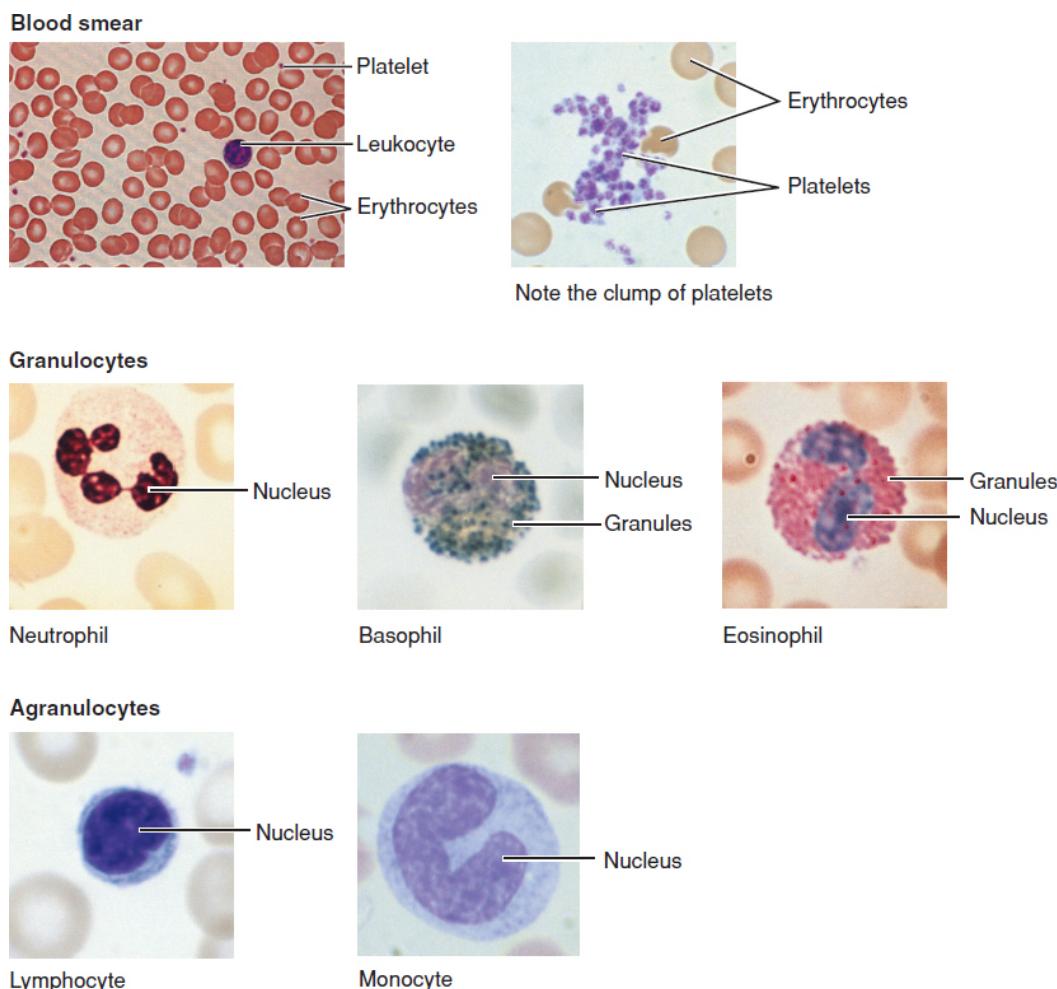


Figure 28-2 • Normal types of blood cells. Reprinted with permission from Cohen, B. J. (2005). *Memmler's the human body in health and disease* (10th ed.). Philadelphia, PA: Lippincott Williams & Wilkins.

The normal findings for concentration of iron in blood can range from 50 to 250 µg/dL depending on age and gender (Fischbach & Fischbach, 2018). With iron deficiency, bone marrow iron stores are rapidly depleted; hemoglobin synthesis is depressed, and the erythrocytes produced by the marrow are small and low in hemoglobin. Iron deficiency in the adult generally indicates blood loss (e.g., from bleeding in the GI tract or heavy menstrual flow). Lack of dietary iron is rarely the sole cause of iron deficiency anemia in adults. The source of iron deficiency should be investigated promptly, because iron deficiency in an adult may be a sign of bleeding in the GI tract or colon cancer.

Vitamin B₁₂ and Folate Metabolism

Vitamin B₁₂ and folate are required for the synthesis of deoxyribonucleic acid (DNA) in RBCs. Both vitamin B₁₂ and folate are derived from the diet. Folate

is absorbed in the proximal small intestine, but only small amounts are stored within the body. If the diet is deficient in folate, stores within the body quickly become depleted. Because vitamin B₁₂ is found only in foods of animal origin, strict vegetarians may ingest little vitamin B₁₂. Vitamin B₁₂ combines with intrinsic factor produced in the stomach. The vitamin B₁₂-intrinsic factor complex is absorbed in the distal ileum. People who have had a partial or total gastrectomy may have limited amounts of intrinsic factor, and therefore the absorption of vitamin B₁₂ may be diminished. The effects of either decreased absorption or decreased intake of vitamin B₁₂ are not apparent for 2 to 4 years.

Vitamin B₁₂ and folate deficiencies are characterized by the production of abnormally large erythrocytes called *megaloblasts*. Because these cells are abnormal, many are sequestered (trapped) while still in the bone marrow, and their rate of release is decreased. Some of these cells actually die in the marrow before they can be released into the circulation. This results in megaloblastic anemia.

Red Blood Cell Destruction

The average lifespan of a normal circulating erythrocyte is 120 days. Often, older erythrocytes lose elasticity and become trapped in small blood vessels and the spleen. These older erythrocytes are removed from the blood by the reticuloendothelial cells, particularly in the liver and the spleen. As the erythrocytes are destroyed, most of their hemoglobin is recycled. Some hemoglobin also breaks down to form bilirubin and is secreted in the bile. Most of the iron is recycled to form new hemoglobin molecules within the bone marrow; small amounts are lost daily in the feces and urine and monthly in menstrual flow.

Leukocytes (White Blood Cells)

Leukocytes are divided into two general categories: granulocytes and lymphocytes. In normal blood, the total leukocyte count is 4000 to 11,000 cells/mm³. Of these, approximately 60% to 80% are granulocytes and 20% to 40% are lymphocytes. Both of these types of leukocytes primarily protect the body against infection and tissue injury.

Granulocytes

Granulocytes are defined by the presence of granules in the cytoplasm of the cell. Granulocytes are divided into three main subgroups—eosinophils, basophils, and neutrophils—that are characterized by the staining properties of these granules (see Fig. 28-2). Eosinophils have bright-red granules in their cytoplasm, whereas the granules in basophils stain deep blue. The third and most numerous cell in this class is the neutrophil, with granules that stain a

pink to violet hue. Neutrophils are also called *polymorphonuclear neutrophils* (PMNs, or polys) or *segmented neutrophils* (segs).

The nucleus of the mature neutrophil has multiple lobes (usually two to five) that are connected by thin filaments of nuclear material, or a “segmented” nucleus; it is usually two times the size of an erythrocyte. The somewhat less mature granulocyte has a single-lobed, elongated nucleus and is called a **band cell**. Ordinarily, band cells account for only a small percentage of circulating granulocytes, although their percentage can increase greatly under conditions in which neutrophil production increases, such as infection. The increased number of band cells is sometimes called a left shift or shift to the left. (Traditionally, the diagram of neutrophil maturation showed the myeloid stem cell on the left with progressive maturation stages toward the right, ending with a fully mature neutrophil on the far right side. A shift to the left indicates that more immature cells are present in the blood than normal.)

Fully mature neutrophils result from the gradual differentiation of myeloid stem cells, specifically myeloid **blast cells** (i.e., immature white blood cells). The process, called **myelopoiesis**, is highly complex and depends on many factors. These factors, including specific **cytokines** (i.e., regulatory proteins produced by leukocytes) such as growth factors, are normally present within the marrow itself. As the blast cell matures, the cytoplasm of the cell changes in color (from blue to violet) and granules begin to form with the cytoplasm. The shape of the nucleus also changes. The entire process of maturation and differentiation takes about 10 days (see [Fig. 28-1](#)). Once the neutrophil is released into the circulation from the marrow, it stays there for only about 6 hours before it migrates into the body tissues to perform its function of **phagocytosis** (ingestion and digestion of foreign bodies, such as bacteria). Neutrophils die here within 1 to 2 days. The number of circulating granulocytes found in the healthy person is relatively constant; however, in infection, large numbers of these cells are rapidly released into the circulation.

Agranulocytes

Monocytes

Monocytes (also called *mononuclear leukocytes*) are leukocytes with a single-lobed nucleus and a granule-free cytoplasm—hence the term *agranulocyte* (see [Fig. 28-2](#)). In normal adult blood, monocytes account for approximately 5% of the total leukocytes. Monocytes are the largest of the leukocytes. Produced by the bone marrow, they remain in the circulation for a short time before entering the tissues and transforming into **macrophages**. Macrophages are particularly active in the spleen, liver, peritoneum, and alveoli; they remove debris from these areas and phagocytize bacteria within the tissues.

Lymphocytes

Mature **lymphocytes** are small cells with scanty cytoplasm (see Fig. 28-2). Immature lymphocytes are produced in the marrow from the lymphoid stem cells. A second major source of production for lymphocytes is the thymus. Cells derived from the thymus are known as T lymphocytes (or T cells); those derived from the marrow can also be T cells but are more commonly B lymphocytes (or B cells). Lymphocytes complete their differentiation and maturation primarily in the lymph nodes and in the lymphoid tissue of the intestine and spleen after exposure to a specific antigen. Mature lymphocytes are the principal cells of the immune system, producing antibodies and identifying other cells and organisms as “foreign.” **Natural killer (NK) cells** serve an important role in the body’s immune defense system. Like other lymphocytes, NK cells accumulate in the lymphoid tissues (especially spleen, lymph nodes, and tonsils), where they mature. When activated, they serve as potent killers of virus-infected and cancer cells. They also secrete cytokines to mobilize the T and B cells into action.

Function of Leukocytes

Leukocytes protect the body from invasion by bacteria and other foreign entities. The major function of neutrophils is phagocytosis. Neutrophils arrive at a given site within 1 hour after the onset of an inflammatory reaction and initiate phagocytosis, but they are short-lived. An influx of monocytes follows; these cells continue their phagocytic activities for long periods as macrophages. This process constitutes a second line of defense for the body against inflammation and infection. Although neutrophils can often work adequately against bacteria without the help of macrophages, macrophages are particularly effective against fungi and viruses. Macrophages also digest senescent (aging or aged) blood cells, primarily within the spleen.

The primary function of lymphocytes is to attack foreign material. One group of lymphocytes (T lymphocytes) kills foreign cells directly or releases lymphokines, substances that enhance the activity of phagocytic cells. T lymphocytes are responsible for delayed allergic reactions, rejection of foreign tissue (e.g., transplanted organs), and destruction of tumor cells. This process is known as *cellular immunity*. The other group of lymphocytes (B lymphocytes) is capable of differentiating into plasma cells. Plasma cells, in turn, produce antibodies called *immunoglobulins* (Igs), which are protein molecules that destroy foreign material by several mechanisms. This process is known as *humoral immunity*.

Eosinophils and basophils function in hypersensitivity reactions. Eosinophils are important in the phagocytosis of parasites. The increase in eosinophil levels in allergic states indicates that these cells are involved in the hypersensitivity reaction; they neutralize histamine. Basophils produce and store histamine as well as other substances involved in hypersensitivity

reactions. The release of these substances provokes allergic reactions. See [Chapter 31](#) for further information on the immune response.

Platelets (Thrombocytes)

Platelets, or thrombocytes, are not technically cells; rather, they are granular fragments of giant cells in the bone marrow called *megakaryocytes* (see [Fig. 28-2](#)). Platelet production in the marrow is regulated in part by the hormone thrombopoietin, which stimulates the production and differentiation of megakaryocytes from the myeloid stem cell. Each megakaryocyte has the capacity to produce approximately 2000 platelets; 80% of these platelets are active in the circulation and 20% are stored in the spleen (Ciesla, 2019a).

Platelets play an essential role in the control of bleeding. They circulate freely in the blood in an inactive state, where they nurture the endothelium of the blood vessels, maintaining the integrity of the vessel. When vascular injury occurs, platelets collect at the site and are activated. They adhere to the site of injury and to each other, forming a platelet plug that temporarily stops bleeding. Substances released from platelet granules activate coagulation factors in the blood plasma and initiate the formation of a stable clot composed of **fibrin**, a filamentous protein. Platelets have a normal lifespan of 7 to 10 days (Ciesla, 2019b).

Plasma and Plasma Proteins

After cellular elements are removed from blood, the remaining liquid portion is called *plasma*. More than 90% of plasma is water. The remainder consists primarily of plasma proteins; clotting factors (particularly fibrinogen); and small amounts of other substances, such as nutrients, enzymes, waste products, and gases. If plasma is allowed to clot, the remaining fluid is called *serum*. Serum has essentially the same composition as plasma, except that fibrinogen and several clotting factors have been removed during the clotting process.

Plasma proteins consist primarily of albumin and globulins. The globulins can be separated into three main fractions (alpha, beta, and gamma), each of which consists of distinct proteins that have different functions. Important proteins in the alpha and beta fractions are the transport globulins and the clotting factors that are made in the liver. The transport globulins carry various substances in bound form in the circulation. For example, thyroid-binding globulin carries thyroxin, and transferrin carries iron. The clotting factors, including fibrinogen, remain in an inactive form in the blood plasma until activated by the clotting cascade. The gamma-globulin fraction refers to the Ig's, or antibodies. These proteins are produced by well-differentiated B lymphocytes and plasma cells. The actual fractionation of the globulins can be seen on a specific laboratory test (serum protein electrophoresis).

Albumin is particularly important for the maintenance of fluid balance within the vascular system. Capillary walls are impermeable to albumin, so its presence in the plasma creates an osmotic force that keeps fluid within the vascular space. Albumin, which is produced by the liver, has the capacity to bind to several substances that are transported in plasma (e.g., certain medications, bilirubin, and some hormones). People with impaired hepatic function may have low concentrations of albumin, with a resultant decrease in osmotic pressure and the development of edema.

Reticuloendothelial System (RES)

The **reticuloendothelial system (RES)** is composed of special tissue macrophages. When released from the marrow, monocytes spend a short time in the circulation (about 24 hours) and then enter the body tissues. Within the tissues, the monocytes continue to differentiate into macrophages, which can survive for months or years. Macrophages have a variety of important functions. They defend the body against foreign invaders (i.e., bacteria and other pathogens) via phagocytosis. They remove old or damaged cells from the circulation. They stimulate the inflammatory process and present antigens to the immune system (Banaski, 2019). Macrophages give rise to tissue histiocytes, phagocytic cells that are present in loose connective tissue. These include Kupffer cells of the liver, peritoneal macrophages, alveolar macrophages, and other components of the RES. Thus, the RES is a component of many other organs within the body, particularly the spleen, lymph nodes, lungs, and liver.

The spleen is the site of activity for most macrophages. Most of the spleen (75%) is made of red pulp; here, the blood enters the venous sinuses through capillaries that are surrounded by macrophages. Within the red pulp are tiny aggregates of white pulp, consisting of B and T lymphocytes. The spleen sequesters newly formed reticulocytes from the marrow, removing nuclear fragments and other materials (e.g., damaged or defective hemoglobin, iron) before the now fully mature erythrocyte returns to the circulation. If the spleen is enlarged, a greater number of red cells and platelets can be sequestered. The spleen is a major source of hematopoiesis in fetal life. It can resume hematopoiesis later in adulthood if necessary, particularly when marrow function is compromised (e.g., in bone marrow fibrosis). The spleen has important immunologic functions as well. It forms substances called *opsonins* that promote the phagocytosis of neutrophils; it also forms the antibody immunoglobulin M (IgM) after exposure to an antigen.

Hemostasis is the process of preventing blood loss from intact vessels and of stopping bleeding from a severed vessel, which requires adequate numbers of functional platelets. Platelets nurture the endothelium and thereby maintain the structural integrity of the vessel wall. Two processes are involved in arresting bleeding: primary and secondary hemostasis (see [Fig. 28-3](#)).

In primary hemostasis, the severed blood vessel constricts. Circulating platelets aggregate at the site and adhere to the vessel and to one another. An unstable hemostatic plug is formed. For the coagulation process to be correctly activated, circulating inactive coagulation factors must be converted to active forms. This process occurs on the surface of the aggregated platelets at the site of vessel injury.

Physiology/Pathophysiology

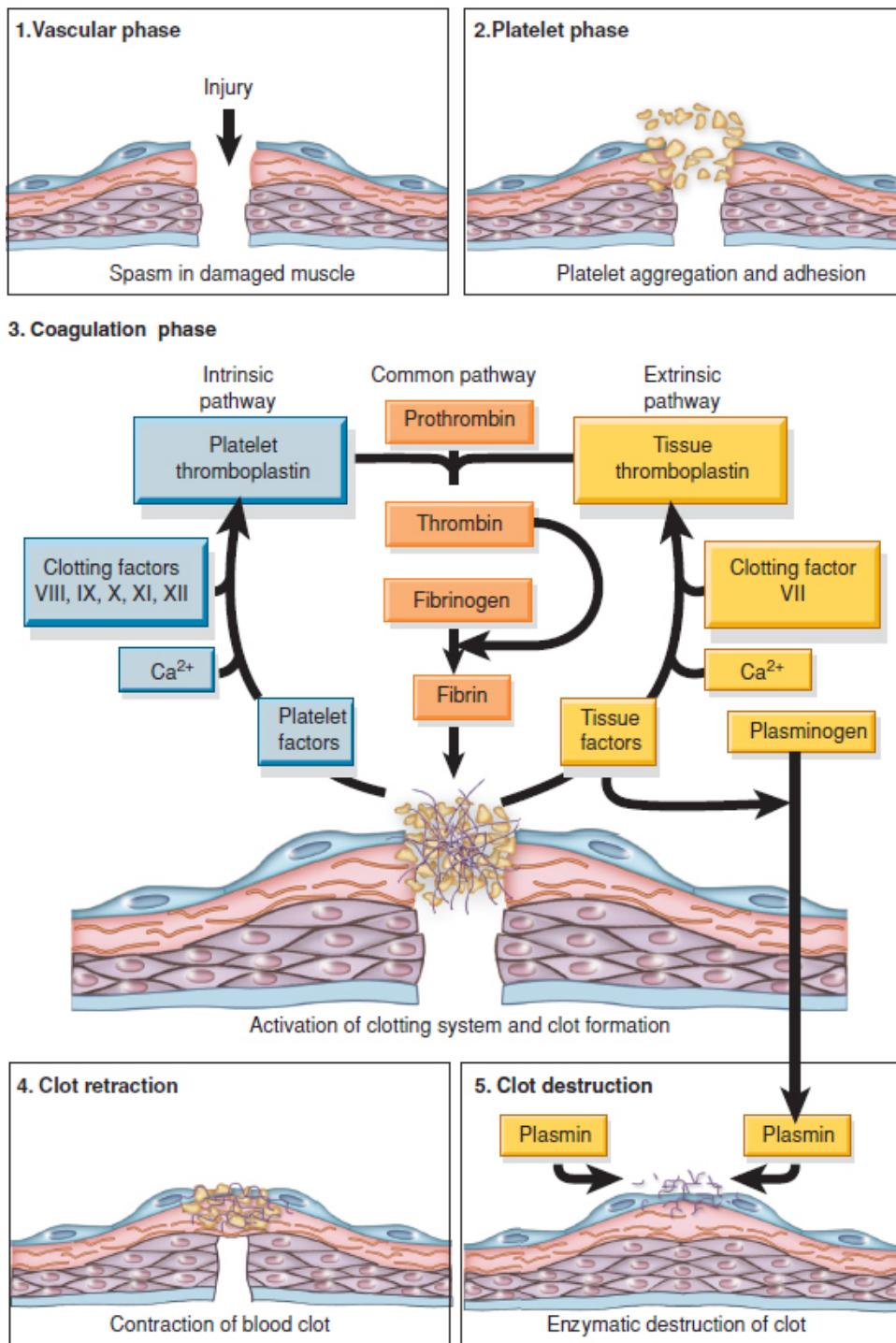


Figure 28-3 • Hemostasis. When the endothelial surface of a blood vessel is injured, several processes occur. In primary hemostasis, platelets within the circulation are attracted to the exposed layer of collagen at the site of injury. They adhere to the site of injury, releasing factors that stimulate other platelets to aggregate at the

site, forming an unstable platelet plug. In secondary hemostasis, based on the type of stimulus, one of two clotting pathways is initiated—the intrinsic or extrinsic pathway—and the clotting factors within that pathway are activated. The end result from either pathway is the conversion of prothrombin to thrombin. Thrombin is necessary for fibrinogen to be converted into fibrin, the stabilizing protein that anchors the fragile platelet plug to the site of injury to prevent further bleeding and permit the injured vessel or site to heal.

Modified from www.irvingcrowley.com/cls/clotting.gif

The end result is the formation of fibrin, which reinforces the platelet plug and anchors it to the injury site. This process is referred to as secondary hemostasis. Blood coagulation is highly complex. It can be activated by the extrinsic pathway (also known as the tissue factor pathway) or the intrinsic pathway (also known as the contact activation pathway). Both pathways are needed for maintenance of normal hemostasis. Many factors are involved in the reaction cascade that forms fibrin. When tissue is injured, the extrinsic pathway is activated by the release of thromboplastin from the tissue. As the result of a series of reactions, prothrombin is converted to thrombin, which in turn catalyzes the conversion of fibrinogen to fibrin. Clotting by the intrinsic or contact activation pathway is activated when the collagen that lines blood vessels is exposed. Clotting factors are activated sequentially until, as with the extrinsic pathway, fibrin is ultimately formed (Rockwell, 2019). The intrinsic pathway is slower, and this sequence is less often responsible for clotting in response to tissue injury. However, it is important if a noninjured vessel wall comes into contact with lipoproteins (e.g., atherosclerosis) or with bacteria, resulting in a clot that is formed for purposes other than protection from trauma or bleeding.

As the injured vessel is repaired and again covered with endothelial cells, the fibrin clot is no longer needed. The fibrin is digested via two systems: the plasma fibrinolytic system and the cellular fibrinolytic system. The protein **plasminogen** is required to lyse (break down) the fibrin. Plasminogen, which is present in all body fluids, circulates with fibrinogen and is therefore incorporated into the fibrin clot as it forms. When the clot is no longer needed (e.g., after an injured blood vessel has healed), the plasminogen is activated to form plasmin. Plasmin digests the fibrinogen and fibrin. The breakdown particles of the clot, called *fibrin degradation products*, are released into the circulation. Through this system, clots are dissolved as tissue is repaired, and the vascular system returns to its normal baseline state.



Gerontologic Considerations

In older adults, the bone marrow's ability to respond to the body's need for blood cells (erythrocytes, leukocytes, and platelets) may be decreased, resulting in **leukopenia** (a decreased number of circulating leukocytes) or anemia. This decreased ability is a result of many factors, including diminished production of the growth factors necessary for hematopoiesis by stromal cells within the marrow or a diminished response to the growth factors (in the case of erythropoietin). Over time, stem cells within the marrow acquire damage to their DNA, which compromises their function. T- and B-cell development is also decreased. This age-related decrease in immune system response due to diminished production and function of blood cells designed to protect the body is called immunosenescence (Yeager, 2019).

Assessment

Health History

A careful health history and physical assessment can provide important information related to a patient's known or potential hematologic diagnosis. Because many hematologic disorders are more prevalent in certain ethnic groups, assessments of ethnicity and family history are useful (see [Chart 28-1](#)). Similarly, obtaining a nutritional history and assessing the use of prescription and over-the-counter medications, as well as herbal supplements, are important to note, because several conditions can result from nutritional deficiencies, or from the use of certain herbs or medications. Careful attention to the onset of a symptom or finding (e.g., rapid vs. gradual; persistent vs. intermittent), its severity, and any contributing factors can further differentiate potential causes. Of equal importance is assessing the impact of these findings on the patient's functional ability, manifestations of distress, and coping mechanisms.

Chart 28-1



GENETICS IN NURSING PRACTICE

Hematologic Disorders

Hematologic disorders are marked by aberrations in the structure or function of the blood cells or the blood clotting mechanism. Some examples of genetic hematologic disorders are:

Autosomal Dominant:

- Factor V Leiden
- Familial hypercholesterolemia
- Hereditary angioedema
- Hereditary spherocytosis
- von Willebrand disease

Autosomal Recessive:

- Hemochromatosis
- Sickle cell disease
- Thalassemia

X-Linked:

- Hemophilia

Nursing Assessments

Refer to Chapter 4, Chart 4-2: Genetics in Nursing Practice: Genetic Aspects of Health Assessment

Family History Assessment Specific to Hematologic Disorders

- Collect family history information on maternal and paternal relatives from three generations of the family.
- Assess family history for other family members with histories of blood disorders or episodes of abnormal bleeding.
- If a family history or personal risk is suspected, the person should be carefully screened for bleeding disorders prior to surgical procedures.

Patient Assessment Specific to Hematologic Disorders

- Assess for specific symptoms of hematologic diseases:
 - Extreme fatigue (the most common symptom of hematologic disorders)
 - Delayed clotting of blood
 - Easy or deep bruising

- Abnormal bleeding (e.g., frequent nosebleeds)
- Abdominal pain (hemochromatosis) or joint pain (sickle cell disease)
- Review blood cell counts for abnormalities.
- Assess for presence of illness despite low risk for the illness (e.g., a young adult with a blood clot)

Resources

Hemophilia Federation of America, www.hemophiliafed.org

Iron Disorders Institute: Hemochromatosis, www.hemochromatosis.org

Sickle Cell Association of America, www.sicklecelldisease.org

See [Chapter 6, Chart 6-7](#), for components of genetic counseling.

Physical Assessment

The physical assessment should be comprehensive and include careful attention to the skin, oral cavity, lymph nodes, and spleen (see [Fig. 28-4](#)). [Table 28-2](#) highlights a general approach to the physical assessment findings in hematologic disorders (more specific findings are presented in Chapters 29 and 30).

Diagnostic Evaluation

Most hematologic diseases reflect a defect in the hematopoietic, hemostatic, or reticuloendothelial systems. The defect can be quantitative (e.g., increased or decreased production of cells), qualitative (e.g., the cells that are produced are defective in their expected functional capacity), or both. Initially, many hematologic conditions cause few symptoms, and extensive laboratory tests are often required to establish a diagnosis. For most hematologic conditions, continued monitoring via specific blood tests is required because it is very important to assess for changes in test results over time. In general, it is important to assess trends in test results because these trends help the clinician decide whether the patient is responding appropriately to interventions.

Hematologic Studies

The most common tests used are the complete blood count (CBC) and the peripheral blood smear. The CBC identifies the total number of blood cells (leukocytes, erythrocytes, and platelets) as well as the hemoglobin, **hematocrit** (percentage of blood volume consisting of erythrocytes), and RBC indices. Because cellular morphology (shape and appearance of the cells) is

particularly important in accurately diagnosing most hematologic disorders, the blood cells involved must be examined. This process is referred to as the manual examination of the peripheral smear, which may be part of the CBC. In this test, a drop of blood is spread on a glass slide, stained, and examined under a microscope. The shape and size of the erythrocytes and platelets, as well as the actual appearance of the leukocytes, provide useful information in identifying hematologic conditions. Blood for the CBC is typically obtained by venipuncture (Fischbach & Fischbach, 2018).

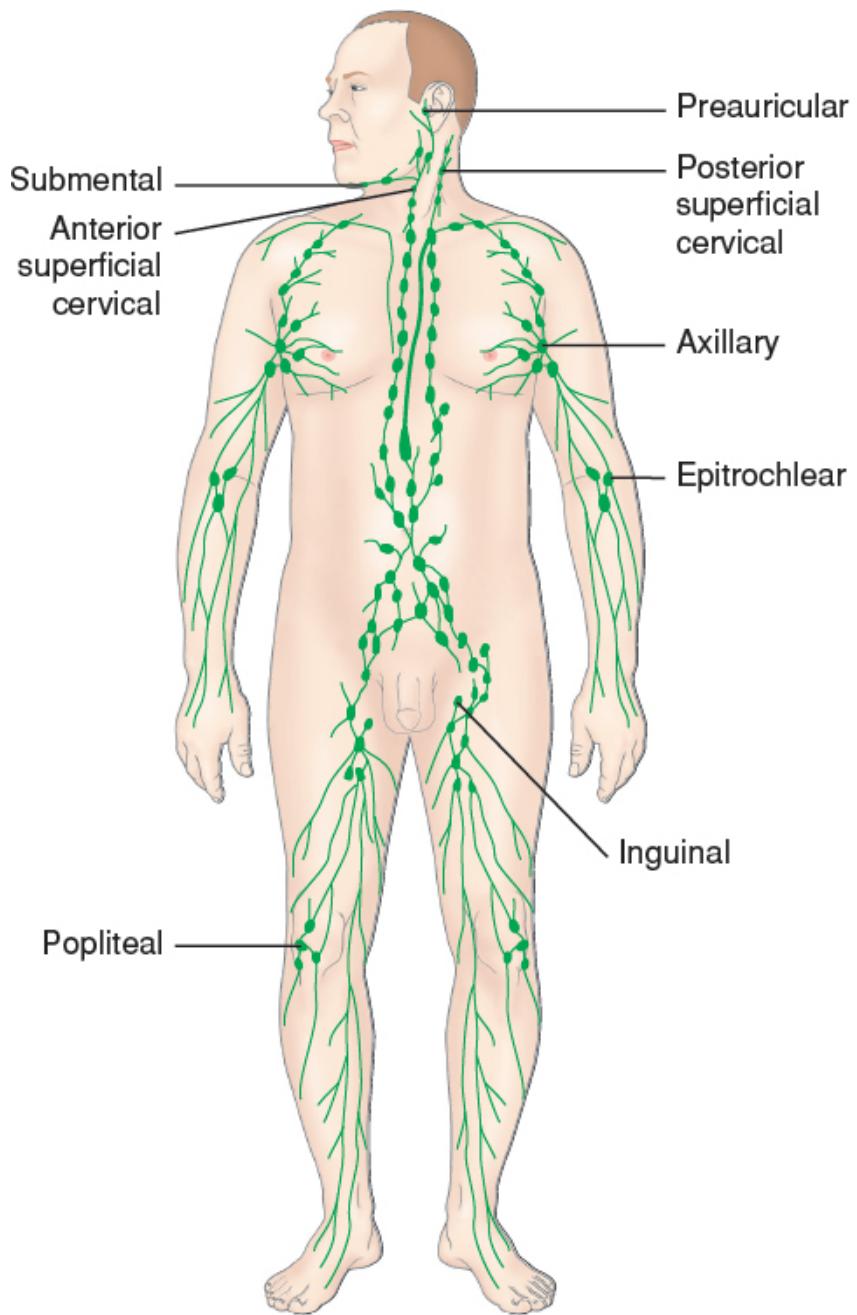


Figure 28-4 • Lymphatic system. Sites where lymph nodes are accessible for palpation. Developed by Thomas, M., & Morrow, K. (2011). Veterans Administration Palo Alto Health Care System.

TABLE 28-2

Health History and Physical Assessment in
Hematologic Disorders^a

	Findings	Potential Indications of Hematologic Disorder
Health History	Prior episodes of bleeding (epistaxis, tooth, gum, hematuria, menorrhagia, hematochezia, gastrointestinal bleeding and/or ulcers)	Thrombocytopenia, coagulopathy, anemia
	Prior blood clots, pulmonary emboli, miscarriages	Thrombotic disorder
	Fatigue and weakness	Anemia, infection, malignancy, clonal disorders
	Dyspnea, particularly dyspnea on exertion, orthopnea, shortness of breath	Anemia, infection
	Prior radiation therapy (especially pelvic irradiation)	Anemia, pancytopenia, myelodysplastic syndrome, leukemia
	Prior chemotherapy	Myelodysplastic syndrome, leukemia
	Hobbies/occupational/military exposure history (especially benzene, Agent Orange)	Myelodysplastic syndrome, leukemia, myeloma, lymphoma
	Diet history	Anemia (due to vitamin B ₁₂ , folate, iron deficiency)
	Alcohol consumption	Anemia (effect on hematopoiesis, nutritional deficiency)
	Use of herbal supplements	Platelet dysfunction
	Concurrent medications	Neutropenia, anemia, hemolysis, thrombocytopenia
	Family history/ethnicity	Some hematologic disorders have a higher prevalence in certain ethnic groups and families (see Chart 28-1)
Physical Assessment		
Skin	Gray-tan or bronze skin color (especially genitalia, scars, exposed areas)	Hemochromatosis (primary or secondary)
	Ruddy complexion (face, conjunctiva, hands, feet)	Polycythemia
	Ecchymoses (i.e., bruises)	Thrombocytopenia, coagulopathy
	Petechiae (i.e., pinpoint hemorrhagic	Severe thrombocytopenia

		lesions, usually more prominent on trunk or anterior aspects of lower extremities)
	Rash	Variable; if pruritic, may indicate polycythemia, other non-hematologic-related disorders (see Chapter 56)
	Bleeding (including around vascular lines, tubes)	Thrombocytopenia, coagulopathy
	Conjunctival hemorrhage	Severe thrombocytopenia, coagulopathy
	Pallor, especially in mucous membranes (including conjunctiva), nail beds	Anemia
	Jaundice in mucous membranes (including conjunctiva), nail beds, palate	Hemolysis
Oral cavity	Petechiae in the buccal mucosa, gingiva, hard palate	Severe thrombocytopenia
	Ulceration of oral mucosa	Infection, leukemia
	Tongue: Smooth	Pernicious anemia
	Beefy red	Vitamin B ₁₂ /folate deficiency
	Enlarged	Amyloidosis
	Angular cheilosis (ulceration at corners of mouth)	Anemia
	Enlarged gums: hyperplasia	Leukemia
Lymph nodes	Enlarged size, firm and fixed vs. mobile and tender	Leukemia, lymphoma
Respiratory	Increased rate and depth of respirations; adventitious breath sounds	Anemia; infection
Cardiovascular	Distended neck veins, edema, chest pain on exertion, murmurs, gallops	Severe anemia
	Hypotension (below baseline)	Polycythemia
	Hypertension (above baseline)	
Genitourinary	Hematuria	Hemolysis, thrombocytopenia
	Proteinuria	Myeloma
Musculoskeletal	Rib/sternal tenderness to palpation	Leukemia, myeloma
	Back pain; tenderness to palpation over spine, loss of height, kyphosis	Myeloma
	Pain/swelling in knees, wrists, hands	Hemophilia, sickle cell disease
Abdominal	Enlarged spleen	Leukemia, myelofibrosis
	Enlarged liver	Myelofibrosis

	Stool positive for occult blood	Anemia, thrombocytopenia
Central nervous system	Cranial nerve dysfunction	Vitamin B ₁₂ deficiency
	Peripheral nerve dysfunction (especially sensory)	Vitamin B ₁₂ deficiency, amyloidosis, myeloma
	Visual changes, headache, alteration in mental status	Severe thrombocytopenia
Gynecologic	Menorrhagia	Thrombocytopenia, coagulopathy
Constitutional	Fever, chills, sweats, asthenia	Leukemia, lymphoma; infection

^aCommon findings (obtained via health history and physical assessment) that occur in patients with hematologic disorders. Note that signs and symptoms are not disease specific but are useful in guiding the nurse to establishing an etiology for the findings noted.

Adapted from Bickley, L. S. (2016). *Bates' guide to physical examination and history taking* (12th ed.). Philadelphia, PA: Lippincott Williams & Wilkins; Weber, J. W., & Kelley, J. (2018). *Health assessment in nursing* (6th ed.). Philadelphia, PA: Wolters Kluwer.

Other common tests of coagulation are the prothrombin time (PT), typically replaced by the standardized test, international normalized ratio (INR), and the activated partial thromboplastin time (aPTT). The INR and aPTT serve as useful screening tools for evaluating a patient's clotting ability and monitoring the therapeutic effectiveness of anticoagulant medications. In both tests, specific reagents are mixed into the plasma sample, and the time taken to form a clot is measured. For these tests to be accurate, the test tube must be filled with the correct amount of the patient's blood; either excess or inadequate blood volume within the tube can render the results inaccurate.

Bone Marrow Aspiration and Biopsy

Bone marrow aspiration and biopsy are crucial when additional information is needed to assess how a patient's blood cells are being formed and to assess the quantity and quality of each type of cell produced within the marrow. Also, results of these tests can be used to document infection or tumor within the marrow. Other specialized tests can be performed on the marrow aspirate, such as cytogenetic analysis or immunophenotyping (i.e., identifying specific proteins expressed by cells), and are useful to identify certain malignant conditions and form a prognosis.

Normal bone marrow is in a semifluid state and can be aspirated through a special large needle. In adults, bone marrow is usually aspirated from the iliac crest and occasionally from the sternum. The bone marrow aspirate provides a sample of cells from the more fluid part of the bone marrow and may not be adequate for evaluating certain conditions, such as anemia. When more

information is required, a bone marrow biopsy is performed, which examines a solid part of the bone marrow. Biopsy samples are taken from the posterior iliac crest; although occasionally, an anterior approach is required. A marrow biopsy shows the architecture of the bone marrow as well as its degree of cellularity.

Patient preparation includes a careful explanation of the procedure, which may be done at the patient's bedside (for a patient who is hospitalized) or in the outpatient setting. Some patients may be anxious, thus an anxiolytic agent may be prescribed. It is essential the physician or nurse explain the procedure, including risks, benefits and alternatives, and describe sensations the patient may experience. A signed informed consent is required for a bone marrow aspiration and biopsy.

Before aspiration, the skin is cleansed using aseptic technique. Next, a small area is anesthetized with a local anesthetic agent through the skin and subcutaneous tissue to the periosteum of the bone; it is not possible to anesthetize the bone itself. The bone marrow needle is introduced with a stylet in place. When the needle moves through the outer cortex of bone and enters the marrow cavity, the stylet is removed, and a syringe is attached. A small volume (5 mL) of blood and marrow is then aspirated. Patients typically feel a pressure sensation as the needle is advanced into position. The actual aspiration always causes sharp but brief pain, resulting from the suction exerted as the marrow is aspirated into the syringe. Taking deep breaths or using relaxation techniques often helps ease the discomfort (see [Fig. 28-5](#)).

A bone marrow biopsy is most often performed with a bone marrow aspiration and is called a bone marrow exam (Mayo Clinic, 2018a). The bone marrow aspirate is used to determine types and numbers of cells present in the bone marrow. The bone marrow biopsy consists of an actual tissue sample used to study the architecture of the bone marrow and confirm diagnoses (Wimberly, 2019). For a bone marrow biopsy, a special biopsy needle is used. Because these needles are large, the skin may be punctured first with a surgical blade to make a 3- to 4-mm incision. The biopsy needle is advanced well into the marrow cavity. When the needle is properly positioned, a portion of marrow is cored out. The patient feels a pressure sensation but should not feel actual pain. The nurse should assist the patient in maintaining a comfortable position and encourage relaxation and deep breathing throughout the procedure. The patient should be instructed to inform the physician if pain occurs so that an additional anesthetic agent can be given.

Potential complications of either bone marrow aspiration or biopsy include bleeding and infection. The risk of bleeding is somewhat increased if the patient's platelet count is low or if the patient has been taking a medication that alters platelet function (e.g., aspirin). After the marrow sample is obtained, pressure is applied to the site for several minutes. The site is then covered with a sterile dressing. Most patients have no discomfort after a bone marrow

aspiration, but the site of a biopsy may ache for 1 or 2 days. Warm tub baths and a mild analgesic agent (e.g., acetaminophen) may be useful. Aspirin-containing analgesic agents should be avoided in the immediate postprocedure period because they can aggravate or potentiate bleeding. Also, no rigorous activity or exercise for 1 to 2 days is recommended (Mayo Clinic, 2018a).

Unfolding Patient Stories: Lloyd Bennett • Part 1



Lloyd Bennett is a 76-year-old male who fell while working outdoors. He presents to the emergency department with a hip fracture. What physical assessment and laboratory data can assist the nurse in evaluation for possible internal blood loss from the fracture or indications that the patient is at higher risk of bleeding? (Lloyd Bennett's story continues in Chapter 47.)

Care for Lloyd and other patients in a realistic virtual environment: **vSim**(thepoint.lww.com/vSimMedicalSurgical). Practice documenting these patients' care in DocuCare (thepoint.lww.com/DocuCareEHR).

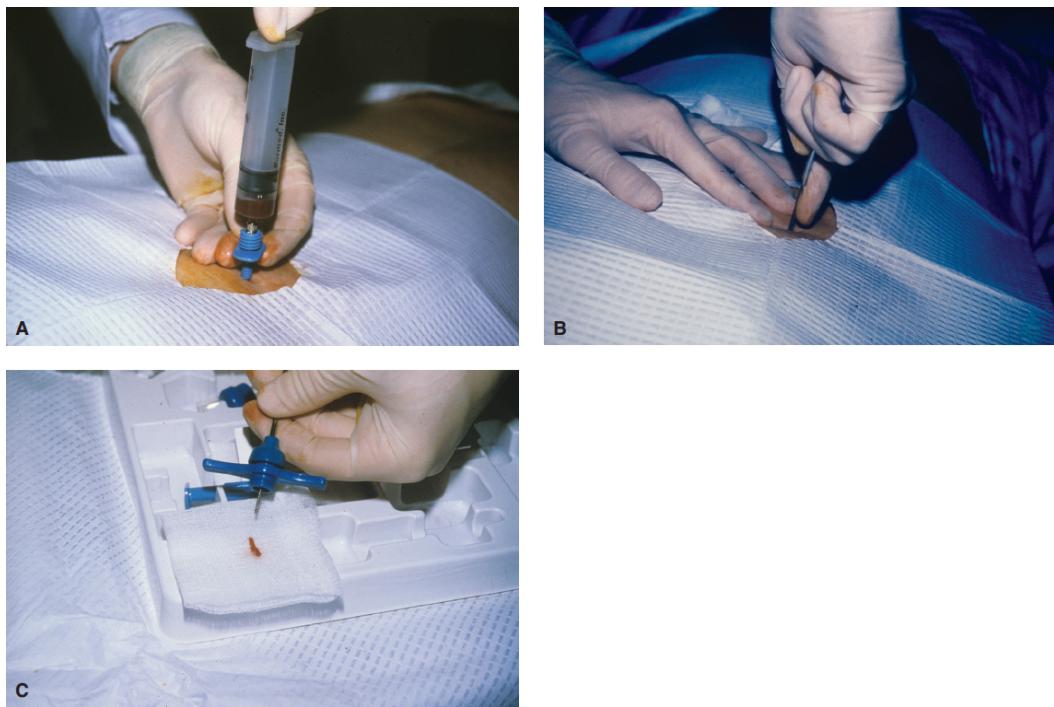


Figure 28-5 • Bone marrow aspiration procedure. The posterior superior iliac crest is the preferred site for bone marrow aspiration and biopsy because no vital organs or vessels are nearby. The patient is placed either in the lateral position with one leg flexed or in the prone position. The anterior iliac crest or sternum may also be used. Note that the sternum cannot be used for a marrow biopsy. **A.** Bone marrow aspiration. **B.** Inserting a Jamshidi biopsy needle. **C.** Dispensing the bone marrow core. Reprinted with permission from Farhi, D. C. (2009). *Pathology of bone marrow and blood cells* (2nd ed.). Philadelphia, PA: Lippincott Williams & Wilkins.

Therapeutic Approaches to Hematologic Disorders

Splenectomy

The surgical removal of the spleen, called splenectomy, is a possible treatment for some hematologic disorders. For example, an enlarged spleen may be the site of excessive destruction of blood cells. In addition, some patients with grossly enlarged spleens develop severe thrombocytopenia as a result of platelets being sequestered in the spleen. Splenectomy removes the “trap,” and platelet counts may normalize over time.

Laparoscopic splenectomy is associated with decreased postoperative morbidity compared to open splenectomy. Acute risks associated with a splenectomy include hemorrhage, increased clotting, and injury to surrounding

organs and tissues. Long-term risks post splenectomy includes greater likelihood to develop life-threatening infections. Patients should be vaccinated for pneumonia before undergoing splenectomy, if possible. The patient is instructed to seek prompt medical attention for even minor symptoms of infection. The Centers for Disease Control and Prevention (CDC, 2020) recommends patients without spleens receive vaccines for influenza, pneumonia, and meningococci. Also, if a patient has other conditions that increase risk of serious infection in addition to a history of splenectomy, they may need antibiotic prophylaxis (Mayo Clinic, 2018b).

Therapeutic Apheresis

Apheresis is a Greek word meaning “separation.” In therapeutic apheresis (or pheresis), blood is taken from the patient and passed through a centrifuge, where a specific component is separated from the blood, removed (see [Table 28-3](#)), and the remaining blood is returned to the patient. The entire system is closed, so the risk of bacterial contamination is low. When platelets or leukocytes are removed, the decrease in these cells within the circulation is temporary. Platelet donors can have their platelets apheresed as often as every 14 days. Leukocytes can be obtained similarly, typically after the donor has received growth factors (granulocyte colony-stimulating factor, granulocyte-macrophage colony-stimulating factor) to stimulate the formation of additional leukocytes and thereby increase the leukocyte count. The use of these growth factors also stimulates the release of stem cells within the circulation. Apheresis is used to harvest these stem cells (typically over a period of several days) for use in peripheral blood stem cell transplant (Padmanabhan, Smith, Aqui, et al., 2019). Sometimes plasma is removed rather than blood cells, and this process is called plasmapheresis. Indications for plasmapheresis include obtaining plasma for transfusion and removing dangerous substances such as immune complexes and autoantibodies (Sarode, 2018).

Hematopoietic Stem Cell Transplantation

Hematopoietic stem cell transplantation (HSCT) is a therapeutic modality that offers the possibility of cure for some patients with hematologic disorders such as severe aplastic anemia, some forms of leukemia, and thalassemia. It can also provide longer remission from disease even when cure is not possible, such as in multiple myeloma. Hematopoietic stem cells may be transplanted from either allogeneic or autologous donors. For most hematologic diseases, allogeneic transplant is more effective (Bazinet & Popradi, 2019); here, stem cells are obtained from a donor whose cells match those of the patient. In contrast, the patient’s own stem cells are harvested and then used in autologous transplant. (See [Chapter 12](#) for a detailed discussion of HSCT.)

TABLE 28-3 Types of Apheresis^a

Procedure	Purpose	Examples of Clinical Use
Plateletpheresis	Remove platelets	Extreme thrombocytosis, essential thrombocythemia (temporary measure); single-donor platelet transfusion
Leukapheresis	Remove WBCs (can be specific to neutrophils or lymphocytes)	Extreme leukocytosis (e.g., AML, CML) (very temporary measure); harvest WBCs for transfusion
Erythrocytapheresis (RBC exchange)	Remove RBCs	RBC dyscrasias (e.g., sickle cell disease); RBCs replaced via transfusion
Plasmapheresis (plasma exchange)	Remove plasma proteins	Hyperviscosity syndromes; treatment for some renal and neurologic diseases (e.g., Goodpasture syndrome, TTP, Guillain–Barré, myasthenia gravis)
Stem cell harvest	Remove circulating stem cells	Transplantation (donor harvest or autologous)

^aTherapeutic apheresis can be used to treat a wide variety of conditions. When it is used to treat a disease that causes an increase in a specific cell type with a short life in circulation (i.e., WBCs, platelets), the reduction in those cells is temporary. However, this temporary reduction permits a margin of safety while waiting for a longer-lasting treatment modality (e.g., chemotherapy) to take effect. Apheresis can also be used to obtain stem cells for transplantation, either from a matched donor (allogeneic) or from the patient (autologous).

AML, acute myeloid leukemia; CML, chronic myeloid leukemia; RBC, red blood cell; TTP, thrombotic thrombocytopenic purpura; WBCs, white blood cells.

Adapted from Padmanabhan, A., Smith, L., Aqui, N., et al. (2019). Guidelines on the use of therapeutic apheresis in clinical practice—evidence-based approach from the Writing Committee of the American Society for Apheresis: The eighth special issue. *Journal of Clinical Apheresis*, 34(3), 171–354.

Therapeutic Phlebotomy

Therapeutic phlebotomy is the removal of a certain amount of blood under controlled conditions. Patients with elevated hematocrits (e.g., those with polycythemia vera) or excessive iron absorption (e.g., hemochromatosis) can usually be managed by periodically removing 1 unit (about 500 mL) of whole blood. Over time, this process can produce iron deficiency, leaving the patient unable to produce as many erythrocytes. The actual procedure for therapeutic phlebotomy is similar to that for blood donation (see later discussion).

Blood Component Therapy

A single unit of whole blood contains 450 mL of blood and 50 mL of an anticoagulant, which can be processed and dispensed for administration.

However, it is more appropriate, economical, and practical to separate that unit of whole blood into its primary components: erythrocytes, platelets, and plasma (leukocytes are rarely used; see later discussion).

Each component must be processed and stored differently to maximize the longevity of the viable cells and factors within it; thus, each individual blood component has a different storage life. Because the plasma is removed, a unit of packed red blood cells (PRBCs) is very concentrated (hematocrit approximately 70%) (Butterworth, Mackey, & Wasnick, 2018). PRBCs are stored at 4°C (39.2°F). With special preservatives, they can be stored safely for up to 42 days before they must be discarded (American Red Cross, 2020a).

In contrast, platelets must be stored at room temperature because they cannot withstand cold temperatures, and they last for only 5 days before they must be discarded. To prevent clumping, platelets are gently agitated while stored. Plasma is immediately frozen to maintain the activity of the clotting factors within; it lasts for 1 year if it remains frozen. Alternatively, plasma can be further pooled and processed into blood derivatives, such as albumin, immune globulin, factor VIII, and factor IX. [Table 28-4](#) describes each blood component and how it is commonly used.

Special Preparations

Factor VIII concentrate (antihemophilic factor) is a lyophilized, freeze-dried concentrate of pooled fractionated human plasma used in treating hemophilia A. Factor IX concentrate (prothrombin complex) is similarly prepared and contains factors II, VII, IX, and X. It is used primarily for the treatment of factor IX deficiency (hemophilia B). Factor IX concentrate is also useful in treating congenital factor VII and factor X deficiencies. Recombinant forms of factor VIII, such as Humate-P or Alphanate, are also useful. Because they contain von Willebrand factor, these agents are used in von Willebrand disease as well as in hemophilia A, particularly when patients develop factor VIII inhibitors.

Plasma albumin is a large protein molecule that usually stays within vessels and is a major contributor to plasma oncotic pressure. This protein is used to expand the blood volume of patients in hypovolemic shock and, rarely, to increase the concentration of circulating albumin in patients with hypoalbuminemia.

Immune globulin is a concentrated solution of the antibody immunoglobulin G (IgG), prepared from large pools of plasma. It contains very little immunoglobulin A (IgA) or IgM. Intravenous immunoglobulin (IVIG) is used in various clinical situations to replace inadequate amounts of IgG in patients who are at risk for recurrent bacterial infection (e.g., those with chronic lymphocytic leukemia, those receiving HSCT). It is also used in certain autoimmune disorders, such as idiopathic thrombocytopenic purpura (ITP). Albumin, antihemophilic factors, and IVIG, in contrast to all other

fractions of human blood, cells, or plasma, can survive being subjected to heating at 60°C (140°F) for 10 hours to free them of the viral contaminants that may be present.

TABLE 28-4 Blood and Blood Components Commonly Used in Transfusion Therapy^a

Component	Composition	Indications and Considerations
Whole blood	Cells and plasma; hematocrit about 40%	Volume replacement and oxygen-carrying capacity; usually used only in significant bleeding (>25% blood volume lost)
PRBCs	RBCs with little plasma (hematocrit about 75%); some platelets and WBCs remain	↑ RBC mass; symptomatic anemia: <ul style="list-style-type: none"> • Platelets within the unit are not functional • WBCs within the unit may cause reaction and are not functional
Platelets—random	Platelets (5.5×10^{10} platelets/unit), plasma; some RBCs, WBCs	Bleeding due to severe ↓ platelets Prevent bleeding when platelets $<5,000\text{--}10,000/\text{mm}^3$ Survival ↓ in presence of fever, chills, infection Repeated treatment leads to ↓ survival due to alloimmunization
Platelets—single donor	Platelets (3×10^{11} platelets/unit) 1 unit is equivalent to 6–8 units of random platelets	Used for repeated treatment: <ul style="list-style-type: none"> • darr; alloimmunization risk by limiting exposure to multiple donors
Plasma	Plasma; all coagulation factors Complement	Bleeding in patients with coagulation factor deficiencies; plasmapheresis
Granulocytes	Neutrophils ($>1 \times 10^{10}/\text{unit}$); some lymphocytes, RBCs, and platelets will remain within the unit	Severe neutropenia in select patients; controversial
Lymphocytes	Lymphocytes (number varies)	Stimulate graft-vs.-host disease effect
Cryoprecipitate	Fibrinogen ≥ 150 mg/bag, AHF (VIII:C) 80–110 units/bag, von Willebrand factor; fibronectin	von Willebrand disease Hypofibrinogenemia Hemophilia A
AHF	Factor VIII	Hemophilia A
Factor IX concentrate	Factor IX	Hemophilia B (Christmas disease)
Factor IX complex	Factors II, VII, IX, X	Hereditary factor VII, IX, X deficiency; hemophilia A with factor VII inhibitors
Albumin	Albumin 5%, 25%	Hypoproteinemia; burns; volume expansion by 5% to ↑ blood volume; 25% leads to ↓ hematocrit
IV gamma-globulin	Immunoglobulin G antibodies	Hypogammaglobulinemia (in CLL, recurrent infections); ITP; primary

		immunodeficiency states
Antithrombin III concentrate (AT III)	AT III (trace amounts of other plasma proteins)	AT III deficiency with or at risk for thrombosis

^aThe composition of each type of blood component is described as well as the most common indications for using a given blood component. RBCs, platelets, and fresh-frozen plasma are the blood products most commonly used. When transfusing these blood products, it is important to realize that the individual product is always “contaminated” with very small amounts of other blood products (e.g., WBCs mixed in a unit of platelets). This contamination can cause some difficulties, particularly isosensitization, in certain patients.

↑, increased; ↓, decreased; AHF, antihemophilic factor; CLL, chronic lymphocytic leukemia; ITP, idiopathic thrombocytopenic purpura; IV, intravenous; PRBCs, packed red blood cells; RBCs, red blood cells; WBCs, white blood cells.

Adapted from American Red Cross. (2020b). How can one donation help multiple people? Retrieved on 1/15/2020 at: www.redcrossblood.org/faq.html#eligibility; Stowell, C. P. (2019). Transfusion medicine. In M. Laposata (Ed.). *Laboratory medicine: Diagnosis of disease in the clinical laboratory* (3rd ed., pp. 321–348). New York: McGraw-Hill.

Procuring Blood and Blood Products

The process of procuring blood and blood products includes donation and processing.

Blood Donation

To protect both the donor and the recipients, all prospective donors are examined and interviewed before they are allowed to donate their blood. The intent of the interview is to assess the general health status of the donor and to identify risk factors that might harm a recipient of the donor’s blood. There is no upper age limit to donation. The American Red Cross (2020c) requires that donors be in good health and meet specific eligibility criteria related to medications and vaccinations, medical conditions and treatments, travel outside the United States, lifestyle and life events, and so on. Detailed information about these criteria is available on the American Red Cross Web site (see the Resources section). Examples of these minimal requirements include (American Red Cross, 2020a, 2020d):

- Body weight should be at least 50 kg (110 lb) for a standard 450-mL donation.
- Donors must wait at least 8 weeks between whole blood (standard) donations.
- People younger than 17 years require parental consent in some states.
- The oral temperature should not exceed 37.5°C (99.6°F).

- The systolic arterial blood pressure should be 80 to 180 mm Hg, and the diastolic pressure should be 50 to 100 mm Hg.
- The hemoglobin level should be at least 12.5 g/dL.
- The destinations of people who traveled outside the United States and Canada within the past 3 years are reviewed; a waiting period maybe required before a donation is accepted.
- Prospective donors who received a blood transfusion must wait 12 months before a donation is accepted.
- Men who have sexual relations with men must wait 3 months from their last sexual encounter before a donation is accepted.

The American Red Cross follows the U.S. Food and Drug Administration (FDA) policy for donors who are lesbian, gay, bisexual, transgender, or queer (LGBTQ) and provides support for these individuals through the American Red Cross LGBTQ+ Team Member Resource Group (see Resources section at the end of the chapter).

Directed Donation

At times, friends and family of a patient wish to donate blood for that person. These blood donations are referred to as directed donations. These donations are not any safer than those provided by random donors, because directed donors may not be as willing to identify themselves as having a history of any of the risk factors that disqualify a person from donating blood. Therefore, many blood centers no longer accept directed donations.

Standard Donation

Phlebotomy consists of venipuncture and blood withdrawal. Standard precautions are used. Donors are placed in a semirecumbent position. The skin over the antecubital fossa is carefully cleansed with an antiseptic preparation, a tourniquet is applied, and venipuncture is performed. Withdrawal of 450 mL of blood usually takes less than 15 minutes. After the needle is removed, donors are asked to hold the involved arm straight up, and firm pressure is applied with sterile gauze for 2 to 3 minutes. A firm bandage is then applied. The donor remains recumbent until they feel able to sit up, usually within a few minutes. Donors who experience weakness or faintness should rest for a longer period. The donor then receives food and fluids and is asked to remain another 15 minutes.

The donor is instructed to leave the dressing on and to avoid heavy lifting for several hours, to avoid smoking for 1 hour, to avoid drinking alcoholic beverages for 3 hours, to increase fluid intake for 2 days, and to eat healthy meals for at least 2 weeks. Specimens from the donated blood are tested to

detect infections and to identify the specific blood type (see later discussion under Blood Processing).

Autologous Donation

A patient's own blood may be collected for future transfusion; this method is useful for many elective surgeries where the potential need for transfusion is high (e.g., orthopedic surgery). Preoperative donations are ideally collected 4 to 6 weeks before surgery. Iron supplements are prescribed during this period to prevent depletion of iron stores. Typically, 1 unit of blood is drawn each week; the number of units obtained varies with the type of surgical procedure to be performed (i.e., the amount of blood anticipated to be transfused). Phlebotomies are not performed within 72 hours of surgery. Individual blood components can also be collected.

The primary advantage of autologous transfusions is the prevention of viral infections from another person's blood. Other advantages include safe transfusion for patients with a history of transfusion reactions, prevention of alloimmunization, and avoidance of complications in patients with alloantibodies. It is the policy of the American Red Cross that autologous blood is transfused only to the donor. If the blood is not required, it is discarded. The blood is never returned to the general donor supply of blood products to be used by another person (American Red Cross, 2020a).

Needless autologous donation (i.e., performed when the likelihood of transfusion is small) is discouraged because it is expensive, takes time, and uses resources inappropriately. Moreover, in an emergency situation, the autologous units available may be inadequate, and the patient may still require additional units from the general donor supply. Furthermore, although autologous transfusion can eliminate the risk of viral contamination, the risk of bacterial contamination is the same as that in transfusion from random donors (Stowell, 2019).

Contraindications to donation of blood for autologous transfusion are acute infection, severely debilitating chronic disease, hemoglobin level less than 11 g/dL, unstable angina, and acute cardiovascular or cerebrovascular disease. A history of poorly controlled epilepsy may be considered a contraindication in some centers.

Intraoperative Blood Salvage

This transfusion method provides replacement for patients who cannot donate blood before surgery and for those undergoing vascular, orthopedic, or thoracic surgery. During a surgical procedure, blood lost into a sterile cavity (e.g., hip joint) is suctioned into a cell-saver machine. The whole blood or PRBCs are washed, often with saline solution; filtered; and then returned to the patient as

an IV infusion. Salvaged blood cannot be stored, because bacteria cannot be completely removed from the blood and thus cannot be used when it is contaminated with bacteria. The use of intraoperative blood salvage has decreased the need for autologous blood donation but has not affected the need for allogeneic blood products (Sikorski, Rizkalla, Yang, et al., 2017).

Hemodilution

This transfusion method may be initiated before or after induction of anesthesia. About 1 to 2 units of blood are removed from the patient through a venous or arterial line and simultaneously replaced with a colloid or crystalloid solution. The blood obtained is then reinfused after surgery. The advantage of this method is that the patient loses fewer erythrocytes during surgery, because the added IV solutions dilute the concentration of erythrocytes and lower the hematocrit. However, patients who are at risk for myocardial injury should not be further stressed by hemodilution. Hemodilution has been associated with adverse outcomes in patients having cardiopulmonary bypass; it has also been linked to tissue ischemia, particularly in the kidneys (Hare, Han, Leshchyshyn, et al., 2018).

Complications of Blood Donation

Excessive bleeding at the donor's venipuncture site is sometimes caused by a bleeding disorder but more often results from a technique error: laceration of the vein, excessive tourniquet pressure, or failure to apply enough pressure after the needle is withdrawn.

Fainting may occur after blood donation and may be related to emotional factors, a vasovagal reaction, or prolonged fasting before donation. Because of the loss of blood volume, hypotension and syncope may occur when the donor assumes an erect position (John, Theodora, Gloria, et al., 2017). A donor who appears pale or complains of faintness should immediately lie down or sit with the head lowered below the knees. The donor should be observed for another 30 minutes.

Anginal chest pain may be precipitated in patients with unsuspected coronary artery disease. Seizures can occur in donors with epilepsy, although the incidence is very low. Both angina and seizures require further medical evaluation and treatment.

Blood Processing

Samples of the unit of blood are always taken immediately after donation so that the blood can be typed and tested. Each donation is tested for antibodies to human immune deficiency virus (HIV) types 1 and 2, hepatitis B core antibody

(anti-HBc), hepatitis C virus (HCV), human T-cell lymphotropic virus type I (anti-HTLV-I/II), hepatitis B surface antigen (HbsAG), and syphilis. Negative reactions are required for the blood to be used, and each unit of blood is labeled to certify the results. Nucleic acid amplification testing has increased the ability to detect the presence of HCV, HIV, and West Nile virus infections, because it directly tests for genomic nucleic acids of the viruses rather than for the presence of antibodies to the viruses. This testing significantly shortens the “window” of inability to detect HIV and HCV from a donated unit, further ensuring the safety of the blood; the risk of transmission of HIV or HCV is now estimated at 1 in 2 million units and 1 in 1.6 million units of blood donated, respectively (American Cancer Society, 2017). Blood is also screened for cytomegalovirus (CMV). If it tests positive for CMV, it can still be used, except in recipients who are negative for CMV and who are severely immunocompromised; any components are labeled as CMV positive.

Equally important is accurate determination of the blood type. More than 200 antigens have been identified on the surface of RBC membranes. Of these, the most important for safe transfusion are the ABO and Rh systems. The ABO system identifies which sugars are present on the membrane of a person’s erythrocytes: A, B, both A and B, or neither A nor B (type O). To prevent a significant reaction, the same type of PRBCs should be transfused. Previously, it was thought that in an emergency situation in which the patient’s blood type was not known, type O blood could be safely transfused. This practice is no longer recommended.

The Rh antigen (also referred to as D) is present on the surface of erythrocytes in 85% of the population (Rh positive). Those who lack the D antigen are referred to as being Rh negative. PRBCs are routinely tested for the D antigen as well as ABO. Patients should receive PRBCs with a compatible Rh type.

The majority of transfusion reactions are due to clerical errors, including mislabeling, inaccuracy transcribing orders and incorrect verification of product and patient. When these errors occur, the patient is transfused an incompatible unit of blood product (Stubbs, 2018). Reactions (other than those due to procedural error) are most frequently due to the presence of donor leukocytes within the blood component unit (PRBCs or platelets); the recipient may form antibodies to the antigens present on these leukocytes. PRBC components typically have 1 to 3×10^9 leukocytes remaining in each unit. Leukocytes from the blood product are frequently filtered to diminish the likelihood of developing reactions and refractoriness to transfusions, particularly in patients who have long-term transfusion needs. The process of leukocyte filtration renders the blood component “leukocyte poor” (i.e., leukopenic). Filtration can occur at the time the unit is collected from the donor and processed, which achieves better results but is more expensive, or at the time the blood component is transfused by attaching a leukocyte filter to the

blood administration tubing. Many centers advocate routinely using leukopenic filtered blood components for people who have or are likely to develop long-term transfusion requirements.

When a patient is immunocompromised, as in the case following stem cell transplant, any donor lymphocytes must be removed from the blood components. In this situation, the blood component is exposed to low amounts of radiation (25 Gy) that kill any lymphocytes within the blood component. Irradiated blood products are highly effective in preventing transfusion-associated graft-versus-host disease, which is fatal in most cases. Irradiated blood products have a shorter shelf life.

Transfusion

Administration of blood and blood components requires knowledge of correct administration techniques and possible complications. It is very important to be familiar with the agency's policies and procedures for transfusion therapy.

Most blood transfusions are performed in the acute care setting, and sometimes must be done emergently. Patients with long-term transfusion requirements (i.e., patients who require transfusions on an ongoing, periodic basis) often can receive transfusions in other settings. Freestanding infusion centers, ambulatory care clinics, physicians' offices, and even patients' homes may be appropriate settings for transfusion. Typically, patients who need long-term transfusions but are otherwise stable physically are appropriate candidates for outpatient therapy. Verification and administration of the blood product are performed as in a hospital setting. Although most blood products can be transfused in the outpatient setting, the home is typically limited to transfusions of PRBCs and factor components (e.g., factor VIII for patients with hemophilia).

Pretransfusion Assessment

Patient History

The patient history is an important component of the pretransfusion assessment to determine the history of previous transfusions as well as previous reactions to transfusion. The history should include the type of reaction, its manifestations, the interventions required, and whether any preventive interventions were used in subsequent transfusions. The nurse assesses the number of pregnancies a woman has had, because a high number can increase her risk of reaction due to antibodies developed from exposure to fetal circulation. Other concurrent health problems should be noted, with careful

attention to cardiac, pulmonary, and vascular disease. Informed consent must be obtained preprocedure (see [Chart 28-2](#)).

Physical Assessment

A systematic physical assessment and measurement of baseline vital signs and fluid status are important before transfusing any blood product. The respiratory system should be assessed, including careful auscultation of the lungs and the patient's use of accessory muscles. Cardiac system assessment should include careful inspection for any edema as well as other signs of heart failure (e.g., jugular venous distention; see [Chapter 25](#)). The skin should be observed for rashes, petechiae, and ecchymoses. The sclera should be examined for icterus. In the event of a transfusion reaction, a comparison of findings can help differentiate between types of reactions.

Chart 28-2 ETHICAL DILEMMA

Can Surrogates Refuse Life-Saving Treatment?

Case Scenario

L.C. is a 34-year-old woman who was an unrestrained front-seat passenger in a motor vehicle crash 2 days ago. She sustained multiple trauma, including a fractured skull, traumatic brain injury, several fractured ribs, a pulmonary contusion, and a fractured right femur. After stabilization in the emergency department, she was admitted to the intensive care unit (ICU) endotracheally intubated and mechanically ventilated. You are a staff nurse in the ICU and have been assigned as L.C.'s nurse since her admission. You have come to know her family members, including her parents and her boyfriend, whom she has lived with for the past 10 months. During interdisciplinary rounds, L.C.'s trauma surgeon notes that her hemoglobin continues to drop since admission, and is now 7.7 g/dL; he asserts that she must receive blood transfusions. L.C.'s parents and her boyfriend are present during these rounds. L.C.'s parents tell the trauma surgeon that they are Jehovah's Witnesses, and that receiving blood transfusions is against their religious beliefs. L.C.'s boyfriend notes that she no longer adheres to the tenets of Jehovah's Witnesses and does not attend any religious meetings or services. L.C.'s parents become angry and tell her boyfriend that they are the ones to make decisions on L.C.'s behalf. L.C. does not have an advance directive or a power-of-attorney for health care.

Discussion

Whenever a patient lacks capacity to make their own health care decisions, those decisions are made by a legally identified surrogate. Had L.C. identified who that surrogate should be in a power-of-attorney for health care document, that person would have the rights and responsibilities to make those decisions. Since that document does not exist, and since L.C. does not have a spouse, her parents are her legal surrogates and authorized to make those decisions on her behalf.

Had L.C. written an advance directive and specified whether or not she would wish to receive blood transfusions for life-threatening contingencies, that specification would be legally binding. For instance, had she noted in an advance directive that she would *not* wish to receive blood transfusions, even if that meant that she would die, that would be a legally binding decision, even if her parents wished for her to receive blood transfusions.

However, L.C.'s parents and her boyfriend disagree about what they believe L.C. would want to be done in this situation. Surrogates are charged with making decisions on behalf of patients who lack capacity. However, that charge is predicated on the belief that surrogates know which decision is consistent with what the patient would have wanted when the patient could have made a reasoned decision. It is noteworthy that L.C.'s parents insist that she not be transfused since it is against *their* religious beliefs. However, they do not note that their beliefs are also consistent with L.C.'s beliefs.

Analysis

- Describe the ethical principles that are in conflict in this case (see [Chapter 1, Chart 1-7](#)). Is it possible to preserve L.C.'s autonomy, given that she lacks capacity at this time, and given the conflict between her family members?
- There is a conflict between legal rights and moral decisions in this case. Are there situations where the decision that a legal surrogate makes for a patient who lacks capacity could and should be overturned?
- What if a family meeting is called to try to resolve the conflict between L.C.'s parents and her boyfriend, and her boyfriend is able to provide evidence that L.C. does not adhere to the tenets of the Jehovah's Witness faith? By contrast, what if her parents are able to provide evidence that L.C. has been faithfully attending Jehovah's Witnesses meetings for the past 10 months and that she has explicitly told her parents that she would not ever wish to have blood transfusions? Finally, what if L.C.'s parents and her boyfriend each express that none of them are certain what decision L.C. would make in this situation? Would the trauma surgeon be justified in then upholding the principle of beneficence and prescribe blood transfusions for L.C., despite her parents' objections? If those transfusions were prescribed, would you administer the blood transfusions or would you object?
- What resources might be mobilized to be of assistance to L.C.'s family and the health care team so that the decision that best respects L.C.'s wishes might be made?

References

Baumrucker, S. J., Stolick, M., Hutchinson, L., et al. (2019). Death or damnation: Surrogacy and religious beliefs. *American Journal of Hospice & Palliative Medicine*, 36(8), 740–745.

Resources

See [Chapter 1, Chart 1-10](#), for Steps of an Ethical Analysis and Ethics Resources.



Patient Education

Reviewing the signs and symptoms of a transfusion reaction is crucial with all patients, including those who have and have not received a previous transfusion. Signs and symptoms of a reaction include fever, chills, respiratory distress, low back pain, nausea, pain at the IV site, or anything "unusual." Although a thorough review is very important, the nurse also reassures the patient that the blood is carefully tested against the patient's own blood (cross-

matched) to diminish the likelihood of any untoward reaction. Similarly, the patient can be reassured about the very low possibility of contracting HIV from the transfusion; this fear persists among many people.

Transfusion Procedures

Methods for transfusing blood components and the role of the nurse in assessing patients before, during, and after these procedures are described in [Charts 28-3 and 28-4](#).

Complications

Any patient who receives a blood transfusion is at risk for developing complications from the transfusion. Nursing management is directed toward preventing complications, promptly recognizing complications if they develop, and promptly initiating measures to control complications. Nurses assess patients' vital signs before, during, and after a blood transfusion is complete to screen for any adverse reactions; however, the optimal frequency for assessing these vital signs during the transfusion is not well established (Cortez-Gann, Gilmore, Foley, et al., 2017) (see the Nursing Research Profile in [Chart 28-5](#)). The following sections describe the most common or potentially severe transfusion-related complications.

Febrile Nonhemolytic Reaction

A febrile nonhemolytic reaction is caused by antibodies to donor leukocytes that remain in the unit of blood or blood component; it is the most common type of transfusion reaction (Stubbs, 2018). It occurs more frequently in patients who have had previous transfusions (exposure to multiple antigens from previous blood products) and in Rh-negative women who have borne Rh-positive children (exposure to an Rh-positive fetus raises antibody levels in the untreated mother).

Chart 28-3

Transfusion of Packed Red Blood Cells

Preprocedure

1. Confirm that the transfusion has been prescribed.
2. Check that patient's blood has been typed and cross-matched.
3. Verify that patient has signed a written consent form per institution or agency policy and agrees to procedure.
4. Explain procedure to patient. Educate patient about signs and symptoms of transfusion reaction (itching, hives, swelling, shortness of breath, fever, chills).
5. Take patient's temperature, pulse, respiration, blood pressure, and assess fluid volume status (e.g., auscultate lungs, assess for jugular venous distention) to serve as a baseline for comparison during transfusion.
6. Note if signs of increased fluid overload present (e.g., heart failure, see [Chapter 25](#)), contact primary provider to discuss potential need for a prescription for diuretic, as warranted.
7. Use hand hygiene and wear gloves in accordance with standard precautions.
8. Use appropriately sized intravenous cannula for insertion in a peripheral vein.^a Use special tubing that contains a blood filter to screen out fibrin clots and other particulate matter. Do not vent blood container.

Procedure

1. Obtain packed red blood cells (PRBCs) from the blood bank *after* the IV line is started. (Institution policy may limit release to only 1 unit at a time.)
2. Double-check labels with another nurse or physician to ensure that the ABO group and Rh type agree with the compatibility record. Check to see that number and type on donor blood label and on patient's medical record are correct. Confirm patient's identification by asking the patient's name and checking the identification wristband.
3. Check blood for gas bubbles and any unusual color or cloudiness. (Gas bubbles may indicate bacterial growth. Abnormal color or cloudiness may be a sign of hemolysis.)
4. Make sure that PRBC transfusion is initiated within 30 minutes after removal of PRBCs from blood bank refrigerator.
5. For the first 15 minutes, run the transfusion slowly—no faster than 5 mL/min. Observe patient carefully for adverse effects. If no adverse effects occur during the first 15 minutes, increase the flow rate unless patient is at high risk for circulatory overload.
6. Monitor closely for 15 to 30 minutes to detect signs of reaction. Monitor vital signs at regular intervals per institution or agency policy; compare results with baseline measurements. Increase frequency of measurements based on patient's condition. Observe patient frequently throughout the

transfusion for any signs of adverse reaction, including restlessness, hives, nausea, vomiting, torso or back pain, shortness of breath, flushing, hematuria, fever, or chills. Should any adverse reaction occur, stop infusion immediately, notify primary provider, and follow the agency's transfusion reaction standard.

7. Note that administration time does not exceed 4 hours because of increased risk of bacterial proliferation.
8. Be alert for signs of adverse reactions: circulatory overload, sepsis, febrile reaction, allergic reaction, and acute hemolytic reaction.
9. Change blood tubing after every 2 units transfused to decrease chance of bacterial contamination.

Postprocedure

1. Obtain vital signs and breath sounds; compare with baseline measurements. If signs of increased fluid overload present (e.g., heart failure), consider obtaining prescription for diuretic as warranted.
2. Dispose of used materials properly.
3. Document procedure in patient's medical record, including patient assessment findings and tolerance to procedure.
4. Monitor patient for response to and effectiveness of procedure. If patient is at risk, monitor for at least 6 hours for signs of transfusion-associated circulatory overload (TACO); also monitor for signs of delayed hemolytic reaction.

Note: Never add medications to blood or blood products; if blood is too thick to run freely, normal saline may be added to the unit. If blood must be warmed, use an in-line blood warmer with a monitoring system.

^aThe size of the peripheral cannula used in a blood transfusion depends on two factors, size and integrity of the vein and desired speed for transfusion.

Adapted from Robinson, S., New, H., Shackleton, T., et al. (2018). The administration of blood components: A British Society for Haematology Guideline. *Transfusion Medicine*, 28(1), 3–21.

Chart 28-4

Transfusion of Platelets or Fresh-Frozen Plasma

Preprocedure

1. Confirm that the transfusion has been prescribed.
2. Verify that patient has signed a written consent form per institution or agency policy and agrees to procedure.
3. Explain procedure to patient. Educate patient about signs and symptoms of transfusion reaction (itching, hives, swelling, shortness of breath, fever, chills).
4. Take patient's temperature, pulse, respiration, blood pressure, and assess fluid status, and auscultate breath sounds to establish a baseline for comparison during transfusion.
5. Note if signs of increased fluid overload present (e.g., heart failure, see [Chapter 25](#)), contact primary provider to discuss potential need for a prescription for diuretic, as warranted; this is particularly important when plasma is also infused.
6. Use hand hygiene and wear gloves in accordance with standard precautions.
7. Use a 22-gauge or larger needle or catheter for placement in a large vein, if possible. Use appropriate tubing per institution policy (platelets often require different tubing from that used for other blood products).

Procedure

1. Obtain platelets or fresh-frozen plasma (FFP) from the blood bank (only after the IV line is started.)
2. Double-check labels with another nurse or physician to ensure that the ABO group matches the compatibility record (not usually necessary for platelets; here only if compatible platelets are ordered). Check to see that the number and type on donor blood label and on patient's medical record are correct. Confirm patient's identification by asking the patient's name and checking the identification wristband.
3. Check blood product for any unusual color or clumps (excessive redness indicates contamination with larger amounts of red blood cells).
4. Make sure that platelets or FFP units are given immediately after they are obtained.
5. Infuse each unit of FFP over 30 to 60 minutes per patient tolerance; be prepared to infuse at a significantly lower rate in the context of fluid overload. Infuse each unit of platelets as fast as patient can tolerate to diminish platelet clumping during administration. Observe patient carefully for adverse effects, especially circulatory overload. Decrease rate of infusion if necessary.
6. Observe patient closely throughout transfusion for any signs of adverse reaction, including restlessness, hives, nausea, vomiting, torso or back pain, shortness of breath, flushing, hematuria, fever, or chills. Should any adverse reaction occur, stop infusion immediately, notify primary provider, and follow the agency's transfusion reaction standard.

7. Monitor vital signs at the end of transfusion per institution policy; compare results with baseline measurements.
8. Flush line with saline after transfusion to remove blood component from tubing.

Postprocedure

1. Obtain vital signs and auscultate breath sounds; compare with baseline measurements. If signs of increased fluid overload present, consider obtaining prescription for diuretic, as warranted.
2. Dispose of used materials properly.
3. Document procedure in patient's medical record, including patient assessment findings and tolerance to procedure.
4. Monitor patient for response to and effectiveness of procedure. A platelet count may be ordered 1 hour after platelet transfusion to facilitate this evaluation.
5. If patient is at risk for transfusion-associated circulatory overload (TACO), monitor closely for 6 hours after transfusion if possible.

Note: FFP requires ABO but not Rh compatibility. Platelets are not typically cross-matched for ABO compatibility. Never add medications to blood or blood products.

Adapted from Robinson, S., New, H., Shackleton, T., et al. (2018). The administration of blood components: A British Society for Haematology Guideline. *Transfusion Medicine*, 28(1), 3–21.

The diagnosis of a febrile nonhemolytic reaction is made by excluding other potential causes, such as a hemolytic reaction or bacterial contamination of the blood product. The signs and symptoms of a febrile nonhemolytic transfusion reaction are chills (minimal to severe) followed by fever (more than 1°C elevation). The fever typically begins within 2 hours after the transfusion has begun. Although the reaction is not life threatening, the fever, and particularly the chills and muscle stiffness, can be frightening to the patient.

This reaction can be diminished, even prevented, by further depleting the blood component of donor leukocytes; this is accomplished by a leukocyte reduction filter. Antipyretic agents can be given to prevent fever; however, routine premedication is not advised because it can mask the beginning of a more serious transfusion reaction.

Acute Hemolytic Reaction

The most dangerous, and potentially life-threatening, type of transfusion reaction occurs when the donor blood is incompatible with that of the recipient (i.e., type II hypersensitivity reaction). Antibodies already present in the recipient's plasma rapidly combine with antigens on donor erythrocytes, and the erythrocytes are destroyed in the circulation (i.e., intravascular hemolysis).

The most rapid hemolysis occurs in ABO incompatibility. Rh incompatibility often causes a less severe reaction. This reaction can occur after transfusion of as little as 10 mL of PRBCs. Although the overall incidence of such reactions is not high (1:20,000 to 1:40,000 units transfused) (Robinson, New, Shackleton, et al., 2018), they are largely preventable. The most common causes of acute hemolytic reaction are errors in blood component labeling, a type of clerical error, and errors in patient identification that result in the administration of an ABO-incompatible transfusion.

Symptoms consist of fever, chills, low back pain, nausea, chest tightness, dyspnea, and anxiety. As the erythrocytes are destroyed, the hemoglobin is released from the cells and excreted by the kidneys; therefore, hemoglobin appears in the urine (hemoglobinuria). Hypotension, bronchospasm, and vascular collapse may result. Diminished renal perfusion results in acute kidney injury, and disseminated intravascular coagulation may also occur. The reaction must be recognized promptly and the transfusion discontinued immediately (see the Nursing Management of Transfusion Reactions section).

Chart 28-5



NURSING RESEARCH PROFILE

Blood Transfusions and Vital Sign Frequency

Cortez-Gann, J., Gilmore, K. D., Foley, K. W., et al. (2017). Blood transfusion vital sign frequency: What does the evidence say? *MEDSURG Nursing*, 26(2), 89–92.

Purpose

Nurses are responsible for assuring patient safety during a blood transfusion through effective monitoring of vital signs. When and how often to take vital signs varies, based upon institutional protocols. There are no evidence-based research findings that provide direction regarding optimal timing and frequency of vital sign monitoring for patients who receive blood transfusions. Therefore, the purpose of this research was to discover the relationship between vital sign findings and blood transfusion-associated adverse events in order to find patterns suggestive of optimal vital sign timing and frequency for patients receiving blood transfusions.

Design

A retrospective descriptive study was conducted in a 921-bed hospital where approximately 77,800 units of blood products were transfused during 2008 through 2012. Of those patients transfused during this time, 116 experienced a blood transfusion reaction. Using a medical record data collection tool, information from these 116 patients was collected including demographics, type of blood product administered, transfusion start and stop times, vital signs before, during, and after transfusion, symptomatology and treatment protocol for the transfusion reaction, and patient outcomes.

Findings

Packed red blood cells were the most commonly transfused product. Of the 116 sampled patients who experienced a transfusion reaction, 67% were over 60 years of age. The most common changes among vital signs were an increase in temperature, blood pressure, and heart rate. Six of the 116 patients with transfusion reactions experienced severe life-threatening complications from the blood transfusion, but none died from them. The average time from the start of transfusion to an adverse reaction was approximately 92 minutes, with the quickest documented response occurring 5 minutes after initiation of the transfusion and the most delayed reaction taking place 2 hours and 30 minutes after the start of the transfusion.

Nursing Implications

Hospitals endorse different protocols that dictate when and how often nurses take vital signs for patients who receive blood products. While it is commonly believed that the most likely time for a patient to experience a transfusion reaction is within the first 15 minutes after the start of a transfusion, findings from this study established an average time to the reaction of 1.5 hours, with the most severe reaction occurring 2 hours after initiation of the transfusion. Only one severe reaction in this study occurred during the first 15 minutes of

the transfusion period. Findings from this study suggest that nurses should take vital signs of patients receiving blood transfusions at periodic intervals during the entire timeframe that a patient receives a blood transfusion.

Acute hemolytic transfusion reactions are preventable. Meticulous attention to detail in labeling blood samples and blood components and accurately identifying the recipient cannot be overemphasized. Bar coding methods can be useful safeguards in matching a patient's wristband with the label on the blood component; however, these methods are not fail proof and do not reduce the nurse's responsibility to ensure the correct blood component is transfused to the correct patient (Robinson et al., 2018).

Allergic Reaction

Some patients develop urticaria (hives) or generalized itching during a transfusion; the cause is thought to be a sensitivity reaction to a plasma protein within the blood component being transfused. Symptoms of an allergic reaction are urticaria, itching, and flushing. The reactions are usually mild and respond to antihistamines. If the symptoms resolve after administration of an antihistamine (e.g., diphenhydramine), the transfusion may be resumed. Rarely, the allergic reaction is severe, with bronchospasm, laryngeal edema, and shock. These reactions are managed with epinephrine, corticosteroids, and vasopressor support, if necessary.

Giving the patient antihistamines or corticosteroids before the transfusion may prevent future reactions. For severe reactions, future blood components are washed to remove any remaining plasma proteins. Leukocyte filters are not useful to prevent such reactions, because the offending plasma proteins can pass through the filter.

Transfusion-Associated Circulatory Overload (TACO)

If too much blood is infused too quickly, hypervolemia can occur. This condition, known as transfusion-associated circulatory overload (TACO), can be aggravated in patients who already have increased circulatory volume (e.g., those with heart failure, renal dysfunction, advanced age, acute myocardial infarction) (Carman, Uhlenbrock, & McClintock, 2018). A careful assessment for signs of circulatory overload or positive fluid status prior to initiating the transfusion is required, particularly in patients at risk for developing transfusion-related acute lung injury (TRALI) (see discussion below). PRBCs are safer to use than whole blood. If the administration rate is sufficiently slow, circulatory overload may be prevented. For patients who are at risk for, or already in, circulatory overload, diuretics are given prior to the transfusion or between units of PRBCs. Patients receiving fresh-frozen plasma or even platelets may also develop circulatory overload. The infusion rate of these blood components must also be titrated to the patient's tolerance. Rates of

transfusion may need to decrease to less than 100 to 120 mL/h (Henneman, 2017).

Signs of circulatory overload include dyspnea, orthopnea, tachycardia, an increase in blood pressure, and sudden anxiety. Jugular vein distention, crackles at the base of the lungs, and hypoxemia will also develop. Pulmonary edema can quickly develop, as manifested by severe dyspnea and coughing of pink, frothy sputum.

If fluid overload is mild, the transfusion can often be continued after slowing the rate of infusion and administering diuretics. However, if the overload is severe, the patient is placed upright with the feet in a dependent position, the transfusion is discontinued, and the primary provider is notified. The IV line is kept patent with a very slow infusion of normal saline solution or a saline lock device to maintain access to the vein in case IV medications are necessary. Oxygen and morphine may be needed to treat severe dyspnea (see [Chapter 25](#)).

TACO can develop as late as 6 hours after transfusion (Henneman, 2017). Therefore, patients need close monitoring after the transfusion is completed, particularly those who are at higher risk for developing this complication (e.g., older adults, those with a positive fluid balance prior to transfusion, patients with renal dysfunction, patients with left ventricular dysfunction). Monitoring vital signs, auscultating breath sounds, and assessing for jugular venous distention should be included in patient monitoring.

Bacterial Contamination

The incidence of bacterial contamination of blood components is very low; however, administration of contaminated products puts the patient at great risk. Contamination can occur at any point during procurement or processing but often results from organisms on the donor's skin. Many bacteria cannot survive in the cold temperatures used to store PRBCs, but some organisms can. Platelets are at greater risk of contamination because they are stored at room temperature. In response to this, blood centers have developed rapid methods of culturing platelet units, thereby diminishing the risk of using a contaminated platelet unit for transfusion (CDC, 2019).

Preventive measures include meticulous care in the procurement and processing of blood components. When PRBCs or whole blood is transfused, it should be given within a 4-hour period, because warm room temperatures promote bacterial growth. A contaminated unit of blood product may appear normal, or it may have an abnormal color.

The signs of bacterial contamination are fever, chills, and hypotension. These manifestations may not occur until the transfusion is complete, and occasionally not until several hours after the transfusion. As soon as the reaction is recognized, any remaining transfusion is discontinued (see the Nursing Management of Transfusion Reactions section). If the condition is not

treated immediately with fluids and broad-spectrum antibiotics, sepsis can occur. Sepsis is treated with IV fluids and antibiotics; corticosteroids and vasopressors are often also necessary (see [Chapter 11](#)).

Transfusion-Related Acute Lung Injury (TRALI)

TRALI is a potentially fatal, idiosyncratic reaction that is defined as the development of acute lung injury occurring within 6 hours after the blood transfusion. All blood components have been implicated in TRALI, including IVIG, cryoprecipitate, and stem cells. TRALI is the most common cause of transfusion-related death (Heering & Karakashian, 2017).

The underlying pathophysiologic mechanism for TRALI is unknown but is thought to involve specific human leukocyte antigen (HLA) or human neutrophil antigen (HNA) antibodies in the donor's plasma that react to the leukocytes in the recipient's blood. Occasionally, the reverse occurs, and antibodies present in the recipient's plasma agglutinate the antigens on the few remaining leukocytes in the blood component being transfused. Another theory suggests that an initial insult to the patient's vascular endothelium can predispose the neutrophils to aggregate at the injured endothelium. Various substances within the transfused blood component (lipids, cytokines) then activate these neutrophils. Each of these pathophysiologic mechanisms can contribute to the process. The end result of this process is interstitial and intra-alveolar edema, as well as extensive sequestration of WBCs within the pulmonary capillaries (Heering & Karakashian, 2017).

Onset is abrupt (usually within 6 hours of transfusion, often within 2 hours). Signs and symptoms include acute shortness of breath, hypoxia (arterial oxygen saturation [SaO_2] less than 90%; partial pressure of arterial oxygen [PaO_2] to fraction of inspired oxygen [FIO_2] ratio of less than 300), hypotension, fever, and eventual pulmonary edema. Diagnostic criteria include hypoxemia, bilateral pulmonary infiltrates (seen on chest x-ray), no evidence of cardiac cause for the pulmonary edema, and no other plausible alternative cause within 6 hours of completing transfusion. Aggressive supportive therapy (e.g., oxygen, intubation, fluid support) may prevent death. Immunologic therapy (e.g., corticosteroids) has not been shown to be effective in this setting; diuretics can worsen the situation (Raja, Rahul, Kumar, et al., 2019).

Although TRALI can occur with the transfusion of any blood component, it is more likely to occur when plasma and, to a lesser extent, platelets are transfused. One commonly used preventive strategy involves limiting the frequency and amount of blood products transfused. Another entails obtaining plasma and possibly platelets only from men because women who have been pregnant may have developed offending antibodies. A third strategy involves screening donors for the presence of these antibodies and discarding any plasma-containing blood products from those donors who screen positive. The

efficacy of these approaches in preventing TRALI remains unclear (Otrack, Liu, & Grossman, 2017).

Delayed Hemolytic Reaction

Delayed hemolytic reactions usually occur within 14 days after transfusion, when the level of antibody has been increased to the extent that a reaction can occur (Siddon, Kenney, Hendrickson, et al., 2018). The hemolysis of the erythrocytes is extravascular via the RES and occurs gradually.

Signs and symptoms of a delayed hemolytic reaction are fever, anemia, increased bilirubin level, decreased or absent haptoglobin, and possibly jaundice. Rarely, there is hemoglobinuria. Generally, these reactions are not dangerous, but it is important to recognize them because subsequent transfusions with blood products containing these antibodies may cause a more severe hemolytic reaction. However, recognition is also difficult because the patient may not be in a health care setting to be tested for this reaction, and even if the patient is hospitalized, the reaction may be too mild to be recognized clinically. Because the amount of antibody present can be too low to detect, it is difficult to prevent delayed hemolytic reactions. Fortunately, the reaction is usually mild and requires no intervention (Siddon et al., 2018).

Disease Acquisition

Despite advances in donor screening and blood testing, certain diseases can still be transmitted by transfusion of blood components (see [Chart 28-6](#)).

Chart 28-6

Diseases Potentially Transmitted by Blood Transfusion

Hepatitis (Viral Hepatitis B, C)

- There is greater risk from pooled blood products and blood of paid donors than from volunteer donors.
- A screening test detects most hepatitis B and C.
- Transmittal risk for Hepatitis B is estimated at 1:350,000 donated units.

AIDS (HIV and HTLV)

- Donated blood is screened for antibodies to HIV.
- Transmittal risk is estimated at 1:1.5 million donated units.
- People with high-risk behaviors (multiple sex partners, anal sex, IV/injection drug use) and people with signs and symptoms that suggest AIDS should not donate blood.

Cytomegalovirus (CMV)

- Transmittal risk is greater for premature newborns with CMV antibody-negative mothers and for immunocompromised recipients who are CMV negative (e.g., those with acute leukemia, organ or tissue transplant recipients).
- Blood products rendered “leukocyte reduced” help reduce transmission of virus.

Graft-Versus-Host Disease (GVHD)

- GVHD occurs only in recipients who are severely immunocompromised (e.g., Hodgkin disease, bone marrow transplantation).
- Transfused lymphocytes engraft in recipient and attack host lymphocytes or body tissues; signs and symptoms are fever, diffuse reddened skin rash, nausea, vomiting, and diarrhea.
- Preventive measures include irradiating blood products to inactivate donor lymphocytes (no known radiation risks to transfusion recipient) and processing donor blood with leukocyte reduction filters.

Creutzfeldt–Jakob Disease (CJD)

- CJD is a rare, fatal disease that causes irreversible brain damage.
- There is no evidence of transmittal by transfusion.
- All blood donors must be screened for positive family history of CJD.
- Potential donors who spent a cumulative time of 5 years or more (January 1980 to present) in certain areas of Europe cannot donate blood; blood products from a donor who develops CJD are recalled.

AIDS, acquired immunodeficiency syndrome; HIV, human immunodeficiency virus; HTLV, human T-lymphotropic virus.

Adapted from Katz, L. M., & Dodd, R. Y. (2018). Transfusion-transmitted diseases. In B. H. Shaz, C. D. Hillyer, & M. R. Gil (Eds.). *Transfusion medicine and hemostasis: Clinical and laboratory aspects* (3rd ed.). Cambridge, MA: Elsevier.

Complications of Long-Term Transfusion Therapy

The complications that have been described represent a real risk to any patient any time a blood component is given. However, patients with long-term transfusion requirements (e.g., those with myelodysplastic syndrome, thalassemia, aplastic anemia, sickle cell disease) are at greater risk for infection transmission and for becoming more sensitized to donor antigens, simply because they are exposed to more units of blood and, consequently, more donors. A summary of complications associated with long-term transfusion therapy is given in [Table 28-5](#).

Iron overload is a complication unique to people who have had long-term PRBC transfusions. One unit of PRBCs contains 250 mg of iron. Patients with long-term transfusion requirements can quickly acquire more iron than they can use, leading to iron overload. Over time, the excess iron deposits in body tissues can cause organ damage, particularly in the liver, heart, testes, and pancreas. Promptly initiating a program of iron chelation therapy can prevent end-organ damage from iron toxicity (see [Chapter 29](#), Hereditary Hemochromatosis, Nursing Management, and Chapter 30, Myelodysplastic Syndrome, Nursing Management).

Nursing Management of Transfusion Reactions

If a transfusion reaction is suspected, the transfusion must be stopped immediately, and the primary provider notified. A thorough patient assessment is crucial because many complications have similar signs and symptoms. The following steps are taken to determine the type and severity of the reaction:

TABLE 28-5 Common Complications Resulting from Long-Term Packed Red Blood Cell Transfusion Therapy^a

Complication	Manifestation	Management
Infection	Hepatitis (B, C)	May immunize against hepatitis B; treat hepatitis C; monitor hepatic function
	CMV	WBC filters to protect against CMV
Iron overload	Heart failure Endocrine failure (diabetes, hypothyroidism, hypoparathyroidism, hypogonadism)	Prevent by chelation therapy
Transfusion reaction	Sensitization	Diminish by RBC phenotyping, using WBC-filtered products
	Febrile reactions	Diminish by using WBC-filtered products

^aPatients with long-term transfusion therapy requirements are at risk not only for the transfusion reactions discussed in the text but also for the complications noted in the table. In many cases, the use of WBC-filtered (i.e., leukocyte-poor) blood products is standard for patients who receive long-term packed RBC transfusion therapy. An aggressive chelation program initiated early in the course of therapy can prevent problems with iron overload.

CMV, cytomegalovirus; RBC, red blood cell; WBC, white blood cell.

Adapted from Carman, M., Uhlenbrock, J. S., & McClintock, S. M. (2018). CE: A review of current practice in transfusion therapy. *The American Journal of Nursing*, 118(5), 36–44.

- Stop the transfusion. Maintain the IV line with normal saline solution through new IV tubing, given at a slow rate.
- Assess the patient carefully. Compare the vital signs with baseline, including oxygen saturation. Assess the patient's respiratory status carefully. Note the presence of adventitious breath sounds; the use of accessory muscles; the extent of dyspnea; and changes in mental status, including anxiety and confusion. Note any chills, diaphoresis, jugular vein distention, and reports of back pain or urticaria.
- Notify the primary provider of the assessment findings and implement any treatments prescribed. Continue to monitor the patient's vital signs and respiratory, cardiovascular, and renal status.
- Notify the blood bank that a suspected transfusion reaction has occurred.
- Send the blood container and tubing to the blood bank for repeat typing and culture. The patient's identity and blood component identifying tags and numbers are verified.

If a hemolytic transfusion reaction or bacterial infection is suspected, the nurse does the following:

- Obtains appropriate blood specimens from the patient.
- Collects a urine sample as soon as possible to detect hemoglobin in the urine.
- Documents the reaction according to the institution's policy.

Pharmacologic Alternatives to Blood Transfusions

Pharmacologic agents that stimulate the production of one or more types of blood cells by the marrow are commonly used (see [Chart 28-7](#)). Researchers continue to seek a blood substitute that is practical and safe. Manufacturing artificial blood is problematic, given the myriad functions of blood components. Currently, there are two types of products in development: hemoglobin-based oxygen carriers and perfluorocarbons (which can dissolve gases and thus carry oxygen indirectly); none are approved for use in humans, to date (Adams, 2019).

Chart 28-7 PHARMACOLOGY

Pharmacologic Alternatives to Blood Transfusions

Growth Factors

Recombinant technology has provided a means to produce hematopoietic growth factors necessary for the production of blood cells within the bone marrow. By increasing the body's production of blood cells, transfusions and complications resulting from diminished blood cells (e.g., infection from neutropenia) may be avoided. However, the successful use of growth factors requires functional bone marrow. Moreover, the safety of these products has been questioned, and the U.S. Food and Drug Administration is limiting their use in some patient populations.

Erythropoietin

Erythropoietin (epoetin alfa; darbopoeitin) is an effective alternative treatment for patients with chronic anemia secondary to diminished levels of erythropoietin, as in chronic kidney disease. This medication stimulates erythropoiesis. It also has been used for patients who are anemic from chemotherapy or zidovudine (AZT) therapy and for those who have diseases involving bone marrow suppression, such as myelodysplastic syndrome (MDS). The use of erythropoietin can also enable a patient to donate several units of blood for future use (e.g., preoperative autologous donation). The medication can be administered IV or subcutaneously, although plasma levels are better sustained with the subcutaneous route. Side effects are rare, but erythropoietin can cause or exacerbate hypertension. If the anemia is corrected too quickly or is overcorrected, the elevated hematocrit can cause headache and, potentially, seizures. Thrombosis has been noted in some patients whose hemoglobins were raised to a high level; thus, it is recommended that a target hemoglobin level of less than 12 g/dL be used. These adverse effects are rare except for patients with renal failure. Serial complete blood counts (CBCs) must be performed to evaluate the response to the medication. The dose and frequency of administration are titrated to the hemoglobin level.

Granulocyte Colony-Stimulating Factor (G-CSF)

G-CSF (filgrastim) is a cytokine that stimulates the proliferation and differentiation of myeloid stem cells; a rapid increase in neutrophils is seen within the circulation. G-CSF is effective in improving transient but severe neutropenia after chemotherapy or in some forms of MDS. It is particularly useful in preventing bacterial infections that would be likely to occur with neutropenia. G-CSF is given subcutaneously on a daily basis. The primary side effect is bone pain; this probably reflects the increase in hematopoiesis within the marrow. Serial CBCs should be performed to evaluate the response to the medication and to ensure that the rise in white blood cells is not excessive. The effect of G-CSF on myelopoiesis is short; the neutrophil count drops once the medication is stopped.

Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF)

GM-CSF (sargramostim) is a cytokine that is naturally produced by a variety of cells, including monocytes and endothelial cells. It works either directly or synergistically with other growth factors to stimulate myelopoiesis. GM-CSF is not as specific to neutrophils as is G-CSF; thus, an increase in erythroid (red blood cell) and megakaryocytic (platelet) production may also be seen. GM-CSF serves the same purpose as G-CSF. However, it may have a greater effect on macrophage function and therefore may be more useful against fungal infections, whereas G-CSF may be better used to fight bacterial infections. GM-CSF is also given subcutaneously. Side effects include bone pain, fevers, and myalgias.

Thrombopoietin

Thrombopoietin (TPO) is a cytokine that is necessary for the proliferation of megakaryocytes and subsequent platelet formation. Nonimmunogenic second-generation thrombopoietic growth factors (romiplostim; eltrombopag) are used for the treatment of idiopathic thrombocytopenic purpura. Eltrombopag is also approved for use in certain situations for patients with aplastic anemia and in patients requiring hepatitis C treatment that can cause significant thrombocytopenia.

Adapted from Hudgins, K., & Carter, E. (2019). Blood conservation: Exploring alternatives to blood transfusions. *Critical Care Nursing Quarterly*, 42(2), 187–191.

CRITICAL THINKING EXERCISES

1 pq A 40-year-old female is receiving one unit of packed red blood cells after admission for trauma as a result of an automobile injury. She is alert and responsive but lost a large amount of blood and presented with a hematocrit of 28% and a hemoglobin of 10 mg/dL. The blood has been transfusing for approximately 15 minutes when the patient complains of a headache and feeling “achy.” Her pulse is 96 bpm, respirations 20 per minute, blood pressure 128/76, and temperature 37.8°C (100.2°F). A nursing co-worker tells you this is a transfusion reaction, and you should stop the transfusion immediately. How would you respond to the nursing co-worker? What would you prioritize as the first three nursing actions most appropriate for this patient?

2 ebp You are a nurse working in a community health clinic and today during a vaccination health fair a 70-year-old male patient presents for varicella and Td/Tdap vaccines. You notice on his health history that he had a blood transfusion 2 months prior during a total hip replacement procedure. Based on this history, would you advise this patient to accept both vaccinations, varicella only, Td/Tdap only, or no vaccines? What is the strength of the evidence supporting the role of vaccinations in patients who have received blood transfusions? Which interprofessional resources and team members would you consult to help determine the best decision for this patient?

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*Asterisk indicates nursing research.

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Resources

- AABB (formerly known as the American Association of Blood Banks), www.aabb.org/Pages/default.aspx
- American Cancer Society, www.cancer.org
- American Red Cross, www.redcross.org
- American Red Cross LGBTQ+ Team Member Resource Group, www.redcrossblood.org/donate-blood/how-to-donate/eligibility-requirements/lgbtq-donors.html
- Blood and Marrow Transplant Information Network, www.bmtinfonet.org
- Infusion Nurses Society, www.ins1.org
- Myelodysplastic Syndromes Foundation, www.mds-foundation.org
- National Cancer Institute, www.cancer.gov
- National Hemophilia Foundation, www.hemophilia.org
- National Marrow Donor Program, www.bethematch.org
- Oncology Nursing Society (ONS), www.ons.org

29 Management of Patients with Nonmalignant Hematologic Disorders

LEARNING OUTCOMES

On completion of this chapter, the learner will be able to:

1. Differentiate between hypoproliferative and hemolytic anemias and compare the physiologic mechanisms, clinical manifestations, medical management, and nursing interventions for each.
2. Describe the processes involved in neutropenia and lymphopenia and the principles involved in medical and nursing management of patients with these disorders.
3. Specify the etiologies and the medical and nursing management of patients with secondary polycythemias and bleeding and thrombotic disorders.
4. Use the nursing process as a framework for care of the patient with anemia, with sickle cell disease, or with disseminated intravascular coagulation.

NURSING CONCEPTS

Cellular Regulation

Clotting

Perfusion

GLOSSARY

absolute neutrophil count (ANC): a calculation of the number of circulating neutrophils, derived from the total number of white blood cells (WBCs) and the percentage of neutrophils counted in a microscope's visual field

anemia: decreased red blood cell (RBC) count

aplasia: lack of cellular development (e.g., of cells within the bone marrow)

cytokines: proteins produced by leukocytes that are critical for regulation of hematopoiesis, apoptosis, and immune responses

erythrocyte: a cellular component of blood essential to the transport of oxygen and carbon dioxide (*synonym:* RBC)

erythroid cells: any cell that is or will become a mature RBC

erythropoietin: hormone produced primarily by the kidneys in response to cellular hypoxia that is necessary for erythropoiesis

haptoglobin: blood protein synthesized by the liver; binds free hemoglobin released from erythrocytes which is then removed by the reticuloendothelial system

hemolysis: destruction of RBCs with release of cellular components into the circulation; may occur within or outside the vasculature

hemosiderin: iron-containing pigment derived from the breakdown of hemoglobin

hypochromia: pallor within the RBCs caused by decreased hemoglobin content

leukemia: uncontrolled proliferation of WBCs

lymphopenia: a lymphocyte count less than 1500/mm³

megaloblastic anemia: a type of anemia characterized by abnormally large, nucleated RBCs

microcytosis: smaller-than normal RBCs

neutropenia: lower-than-normal number of neutrophils

normochromic: normal RBC color, indicating normal amount of hemoglobin

normocytic: normal size of RBC

pancytopenia: abnormal decrease in WBCs, RBCs, and platelets

petechiae: tiny capillary hemorrhages

poikilocytosis: variation in shape of RBCs

polycythemia: excess RBCs

reticulocytes: slightly immature RBCs, usually 1% of total number of circulating RBCs

spherocytes: small, spherically shaped RBCs

thrombocytopenia: lower-than-normal platelet count

thrombocytosis: higher-than-normal platelet count

Hematologic disorders vary widely in their etiologies and manifestations. While some are malignant, most hematologic disorders are benign. Disease processes can be quite complex, so a comprehensive understanding of the processes involved is important so that nurses may effectively assess, intervene, monitor, and educate patients about their conditions.

Anemia

Anemia is a condition characterized by a lower-than-normal hemoglobin concentration. Fewer than the normal number of red blood cells (RBCs), also called **erythrocytes**, are present in the circulation. Subsequently, less oxygen reaches the tissues, causing a variety of signs and symptoms. Rather than a disease state, anemia is a sign of an underlying disorder. It is the most common of all hematologic conditions and is prevalent throughout the world (Bunn, 2017a; Nair, 2018).

Pathophysiology

Anemia is classified in several ways (see [Table 29-1](#)). Most often it is classified according to whether the decreased number of erythrocytes is associated with hypoproliferation (decreased production), hemolysis (increased destruction), or loss of cells through bleeding.

Hypoproliferative anemias occur when the bone marrow produces an inadequate number of erythrocytes. Decreased erythrocyte production results in a low or appropriately normal **reticulocyte** (i.e., immature RBC) count. Causes of hypoproliferative anemia may include bone marrow damage from chemicals (e.g., benzene) or medication (e.g., chloramphenicol), lack of important factors that promote erythrocyte production such as **erythropoietin**, or lack of nutrients, including iron, vitamin B₁₂ and folic acid.

In hemolytic anemias, premature destruction of erythrocytes results in the liberation of hemoglobin from the erythrocytes into the plasma; the released hemoglobin is converted in large part to bilirubin and, therefore, the bilirubin concentration rises. The increased erythrocyte destruction leads to tissue hypoxia, which in turn stimulates erythropoietin production. This increased production is reflected in an increased reticulocyte count as the bone marrow responds to the loss of erythrocytes. **Hemolysis** (destruction of RBCs with release of cellular components into the circulation) can result from an abnormality within the erythrocyte itself (e.g., sickle cell disease [SCD], glucose-6-phosphate dehydrogenase [G-6-PD] deficiency), within the plasma

(e.g., immune hemolytic anemias), or from direct injury to the erythrocyte within the circulation (e.g., hemolysis caused by a mechanical heart valve). [Chart 29-1](#) identifies causes of hemolytic anemias.

It is often possible to determine the cause of anemia in each patient based on the following factors:

- The ability of the bone marrow to respond to the decrease in erythrocytes by producing reticulocytes.
- The degree to which immature erythrocytes proliferate in the bone marrow and their ability to mature (as seen in a bone marrow biopsy).

TABLE 29-1 Classification of Anemias

Type of Anemia	Laboratory Findings	
	CBC	Other
Hypoproliferative (Resulting from Defective RBC Production)		
Iron deficiency (microcytic)	↓ MCV, ↓ reticulocytes	↓ Iron, % saturation, ferritin ↑ TIBC
Vitamin B ₁₂ deficiency (megaloblastic)	↑ MCV	↓ Vitamin B ₁₂
Folate deficiency (megaloblastic)	↑ MCV	↓ Folate
Decreased erythropoietin production (e.g., from chronic kidney disease)	Normal MCV	↓ Erythropoietin level ↑ Creatinine ↑ Ferritin, % saturation
Cancer/inflammation	Normal MCV	↓ Iron, TIBC ↓ Erythropoietin level (usually)
Bleeding (Resulting in RBC Loss)		
Bleeding from gastrointestinal tract, epistaxis (nosebleed), trauma, bleeding from genitourinary tract (e.g., menorrhagia)	↓ Hgb and Hct (Note: Hgb and Hct may be normal if measured soon after bleeding starts) ↓ MCV (normal MCV initially) ↑ Reticulocytes	↓ Iron, % saturation, ferritin (later)
Hemolytic (Resulting from RBC Destruction)		
Altered erythropoiesis (sickle cell disease, thalassemia, other hemoglobinopathies)	↓ MCV ↑ Reticulocytes Fragmented RBCs (various shapes)	
Hypersplenism (hemolysis)	↑ MCV	
Drug-induced anemia	↑ Presence of spherocytes	
Autoimmune anemia	↑ Presence of spherocytes	
Mechanical heart valve-related anemia	Fragmented red cells	

↓, decreased; ↑, increased; %, percent; CBC, complete blood count; Hct, hematocrit; Hgb, hemoglobin; MCV, mean corpuscular volume; RBC, red blood cell; TIBC, total iron-binding capacity.

Adapted from Prchal, J. T. (2016a). Clinical manifestations and classification of erythrocyte disorders. In K. Kaushansky, M. A. Lichtman, J. T. Prchal, et al. (Eds.). *Williams hematology* (9th ed.). New York: McGraw-Hill Medical.

Chart 29-1

Causes of Hemolytic Anemias

Inherited Hemolytic Anemia

Sickle cell disease

Thalassemia

Red Blood Cell Membrane Abnormality

Acanthocytosis

Hereditary elliptocytosis

Hereditary spherocytosis

Stomatocytosis

Enzyme Deficiencies

Glucose-6-phosphate dehydrogenase deficiency

Acquired Hemolytic Anemia

Antibody Related

Autoimmune hemolytic anemia

Iso-antibody/transfusion reaction

Cold agglutinin disease

Not Antibody Related

Disseminated intravascular coagulation

Hypersplenism

Infection

Bacterial

Parasitic

Liver disease

Mechanical heart valve

Microangiopathic hemolytic anemia

Paroxysmal nocturnal hemoglobinuria

Toxins

Trauma

Uremia

- The presence or absence of end products of erythrocyte destruction in the circulation (e.g., increased bilirubin level, decreased haptoglobin level).

Clinical Manifestations

Several factors influence the development of symptoms associated with anemia. The severity of the anemia, the rapidity with which the anemia developed, the duration (chronicity) of the anemia, metabolic requirements of the patient, the presence of other conditions, such as cardiac or pulmonary disease, and complications or related features of the condition that produced the anemia are some of these factors.

In general, the more quickly the anemia develops, the more severe the symptoms (Bunn, 2017a). An otherwise healthy patient may be able to tolerate as much as a 50% reduction in hemoglobin over several months without pronounced symptoms or significant incapacity; however, a rapid loss of 30% of the hemoglobin over minutes may lead to profound vascular collapse in the same person. A patient who gradually becomes anemic, such as a woman experiencing heavy menses over several months with hemoglobin levels between 9 and 11 g/dL, may have few or no symptoms except for slight tachycardia on exertion or fatigue.

People who are more active or who have significant life demands are more likely to have symptoms than those who are more sedentary. Patients with hypothyroidism with decreased oxygen demands may be asymptomatic without tachycardia or dyspnea with a hemoglobin of 10 g/dL. Similarly, those with co-existing cardiac, vascular, or pulmonary disease may develop pronounced symptoms of anemia (e.g., dyspnea, chest pain, muscle pain, or cramping) with a higher hemoglobin level than those without concurrent health problems. Some anemias, such as SCD, or autoimmune diseases are often complicated by other abnormalities that do not result from the anemia but are inherent with the associated disease. Pain and other symptoms may overshadow those caused by the anemia.

Complications of severe anemia include heart failure, paresthesias, and delirium. Patients with underlying heart disease are more likely to have angina and symptoms associated with heart failure than those without heart disease. Complications of specific types of anemia are included in the description of each type.

Assessment and Diagnostic Findings

A number of studies are performed to determine the type and cause of the anemia. Initial evaluation includes hemoglobin, hematocrit, reticulocyte count, and RBC indices, including mean corpuscular volume (MCV), and red cell distribution width (RDW). Other studies may include iron studies (serum iron level, total iron-binding capacity [TIBC], percent saturation, and ferritin), serum vitamin B₁₂, folate levels, haptoglobin, and erythropoietin levels (Elder, Winland-Brown, & Porter, 2019; Nair, 2018). The remaining complete blood count (CBC) values are also useful in determining if the anemia is an isolated condition or associated with another hematologic condition such as **leukemia**.

(i.e., malignancy of the WBCs) or myelodysplastic syndrome (MDS). Bone marrow aspiration may be performed to assess for cellular abnormalities. Additional studies such as colonoscopy or upper endoscopy may be performed to determine if underlying conditions causing the anemia are present. Lesions in the gastrointestinal (GI) tract including ulcers, polyps, or tumors may be sources of blood loss.

Medical Management

Management of anemia is directed toward correcting or controlling the cause of the anemia; if the anemia is severe, the erythrocytes that are lost or destroyed may be replaced with a transfusion of packed red blood cells (PRBCs). Management of the various types of anemia is covered in the discussions that follow.

Gerontologic Considerations

Anemia is the most common hematologic condition affecting older adults, particularly those admitted to hospitals and in long-term care facilities. The overall prevalence of anemia is 17% in older adults, including approximately 10% of community-dwelling older adults, 45% of nursing homes residents, and 40% of those who are hospitalized. Most have mild anemia with hemoglobin level of 11 g/dL or higher, but even mild anemia may be associated with decreased functional ability and increased morbidity and mortality. Mild anemia in older adults is associated with decreased physical performance, decreased mobility, increased frailty, increased depression, increased risk of falls, and delirium (Lanier, Park, & Callahan, 2018). Studies have identified an association between anemia and cognitive decline. Older adults with anemia are more likely to have fatigue, dyspnea, and confusion because of reduced cardiac reserve and inability to respond with an increase in heart rate and increased cardiac output. Those with preexisting renal and cardiac disease and those who have had recent surgery are at increased risk for morbidity and mortality when anemic (Stauder, Valent, & Theurl, 2018).

NURSING PROCESS

The Patient with Anemia

Assessment

The health history and physical examination provide important data about the type of anemia involved, the extent and type of symptoms it produces, and the impact of the symptoms on the patient's life. Weakness, fatigue, and general malaise are common symptoms, and pallor of the skin and mucous membranes (conjunctivae, oral mucosa) are common signs (Fig. 29-1).

Jaundice, angular cheilitis (inflammation and fissures in the corners of the mouth), and brittle, concave, ridged nails may be associated with **megaloblastic anemia** (characterized by abnormally large, nucleated RBCs) or hemolytic anemia. The tongue may be sore and beefy red in megaloblastic anemia, and smooth and red with iron deficiency anemia. Patients with iron deficiency anemia often experience pica, a craving for ice, starch, or dirt (Cadet, 2018). Restless leg syndrome is also common among those with iron deficiency anemia (Van Wyk, 2018). The health history should include a medication history because some medications may depress bone marrow activity, induce hemolysis, interfere with folate metabolism, or cause GI irritation that leads to bleeding. An accurate social history should include alcohol intake, noting the amount consumed and the duration of alcohol use. Family history is also important since some types of anemia are inherited. The nurse should also inquire about athletic endeavors since extreme forms of exercise such as marathon running may influence erythropoiesis and erythrocyte survival (Leung, 2019).

A nutritional assessment is needed because it may indicate deficiencies in essential nutrients such as iron, vitamin B₁₂, and folate. People who follow strict vegetarian diets and do not supplement with vitamin B₁₂ are at risk for megaloblastic anemia. Older adults may also have decreased intake of foods rich in vitamin B₁₂ or folate.

Cardiac status should be assessed carefully. When hemoglobin levels are low, the heart attempts to compensate by pumping faster and harder to deliver more oxygen to hypoxic tissue. This increased cardiac workload can result in symptoms including tachycardia, palpitations, dizziness, orthopnea, and exertional dyspnea. Heart failure may eventually develop, evidenced by cardiomegaly (an enlarged heart), hepatomegaly (an enlarged liver), and peripheral edema.

GI assessment may reveal complaints of nausea, vomiting (with specific questions regarding the appearance of any emesis [e.g., looks like "coffee grounds"]), melena (dark stools), diarrhea, anorexia, and glossitis (inflammation of the tongue). Stool should be tested for occult blood.

Women should be asked about their menstrual periods (e.g., excessive flow, other vaginal bleeding) and the use of iron and vitamin supplements during pregnancy. Neurologic examination is important because pernicious anemia with vitamin B₁₂ deficiency affects the function of the central and peripheral nervous systems (see later discussion). Examination should include assessment for the presence and extent of peripheral numbness and paresthesia, ataxia, impaired coordination, and confusion. Delirium can sometimes result from other types of anemia, particularly in older adults. It is important to monitor relevant laboratory results over time and note any changes (see [Chapter 28](#)).

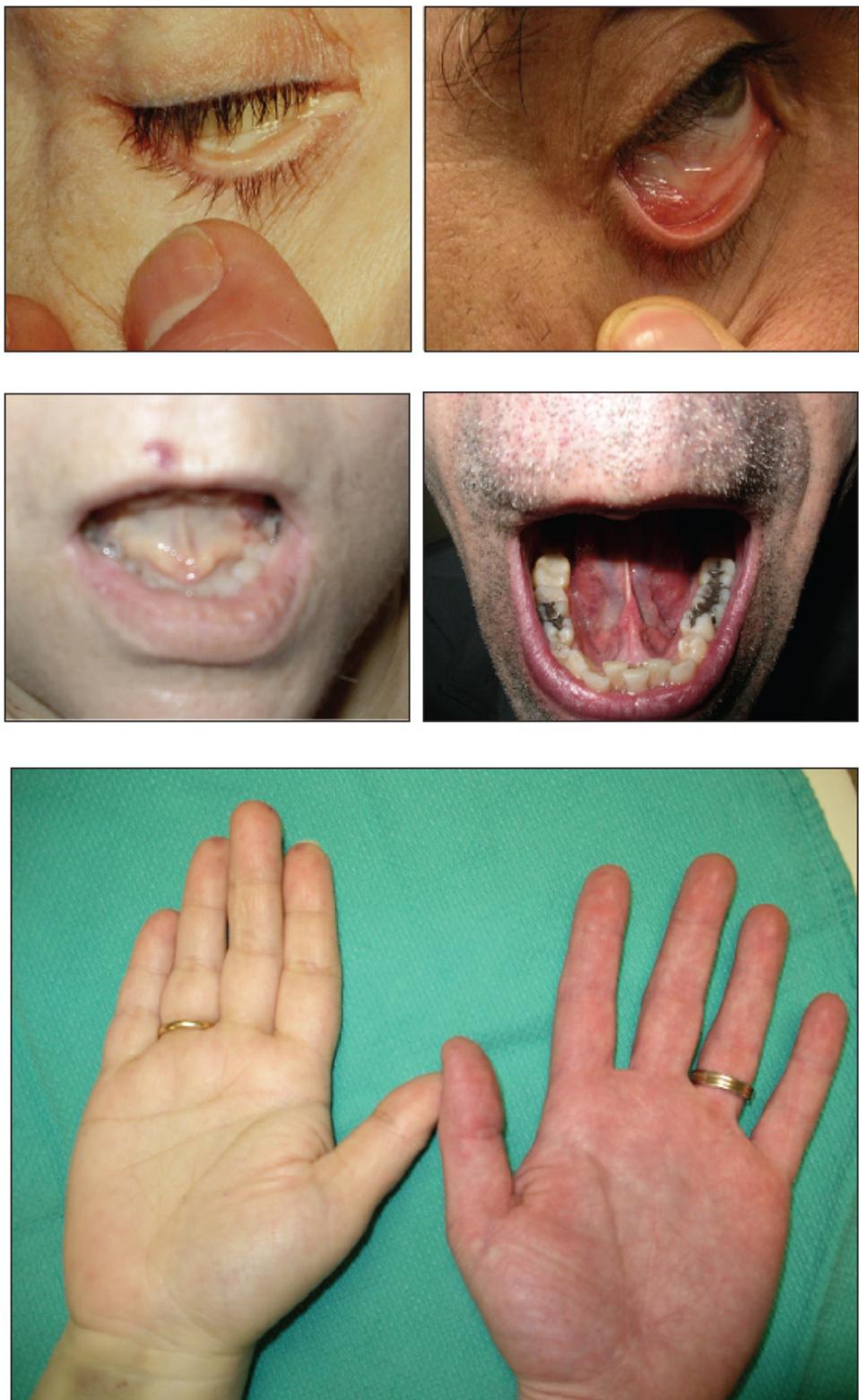


Figure 29-1 • Pallor seen in the patient with anemia. Reprinted with permission from Tkachuk, D. C., & Hirschman, J. V. (2007). *Wintrobe's atlas of clinical hematology* (Fig. 1.1, p. 9). Philadelphia, PA: Lippincott Williams & Wilkins.

Diagnosis

NURSING DIAGNOSES

Based on assessment data, major nursing diagnoses may include:

- Fatigue associated with decreased hemoglobin and diminished oxygen-carrying capacity of the blood
- Impaired nutritional status associated with inadequate intake of essential nutrients
- Activity intolerance associated with inadequate hemoglobin and hematocrit
- Impaired ability to manage regime associated with prescribed therapy

COLLABORATIVE PROBLEMS/POTENTIAL COMPLICATIONS

Potential complications may include the following:

- Heart failure
- Paresthesias
- Confusion
- Injury associated with falls

Planning and Goals

The major goals for the patient with anemia include decreased fatigue, attainment or maintenance of adequate nutrition, attainment or maintenance of adequate tissue perfusion, effective management of prescribed treatment plan, and absence of complications.

Nursing Interventions

MANAGING FATIGUE

The most common symptom and complication of anemia is fatigue. Fatigue is often the symptom with the greatest negative impact on the patient's ability to function and subsequent quality of life. Fatigue is often described as overwhelming or oppressive. The sensation of fatigue may be severe even when the anemia is not severe enough to warrant transfusion. Fatigue may interfere with the patient's ability to engage in work as well as pleasurable activities with family and friends. Significant distress can stem from the inability to meet life's demands and responsibilities and the need to rely on others for assistance.

Nursing interventions can focus on assisting the patient to prioritize activities to establish a balance between activity and rest that is acceptable to the patient. Patients with chronic anemia will need assistance in establishing a program of activity and exercise to avoid deconditioning associated with inactivity. It is also important to assess for other conditions that may contribute to fatigue, such as pain, depression, and sleep disturbances.

MAINTAINING ADEQUATE NUTRITION

Inadequate intake of essential nutrients, including iron, vitamin B₁₂, folic acid and protein, can cause some forms of anemia. The symptoms associated with anemia (fatigue, anorexia) can interfere with maintaining adequate nutritional intake. A well-balanced diet should be encouraged. The nurse should advise the patient that alcohol can interfere with utilization of some essential nutrients and recommend limited alcohol intake (Stouten, Riedel, Droogendijk, et al., 2016). Dietary education involving family members when possible should be individualized to address specific needs and include cultural preferences for food preparation and selection (see [Chapter 4](#)). Dietary supplements (e.g., vitamins and iron) may be prescribed.

Equally important, the patient and family need to understand the role of nutritional supplements in the proper context. Some forms of anemia are not associated with nutritional deficiency. In some cases, excessive use of supplements will not improve the anemia and may be harmful. For example, patients with anemia who receive long-term transfusion therapy are at risk for iron overload from their transfusions. In this situation chelation therapy is implemented to reduce accumulation of excess iron (Murray, De Gelder, Pringle, et al., 2016; see [Chapter 30](#) for discussion of chelation therapy). The use of oral iron supplements may exacerbate the situation.

MANAGING ACTIVITY INTOLERANCE

Patients with severe anemia, with acute blood loss from hemorrhage or severe hemolysis, may not tolerate decreased blood volume or reduced circulating erythrocytes. Lost volume can be replaced with transfusions or intravenous fluids based on symptoms and laboratory test results. Supplemental oxygen may be needed, especially if there is underlying cardiac or pulmonary disease. Monitoring the patient's vital signs and pulse oximetry, especially with activity, is an important nursing action. Medications, including antihypertensive drugs, may need to be adjusted or withheld based on the patient's vital signs.

PROMOTING EFFECTIVE MANAGEMENT OF PRESCRIBED THERAPY

Medications, including nutritional supplements, are frequently prescribed for patients with anemia. It is important that patients understand the purpose of these therapies, how to take them, and how to manage side effects of treatment. Nurses play an important role in promoting adherence to the prescribed plan by educating patients and family caregivers about ways to incorporate the therapeutic plan in daily activities. For example, side effects of oral iron supplements including GI distress may make adherence to treatment difficult for some patients and may contribute to some patients stopping treatment. Nurses can provide important education

and support to assist patients to cope with side effects. Abrupt cessation of some medications, including high-dose steroids for treatment of hemolytic anemia, can have serious consequences for patients. The cost of some medications, such as hematologic growth factors, can be quite high. Patients requiring these medications may need assistance to find alternative ways to obtain the necessary medication. Nurses may need to collaborate with social workers or other health care team members to assist patients in meeting these needs.

MONITORING AND MANAGING POTENTIAL COMPLICATIONS

A significant complication of anemia is heart failure associated with chronic diminished blood volume and the heart's compensatory effort to increase cardiac output. Patients with anemia should be assessed for signs and symptoms of heart failure (see [Chapter 25](#)).

In megaloblastic anemias associated with folate or vitamin B₁₂ deficiency, there is potential for neurologic complications. Neurologic assessment of patients with megaloblastic anemia should be performed. Patients may complain of paresthesias, often manifested by numbness and, as the anemia progresses, symptoms worsen and other signs become apparent. Position and vibration sense may be diminished. Difficulty maintaining balance and gait disturbances may occur. Mental status changes, beginning with confusion and progressing to more severe memory changes and delirium can occur with severe folate or vitamin B₁₂ deficiency (Elder et al., 2019).

Evaluation

Expected patient outcomes may include:

1. Reports less fatigue
 - a. Follows a graduated plan of rest, activity, and exercise
 - b. Prioritizes activities
 - c. Paces activities according to energy level
2. Attains and maintains adequate nutrition
 - a. Eats a healthy diet
 - b. Develops a meal plan that promotes optimal nutrition
 - c. Maintains appropriate amounts of iron, vitamins, and protein from diet and supplements
 - d. Adheres to nutritional supplements when prescribed
 - e. Verbalizes understanding of rationale for using recommended nutritional supplements when prescribed
 - f. Verbalizes understanding of rationale for avoiding nonrecommended nutritional supplements
3. Maintains appropriate activity level

- a. Vital signs will be within baseline for patient
 - b. Pulse oximetry value within normal limits
4. Absence of complications
 - a. Avoids or limits activities that trigger dyspnea, palpitations, dizziness, or tachycardia
 - b. Uses rest and comfort measures to relieve dyspnea
 - c. Has vital signs within baseline for patient
 - d. Has no signs of increased fluid retention (e.g., peripheral edema, decreased urine output, neck vein distention)
 - e. Remains oriented to time, place, and situation
 - f. Verbalizes understanding of importance of serial CBC and other laboratory test measurements
 - g. Maintains safe home environment; obtains and uses assistance as necessary

Hypoproliferative Anemias

The hypoproliferative anemias include iron deficiency anemia, anemias in renal disease, anemia of inflammation, aplastic anemia, and megaloblastic anemias.

Iron Deficiency Anemia

Iron deficiency anemia results when the intake of dietary iron is inadequate for synthesis of hemoglobin. The body is able to store about one fourth to one third of its iron requirements, and it is not until those stores are depleted that iron deficiency anemia develops. Iron deficiency anemia may occur when total body iron stores are adequate, but the amount of iron delivered to the erythroid precursors is inadequate. This is referred to as functional iron deficiency (Hashemi, Mashhadi, Mohammadi, et al., 2017). Iron deficiency anemia is the most common type of anemia in all age groups, and it is the most common form of anemia worldwide, affecting as many as one in eight people (Bunn & Heeney, 2017). It is especially prevalent in developing countries where iron stores may be chronically depleted because of lack of sources for iron-rich foods and from blood loss associated with intestinal parasites (Harper, Besa, & Conrad, 2019).

Iron deficiency anemia is also common among adults in the United States, with the most common cause being blood loss. Blood loss should always be considered as the cause of iron deficiency anemia until proven otherwise. The most common cause of this anemia in men and postmenopausal women is GI bleeding from ulcers, gastritis, tumors, or inflammatory bowel disease. The

most common causes of iron deficiency anemia in premenopausal women are menorrhagia (i.e., excessive menstrual bleeding) and pregnancy with inadequate iron intake. Patients with chronic alcohol abuse and patients who take aspirin, steroids, or nonsteroidal anti-inflammatory drugs (NSAIDs) may have chronic blood loss from the GI tract, leading to iron loss and subsequent anemia. Other causes include iron malabsorption, as seen after gastrectomy or bariatric surgery, or from celiac disease and inflammatory bowel diseases (Harper et al., 2019).

Clinical Manifestations

Patients with iron deficiency primarily have symptoms of anemia. If the deficiency is severe or prolonged, they may also have a smooth, red tongue; brittle and ridged nails; and angular cheilosis. These signs subside after iron replacement therapy. The health history may be significant for multiple pregnancies, GI bleeding, and pica (Camaschella, 2019).

Assessment and Diagnostic Findings

The definitive method of establishing the diagnosis of iron deficiency anemia is bone marrow aspiration (see [Chapter 28](#) for further discussion of bone marrow aspiration). The aspirate is stained to detect iron, which is at a low level or even absent. However, few patients with suspected iron deficiency anemia undergo bone marrow aspiration. In many patients, the diagnosis can be established with other tests, particularly in patients with a history of conditions that predispose them to this type of anemia.

A strong correlation exists between laboratory values that measure iron stores and hemoglobin levels. After iron stores are depleted (as reflected by low serum ferritin levels), the hemoglobin level falls. The diminished iron stores cause small erythrocytes to be produced by the marrow. Therefore, as the anemia progresses, the MCV, which measures the size of the erythrocytes, also decreases. Hematocrit and RBC levels are also low in relation to the hemoglobin level. Other laboratory tests that measure iron stores are useful but not as precise as ferritin levels. Typically, patients with iron deficiency anemia have a low serum iron level and an elevated TIBC, which measures the transport protein supplying the marrow with iron as needed (also referred to as transferrin) (Camaschella, 2019). However, other disease states, such as infection and inflammatory conditions, can also cause a low serum iron level and TIBC, as well as an elevated ferritin level. If these are suspected, measuring the soluble transferring receptor can aid in differentiating the cause of anemia. This test result will be increased in the setting of iron deficiency, but not in chronic inflammation (Camaschella, 2019).

Medical Management

Oral iron supplementation is often the primary mode of treatment for iron deficiency anemia. Several oral iron preparations, including ferrous sulfate, ferrous gluconate, and ferrous fumarate, are available. Ferric maltol, another oral preparation, was approved by the U.S. Food and Drug Administration (FDA) in 2019 for use in iron deficiency anemia in those with inflammatory bowel disease. After taking oral iron preparations, hemoglobin typically begins to increase within a few weeks and the anemia may be corrected within a few months. Replenishing iron stores takes several months so it is important that patients continue taking oral iron supplements for 6 to 12 months. If oral iron is poorly absorbed or poorly tolerated, or large amounts of supplemental iron are needed, intravenous (IV) iron may be given in repeated doses (see [Chart 29-2](#)). Initial evidence has shown that ferric maltol is not inferior to parenteral iron and may be an alternative for patients who cannot tolerate other oral preparations or do not wish to have parenteral iron; however, it is unknown whether use of ferric maltol will decrease demands for parenteral iron preparations (Harper et al., 2019).

Chart 29-2

Parenteral Iron Formulations

- Older formulations of parenteral iron had a high molecular weight and carried a significant risk for hypersensitivity reactions, including anaphylaxis. Newer formulations have a low molecular weight and a markedly lower risk for anaphylaxis.
- Ferric gluconate: Each 5 mL contains 62.5 mg of elemental iron; 125 mg is diluted in 100-mL normal saline and infused over 1 hour, or 5 mL undiluted is given as a slow IV push injection over 5 minutes. Although the likelihood of an allergic reaction is very low, a test dose is often given prior to the first infusion.
- Iron sucrose: Each 5 mL contains 100 mg of elemental iron; 100 to 200 g can be given, undiluted, as a slow IV push over 2 to 5 minutes. This procedure can be repeated as often as every 3 days for a cumulative dose of 1000 mg within a 2-week period.
- Ferumoxytol injection: The 17 mL vial is diluted in 50 to 200 mL of normal saline or 5% dextrose and water and infused over 15 minutes. Close observation for signs and symptoms of hypersensitivity reaction, including monitoring blood pressure and pulse, is recommended.

Adapted from Comerford, K. C., & Durkin, M. T. (2020). *Nursing 2020 drug handbook*. Philadelphia, PA: Wolters Kluwer.

Nursing Management

Preventive education is important for women who are menstruating and for those who are pregnant. Food sources rich in iron include organ meats (e.g., beef or calf's liver, chicken liver), other meats, beans (e.g., pinto, black, and garbanzo beans), leafy green vegetables, raisins, and molasses. Eating iron-rich foods with a source of vitamin C (e.g., orange juice) improves iron absorption.

The nurse assists the patient in selecting healthy diet options. Nutritional counseling can be provided for those who have an inadequate diet. Patients with history of strict vegetarian or other diets lacking in essential nutrients should be counseled about how to meet their dietary needs. The nurse also encourages the patient to continue the prescribed therapy for as long as needed to replenish iron stores even when fatigue and other symptoms have resolved.

Oral iron is best absorbed on an empty stomach, making it important for patients to be instructed to take the supplement approximately 1 hour before or 2 hours after meals. The least expensive, standard form of oral iron, ferrous sulfate, is tolerated by most patients. GI side effects, including constipation, cramping, nausea, and vomiting may result in difficulty adhering to the prescribed regimen. Decreasing the frequency of administration or taking iron supplements with food may reduce symptoms but will diminish iron absorption, thus, it may take longer to replete iron stores. Taking iron with vitamin C can enhance absorption, but it may also increase the frequency of side effects (Heffernan, Evans, Holmes, et al., 2017). Some iron formulations have been designed to limit GI side effects by adding stool softeners to reduce constipation or sustained release formulations to reduce gastritis and nausea. However, enteric-coated tablets may be poorly absorbed. Slow release formulations are absorbed beyond the duodenum; however, the duodenum is the site where maximum iron absorption takes place (Auerbach & Adamson, 2016). Educational materials to assist patients with use of iron supplements are available (see [Chart 29-3](#)).

Chart 29-3



PATIENT EDUCATION

Taking Oral Iron Supplements

The nurse instructs the patient to:

- Take iron on an empty stomach (1 hour before or 2 hours after a meal), preferably with orange juice or other source of vitamin C. Iron absorption is reduced by food, especially dairy products.
- Reduce gastrointestinal distress by using the following schedule when more than one tablet per day is prescribed: Take one tablet per day for the first few days, then increase to two tablets per day, then three tablets per day in divided doses. This allows gradual adjustment to the iron. If unable to tolerate oral supplements due to gastrointestinal distress despite using this intervention, a reduced amount of iron may be used rather than stopping it completely. Reduced doses will require that the treatment duration is extended to adequately replenish iron stores.
- Increase intake of foods rich in vitamin C to enhance iron absorption (citrus fruits and juices, strawberries, tomatoes, broccoli).
- Note that stool will be dark in color and often appear black.
- Eat foods high in fiber to reduce problems with constipation. A stool softener may be needed.
- Be aware that liquid iron preparations may stain the teeth. They may be taken through a straw or by placing the spoon at the back of the mouth. Rinse the mouth thoroughly after each dose.

If taking iron on an empty stomach causes GI distress, the patient may need to take it with meals. However, this may reduce absorption by as much as 40%, therefore increasing the time needed to replenish iron stores. Antacids and dairy products should be avoided with iron as they can greatly diminish its absorption. Polysaccharide iron complex preparations are available. These reduce GI toxicity but are more expensive. Liquid forms of iron that cause less GI distress are also available. Oral iron replacement therapy may change the color of the stool but should not cause a false-positive result for occult blood on stool analysis.

IV supplementation may be used when the patient's iron stores are very low, if the patient cannot tolerate oral forms of iron, or both. The nurse must be aware of the type of parenteral formulation of iron ordered so that risk for anaphylaxis can be determined. High-molecular formulations are associated with a much higher risk for anaphylaxis and are seldom used. Administering a test dose of low-molecular formulations of iron dextran is recommended by many manufacturers. The nurse must assist the patient in understanding the need for repeated doses to replenish iron stores or to maintain iron stores in the setting of chronic blood loss, such as hemodialysis or chronic GI bleeding.

Anemias in Renal Disease

The degree of anemia in patients with chronic kidney disease (CKD) can vary greatly; however, in general, patients do not become severely anemic until the glomerular filtration rate (GFR) is less than 30 mL/min/1.73 m² (Fishbane & Spinowitz, 2018). The symptoms of anemia may be the most troubling of the patient's symptoms. In patients with CKD, anemia contributes to increased cardiac output, reduced oxygen utilization, decreased cognition and ability to concentrate, reduced immune responsiveness, and reduced libido. Anemia may be more severe in patients with both CKD and diabetes (Fishbane & Spinowitz, 2018). Anemia in patients with CKD is discussed in Chapter 48.

Anemia of Inflammation

Anemia of inflammation describes anemia associated with chronic diseases including inflammation, infection, and malignancy. This classification was previously known as anemia of chronic disease (Weiss, Ganz, & Goodnough, 2019). This classification also includes anemia of critical illness that can develop within days after the onset of serious illness, and the anemia associated with aging. Many chronic inflammatory diseases are associated with **normochromic, normocytic** anemia (i.e., RBCs are of normal color and size). These disorders include rheumatoid arthritis, chronic infections, and many cancers. It is important that the underlying condition be identified so that it can be treated appropriately.

The anemia of inflammation is usually mild to moderate and not progressive. The hemoglobin level does not usually fall below 9 g/dL and bone marrow samples have normal cellularity and normal stores of iron. Erythropoietin levels are low and iron use is blocked by **erythroid cells** (cells that are or will become mature RBCs). Erythrocyte survival may also be shortened.

Many patients with anemia of inflammation have few symptoms related to their anemia and do not require treatment. Treatment of the underlying disorder allows iron stored in the bone marrow to be utilized, promoting increased RBC production and facilitating the rise of hemoglobin levels. Iron supplementation is not beneficial for these patients.



Gerontologic Considerations

Evidence suggests that inflammation may have a significant role in the development of anemia in older adults (Price, 2019). Higher-than-normal levels of inflammatory **cytokines** are found in older adults, and this pro-inflammatory state may predispose older adults to frailty. Frailty is manifested by weight loss, impaired mobility, generalized weakness, and loss of balance

and is strongly associated with anemia of inflammation. Erythropoietin levels may not rise as expected in response to decreased hemoglobin (Price, 2019).

Aplastic Anemia

Aplastic anemia is a rare disease caused by a decrease in or damage to bone marrow stem cells, damage to the microenvironment within the bone marrow, and replacement of marrow with fat. Stem cell damage is caused by the body's T cells, which mediate an attack on the bone marrow resulting in **aplasia** (i.e., markedly reduced hematopoiesis). Therefore, in addition to severe anemia, significant **neutropenia** (i.e., lower-than-normal neutrophil count) and **thrombocytopenia** (i.e., lower-than-normal platelet count) also occur.

Pathophysiology

Aplastic anemia is a life-threatening condition associated with bone marrow failure evidenced by **pancytopenia** (i.e., anemia, neutropenia, and thrombocytopenia; lower-than-normal counts of erythrocytes, neutrophils, and platelets) (Peslak, Olson, & Babushok, 2017). It can be acquired, or in rare cases, congenital, but most cases are idiopathic (i.e., without apparent cause) (Young, 2018). It may also be associated with certain medications, chemicals, or radiation damage. Agents that have been associated with bone marrow aplasia include benzene and benzene derivatives (i.e., airplane glues, paint remover, dry cleaning solutions). Certain toxic materials, including inorganic arsenic, glycol ethers, plutonium, and radon, have also been suggested as possible causes (Young, 2018). Nonviral hepatitis may be a precipitating factor in about 10% of cases (Peslak et al., 2017).

Clinical Manifestations

The onset of symptoms of aplastic anemia is often insidious. Complications stemming from bone marrow failure may occur before the diagnosis is made. Typical complications include infection and symptoms of anemia, including fatigue, pallor, and dyspnea. Purpura (bruising) associated with thrombocytopenia may develop. Any combination of these signs and symptoms should prompt a CBC and hematologic evaluation. Lymphadenopathy and splenomegaly may also occur. Retinal hemorrhages are common.

Assessment and Diagnostic Findings

Aplastic anemia occurs in some situations when a medication or chemical is ingested in toxic amounts; however, it may occur even when medications are

taken at the recommended dosage. This is known as an idiosyncratic reaction in those who are highly susceptible, possibly due to a genetic defect in the biotransformation of the medication or elimination process. The CBC reveals pancytopenia. Patients may have neutrophil counts less than 1,500/mm³, hemoglobins less than 10 g/dL, and platelet counts less than 50,000/mm³ (Segel & Lichtman, 2016). A bone marrow biopsy typically reveals an extremely hypoplastic or aplastic bone marrow (i.e., with few or no cells), often replaced with fat.

Medical Management

It is believed that aplastic anemia is an immune-mediated condition in which T lymphocytes attack hematopoietic stem cells with subsequent reduction in production of erythrocytes, leukocytes, and platelets. Aplastic anemia can be successfully treated in many cases. Patients under 60 years of age who are otherwise healthy can often be cured with a hematopoietic stem cell transplant (HSCT) from a compatible donor (see [Chapter 12](#)) (Young, 2018). In other situations, treatment with immunosuppressive therapy using antithymocyte globulin (ATG) and androgens or cyclosporine is useful in managing the disease (Young, 2018). ATG is a purified gamma-globulin solution that is obtained from rabbits or horses immunized with human T lymphocytes. Side effects of such therapy include fever and chills. There is risk for anaphylaxis with associated bronchospasm and hypotension requiring emergency treatment. Serum sickness, associated with rash, fever, arthralgias, and pruritus may occur in some patients but can be prevented or reduced in some cases with premedication with corticosteroids (Segel & Lichtman, 2016). Serum sickness resolves slowly, often over a few weeks when it occurs.

Immunosuppressive therapies prevent T cells from destroying stem cells. If relapse does occur, resuming the same immunosuppressive therapy may induce another remission but the response rate is usually reduced (Segel & Lichtman, 2016). Corticosteroids may be beneficial in the short-term; however, in aplastic anemia, long-term use is associated with bony abnormalities including aseptic necrosis and osteopenia.

Supportive therapies play a critical role in the management of aplastic anemia. All potentially offending medications should be discontinued. Transfusions with PRBCs and platelets are frequently required (see [Chapter 28](#) for discussion of transfusions); however, judicious use of blood products is necessary, especially for patients who are candidates for bone marrow transplant because of the risk for alloimmunization (Peslak et al., 2017). Aggressive treatment of infections is necessary. Deaths associated with aplastic anemia are most often caused by bacterial or fungal infection and bleeding.

Prophylaxis against invasive fungal infection is needed for patients who are severely neutropenic. Patients who become lymphopenic after ATG require prophylaxis for pneumocystis pneumonia.

Nursing Management

Patients with aplastic anemia are at high risk for problems associated with deficiencies of erythrocytes, leukocytes, and platelets. Thorough assessment for signs of infection and bleeding are critical (see later sections on Neutropenia and Thrombocytopenia for specific interventions). Nursing care includes monitoring for side effects of therapy, including hypersensitivity reactions while administering ATG. Patients who require long-term cyclosporine therapy should be monitored for long-term effects, including renal and liver dysfunction, hypertension, pruritus, visual changes, tremor, and skin cancer. Education regarding drug–drug interactions between ATG and many other drugs is necessary. Patients should be informed that stopping immunosuppressive therapy abruptly is not recommended.

Megaloblastic Anemias

Anemias associated with vitamin B₁₂ or folic acid deficiency cause the same bone marrow and peripheral blood changes because both are needed for normal DNA synthesis. The erythrocytes produced with these nutritional deficiencies are abnormally large, thus they are termed megaloblastic red blood cells. Other cells from the myeloid stem cell lines (nonlymphoid leukocytes and platelets) are also abnormal. Bone marrow analysis shows hyperplasia (an abnormal increase in the number of cells) and the precursor erythroid and myeloid cells are abnormally large and irregular in appearance. Many of these abnormal cells are destroyed within the bone marrow leading to an insufficient number of mature cells entering the peripheral blood. Over time, pancytopenia may develop. Cells that enter the circulation are often irregularly shaped; neutrophils are hypersegmented, and platelets may be abnormally large. Erythrocytes are abnormally shaped and shapes can vary greatly; this is known as **poikilocytosis**. Because erythrocytes are very large, the MCV is very high, often exceeding 110 fL. Megaloblastic anemias usually develop over months, allowing the body to compensate; thus, symptoms do not often occur until the anemia is severe (Green, 2016). In patients with light skin, the skin may develop a pale-yellow color resulting from simultaneous pallor and mild jaundice from red blood cell hemolysis.

Pathophysiology

The pathophysiologic mechanisms that undergird megaloblastic anemias are most commonly because of either a folic acid or vitamin B₁₂ deficiency, as noted previously.

Folic Acid Deficiency

Folic acid is stored in the body as compounds known as folates. Folate stores are smaller than those of vitamin B₁₂ and can be depleted within months if dietary intake of folate is deficient (Green, 2016). Folate is found in green vegetables and liver. Folate deficiency is rarely seen in patients who consume uncooked vegetables. Alcohol ingestion increases folic acid requirements and it is not uncommon for those with alcohol abuse disorder to have a diet deficient in folate and other nutrients. Folic acid requirements are also higher in those with liver disease, chronic hemolytic anemias, and in women who are pregnant because erythrocyte production is increased with these conditions. Small bowel diseases such as celiac disease may interfere with normal absorption of folic acid (Green, 2016).

Vitamin B₁₂ Deficiency

Deficiency of vitamin B₁₂ can occur in several ways. Inadequate dietary intake is unusual but sometimes can occur in people who follow a vegan diet and do not consume any meat or dairy products. Impaired absorption from the GI tract is more common, especially in older adults. Nearly 20% of older adults have low vitamin B₁₂ levels; 5% to 10% have symptoms related to vitamin B₁₂ deficiency (Langan & Goodbred, 2017). Vitamin B₁₂ deficiency can occur in patients with disorders such as inflammatory bowel disease, or in patients who have had GI surgery such as ileal resection, bariatric surgery, or gastrectomy. Use of metformin for treatment of type 2 diabetes as well as chronic use of histamine blockers, antacids, and proton pump inhibitors to reduce gastric acid can also inhibit vitamin B₁₂ absorption (Lanier et al., 2018).

Absence of intrinsic factor also impairs vitamin B₁₂ absorption. When associated with lack of intrinsic factor, the anemia is referred to as pernicious anemia. Intrinsic factor is normally secreted by cells in the gastric mucosa; it binds to vitamin B₁₂ and transports it to the ileum where it is absorbed. Without intrinsic factor, vitamin B₁₂ taken orally cannot be absorbed and deficiency with associated anemia eventually results. Diseases of the pancreas and ileum may impair absorption even when adequate intrinsic factor and vitamin B₁₂ are present. Pernicious anemia tends to run in families. It is typically a disease of adults, especially older adults. The body typically has large stores of vitamin B₁₂ so years may pass before deficiency results in anemia. The body is able to compensate over time and the anemia is often severe before the patient becomes symptomatic. Because patients with

pernicious anemia and low vitamin B₁₂ levels have an increased incidence of gastric cancer they may benefit from screening for gastric cancer with endoscopy at regular intervals (Miranti, Stolzenberg-Solomon, Weinstein, et al., 2017).

Clinical Manifestations

Symptoms of folic acid and vitamin B₁₂ deficiencies are similar, and the two anemias may coexist. However, the neurologic manifestations of vitamin B₁₂ deficiency do not occur with folic acid deficiency, and they persist if vitamin B₁₂ is not replaced. Therefore, careful distinction between the two anemias must be made.

After the body's stores of vitamin B₁₂ are depleted, the patient may begin to show signs and symptoms of the anemia. However, because the onset and progression of the anemia are so gradual, the body can compensate well until the anemia is severe, so the typical manifestations of anemia (weakness, listlessness, fatigue) may not be apparent initially. The hematologic effects of vitamin B₁₂ deficiency are accompanied by effects on other organ systems, particularly the GI tract and nervous system. Patients with pernicious anemia develop a smooth, sore, red tongue and mild diarrhea. They are extremely pale, particularly in the mucous membranes. They may become confused; more often, they have paresthesias in the extremities (particularly numbness and tingling in the feet and lower legs). They may have difficulty maintaining their balance because of damage to the spinal cord, and they also lose position sense (proprioception). These symptoms are progressive, although the course of illness may be marked by spontaneous partial remissions and exacerbations. Without treatment, heart failure associated with severe anemia may result, often leading to death several years after onset of symptoms (Leung, 2019).

Assessment and Diagnostic Findings

Serum levels of both folic acid and vitamin B₁₂ are analyzed. Small amounts of folate can increase the serum folate level; therefore, measurement of the amount of folate within the red blood cells is a more sensitive test to determine true folate deficiency although it is not commonly performed.

The traditional method of determining the cause of vitamin B₁₂ deficiency was the Schilling test, but in recent years this has been replaced by other testing methods. A vitamin B₁₂ assay is usually the initial test performed but the reliability of the results is sometimes questionable, when vitamin B₁₂ levels are not unequivocally low. Elevated methylmalonic acid and homocysteine levels are more sensitive for the diagnosis of vitamin B₁₂ deficiency (Lanier et al., 2018). An intrinsic factor antibody test is often more useful in

determining the presence of pernicious anemia. A positive test indicates that antibodies are present that interfere with the binding of the intrinsic factor–vitamin B₁₂ complex to receptors in the ileum, preventing absorption. While not specific for only pernicious anemia, it is useful in helping arrive at the diagnosis.

Medical Management

Folate deficiency is easily treated in most cases by increasing the amount of folic acid in the diet and taking 1 mg of folic acid daily as a supplement. Folic acid can be given intramuscularly to those people with conditions associated with malabsorption. While many multivitamin supplements contain folic acid, the amount may not be enough to replace body stores completely. When folate deficiency is associated with alcohol abuse, supplementation should continue as long as the patient is consuming alcohol.

Vitamin B₁₂ deficiency is treated with vitamin B₁₂ replacement. People who follow a vegan diet can prevent or treat deficiency with oral supplements with vitamins or fortified soy milk. When deficiency is caused by impaired absorption or absence of intrinsic factor (i.e., pernicious anemia), replacement is typically given by monthly intramuscular injections. It is possible to treat patients with oral preparations in the absence of intrinsic factor but much larger doses are required. Intranasal sprays and gels are also available options to avoid the need for intramuscular injections.

As vitamin B₁₂ is replaced, the reticulocyte count rises, often within 1 week, and within 4 to 8 weeks blood counts return to normal (Green, 2016). The tongue begins to feel better and appears less red after several days. Recovery from neurologic symptoms takes more time, and, if the neuropathy is severe, the patient may not fully recover. To prevent a recurrence of pernicious anemia, vitamin B₁₂ supplementation must continue for life.

Nursing Management

Assessment of patients who have or are at risk for megaloblastic anemia includes inspection of the skin, tongue, and mucous membranes. Mild jaundice may be evident and is best seen in the sclera with natural lighting. Vitiligo and premature graying of the hair are frequently present in those with pernicious anemia. Careful neurologic assessment is important to identify neurologic complications. Assessment should include tests of position, vibration sense, and cognitive function. The nurse should pay close attention to the patient's gait and stability with ambulation. Safety is a concern when gait, coordination and position sense are affected. Physical and occupational therapy referrals may be needed to assist in obtaining assistive devices and making sure patients

are instructed in their use. When sensation is impaired, patients should be instructed to avoid excessive heat and cold.

Mouth and tongue soreness may impair nutritional intake. The nurse may instruct the patient to choose soft bland foods that are less likely to cause further discomfort.

Promoting Home, Community-Based and Transitional Care

Education for patients with pernicious anemia must include the chronic nature of this condition and the necessity of monthly vitamin B₁₂ injections or daily oral vitamin B₁₂ supplements even when symptoms have resolved. Patients or a family caregiver can be taught to administer injections. The risk for gastric cancer is increased in patients with gastric atrophy associated with pernicious anemia making it important that patients understand the need for ongoing follow-up care and screening (see [Chapter 40](#) for further discussion on gastric cancer).

Hemolytic Anemias

In hemolytic anemias, the erythrocytes have a shortened lifespan; thus, their number in the circulation is reduced. Fewer erythrocytes result in decreased available oxygen, causing hypoxia, which in turn stimulates an increase in erythropoietin release from the kidney. Erythropoietin then stimulates the bone marrow to compensate by producing new erythrocytes and releasing some of them into the circulation somewhat prematurely as reticulocytes. If the red cell destruction persists, the hemoglobin is broken down excessively; the majority of the heme is converted to bilirubin, conjugated in the liver, and excreted in the bile (Packman, 2016). Hemolytic anemias are far less common than other forms of anemia with approximately 5% of all anemias caused by hemolysis (Schick, 2019).

The mechanisms of erythrocyte breakdown vary, but common laboratory features are characteristic of hemolytic anemia. These include elevated reticulocyte count, increased fraction of indirect (unconjugated) bilirubin, and decreased **haptoglobin** (a binding protein for free hemoglobin) as additional hemoglobin is released from the cells. Anemia worsens if hemolysis persists and the bone marrow is unable to replace the destroyed cells.

Hemolytic anemia is associated with a variety of conditions. Inherited forms include SCD, thalassemias, G-6-PD deficiency, and hereditary spherocytosis. Acquired forms include immune hemolytic anemia, non-immune-mediated paroxysmal nocturnal hemoglobinuria, microangiopathic hemolytic anemia, heart valve-related hemolysis and anemias associated with hypersplenism.

Sickle Cell Disease

SCD is an autosomal recessive disorder caused by inheritance of the sickle hemoglobin (HbS) gene. It is associated with severe hemolytic anemia. The HbS gene results in production of a defective hemoglobin molecule that causes the erythrocyte to change shape when exposed to low oxygen tension. In some circumstances, even the oxygen level in venous blood can cause this change. The erythrocyte usually has a round, biconcave, pliable shape which in SCD can easily become rigid and sickle shaped (see Fig. 29-2). The long, rigid cells can subsequently adhere to the walls of small blood vessels where they accumulate, causing decreased blood flow to the tissues and organs in that region. When blood flow is severely reduced, ischemia or infarction of the tissue can cause severe pain, swelling, and fever referred to as a sickle cell crisis. Because the sickling process takes time, if the patient is exposed to adequate amounts of oxygen, the process can be reversed before the cell membranes become too rigid, allowing the erythrocytes to return to their normal shape. Sickling crises are intermittent and can be triggered by cold because of vasoconstriction that slows blood flow.

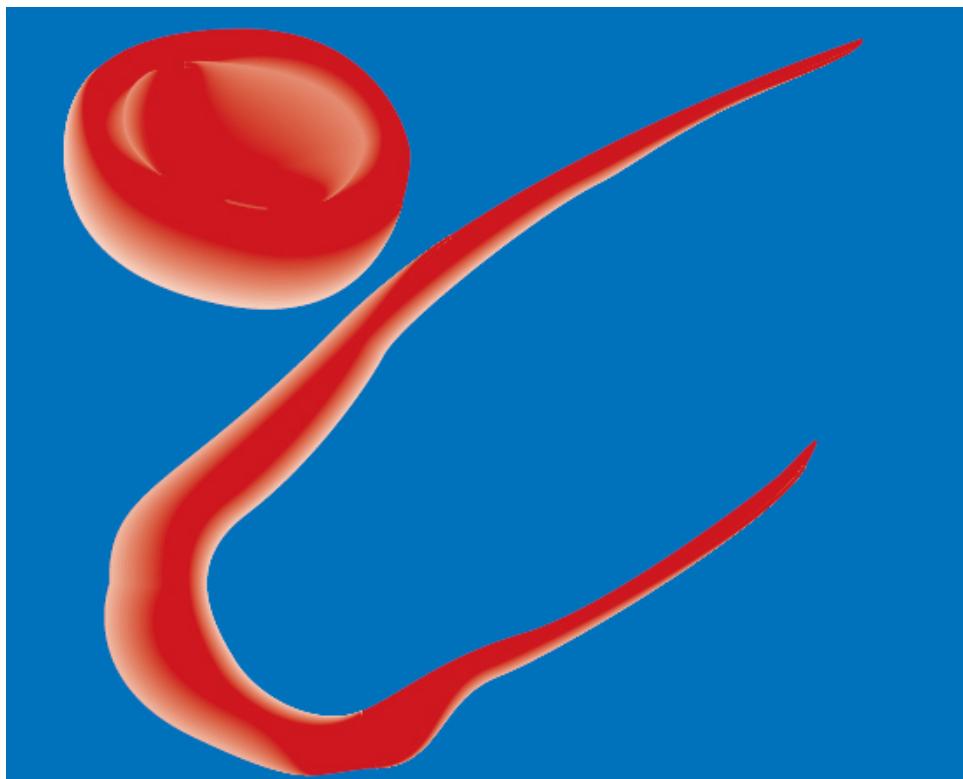


Figure 29-2 • A normal red blood cell (**upper left**) and a sickled red blood cell.

The HbS gene is inherited primarily in people of African descent. It may also be seen to a lesser degree in people of Middle Eastern and Mediterranean descent, and some tribal populations in India (Bunn, 2017b). Sickle cell anemia is the most severe form of SCD and is found in approximately 1 in 365 African Americans (National Heart Lung and Blood Institute, 2014). Other less severe forms of SCD include sickle cell hemoglobin C (SC) disease, sickle cell hemoglobin D (SD) disease, and sickle cell beta-thalassemia. Clinical presentation and treatment for these forms of the disease are the same as for sickle cell anemia.

The term sickle cell trait refers to the carrier state for SCD in which the patient has inherited a sickle gene from one parent and a normal gene from the other parent. Less than 50% of the hemoglobin within the erythrocytes is HbS. Those with sickle cell trait may be unaware that it is present unless severe hypoxia is experienced. Approximately 10% of African Americans have sickle cell trait (Bunn, 2017b). It is important that patients with sickle cell trait understand that if two people with sickle cell trait have children, the children have approximately one in four odds of inheriting two abnormal genes and will manifest SCD (see [Chapter 6](#) for additional discussion of genetic diseases).

Clinical Manifestations

Symptoms of SCD vary and are not solely based on the amount of HbS present. Symptoms and complications are the result of chronic hemolysis and thrombosis. Sickled cells hemolyze rapidly and have a shortened lifespan. Anemia is typically present with hemoglobin values between 5 and 11 g/dL (Natrajan & Kutlar, 2016). Jaundice is often present. The bone marrow expands early in life to compensate for the resulting anemia, sometimes causing enlargement of the bones in the face and skull. Chronic anemia is often associated with tachycardia, cardiac murmurs, and cardiomegaly. Arrhythmias and heart failure may also occur, especially in adults.

Any organ can be affected by thrombosis, but those areas with slower circulation are frequently involved, including the lungs, spleen, and central nervous system (CNS). All tissues and organs can be affected by thrombosis in the microcirculation caused by the sickling process leading to hypoxia and tissue damage and necrosis. Patients with SCD are particularly susceptible to infections, especially pneumonia and osteomyelitis. Additional complications of SCD include stroke, kidney injury, impotence, and pulmonary hypertension (see [Table 29-2](#)).

TABLE 29-2 Complications in Sickle Cell Disease^a

Organ Involved	Mechanisms ^b	Diagnostic Findings	Signs and Symptoms
Spleen	Primary site of sickling → infarctions → ↓ phagocytic function of macrophages	Autosplenectomy; ↑ infection (especially pneumonia, osteomyelitis)	Abdominal pain; fever, other signs of infection
Lungs	Infection Infarction → ↑ pulmonary pressure → pulmonary hypertension	Pulmonary infiltrate ↑ sPLA ₂ ^b	Chest pain; dyspnea Chest pain; dyspnea
Central nervous system	Infarction	Stroke	Weakness; cognitive dysfunction, speech and swallowing dysfunction
Kidney	Sickling → damage to renal medulla	Hematuria; inability to concentrate urine; kidney injury	Dehydration
Heart	Anemia	Tachycardia; cardiomegaly → heart failure	Weakness, fatigue, dyspnea
Bone	↑ Erythroid production Infarction of bone	Widening of medullary spaces and cortical thinning Osteosclerosis → avascular necrosis	Ache, arthralgias Bone pain, especially hips
Liver	Hemolysis	Jaundice and gallstone formation; hepatomegaly	Abdominal pain
Skin and peripheral vasculature	↑ Viscosity/stasis → infarction → skin ulcers	Skin ulcers; ↓ wound healing	Pain
Eye	Infarction	Scarring, hemorrhage, retinal detachment	↓ Vision; blindness
Penis	Sickling → vascular thrombosis	Priapism → impotence	Pain, impotence

→, leading to; ↓, decreased; ↑, increased; sPLA₂, secretory phospholipase A₂.

^aProblems encountered in sickle cell disease vary and are the result of a variety of mechanisms, as depicted in this table. Common physical findings and symptoms are also variable.

^bElevated sPLA₂ levels can predict impending acute chest syndrome (see text).

Adapted from Natrajan K., & Kutlar, A. (2016). Disorders of hemoglobin structure: Sickle cell anemia and related abnormalities. In K. Kaushansky, M. A. Lichtman, J. T. Prchal,

et al. (Eds.). *Williams hematology* (9th ed.). New York: McGraw-Hill Medical.

Sickle Cell Crisis

Three types of sickle cell crises affect adults. The most common is *acute vaso-occlusive crisis* (Kim, Brathwaite, & Kim, 2017). This very painful condition is the result of accumulation of erythrocytes and leukocytes in the microcirculation restricting blood flow to the tissue and causing hypoxia, inflammation, and necrosis. Substances released after tissue perfusion is restored include free radicals and free plasma hemoglobin, which cause oxidative damage to the blood vessel. As a result, the endothelial tissues in the vessel become dysfunctional (Bunn, 2017b). *Aplastic crisis* results from infection with the human parvovirus. The hemoglobin level falls rapidly and the marrow cannot compensate, as evidenced by an absence of reticulocytes (Natrajan & Kutlar, 2016). *Sequestration crisis* results when sickled cells are pooled in organs. In young children, the most common site of sequestration is the spleen; however, in many children with SCD over 10 years of age, the spleen has been infarcted and is no longer functional (Natrajan & Kutlar, 2016). In adults, the most common organs involved are the liver and the lungs.

Acute Chest Syndrome

Acute chest syndrome is a frequent complication in those hospitalized with SCD and is associated with significant morbidity and mortality. Acute chest syndrome is most frequently manifested by fever; respiratory distress that is manifested with tachypnea, cough and wheezing; and new infiltrates on the chest x-ray (Jain, Bakshi, & Krishnamurti, 2017). It is a common cause of death in young adults with SCD (Field, 2019). Infection with atypical bacteria including *Chlamydia pneumoniae* and *Mycoplasma pneumoniae* and viruses, including influenza, are often the cause. Other causes of acute chest syndrome include pulmonary thromboembolism, pulmonary fat embolism, bone marrow embolism, and pulmonary infarction. The patient's clinical condition can deteriorate very quickly leading to respiratory failure. Medical management includes blood transfusion, antibiotics, bronchodilators, inhaled nitric oxide, and when respiratory failure occurs, mechanical ventilation. Risk for acute chest syndrome can be reduced through immunization against influenza and pneumococcal pneumonia, and with use of incentive spirometry during vaso-occlusive crises, and with blood transfusion perioperatively (Jain et al., 2017). Prompt recognition and aggressive treatment can result in good outcomes for this potentially life-threatening condition.

Pulmonary Hypertension

Pulmonary hypertension is a common sequela of SCD and is a common cause of death (Natrajan & Kutlar, 2016). The onset of symptoms of pulmonary

hypertension is insidious; diagnosis is difficult in the early stages and is usually delayed until irreversible damage occurs. Symptoms include fatigue, dyspnea on exertion, dizziness, chest pain, or syncope. Pulse oximetry is usually normal and breath sounds are often clear to auscultation until the condition is quite advanced. Pulmonary artery pressures are elevated above baseline but are generally lower than seen with idiopathic or hereditary pulmonary hypertension. Screening of patients with SCD with Doppler echocardiography may be helpful in identifying increased pulmonary artery pressure (Kling & Farber, 2019). High levels of the amino-terminal form of brain natriuretic peptide can be a biomarker for pulmonary hypertension in people with SCD and serve as a predictor of mortality (Kling & Farber, 2019). Computed tomography (CT) scan of the chest frequently reveals microvascular pulmonary occlusion and decreased lung perfusion while chest x-ray may appear normal.

Stroke

Stroke is a catastrophic consequence of SCD that affects approximately 10% of patients under 20 years of age (Natrajan & Kutlar, 2016). Ischemic stroke is most common, especially in young children and older adults, while hemorrhagic stroke is more common in young adults. The mechanisms vary but often result from decreased blood flow due to anemia, hemolysis, and increased hypoxic stress. Silent cerebral infarction occurs in about 40% of patients with SCD who have strokes, resulting in neurocognitive decline (Vichinsky, 2017). Medical management of stroke includes red blood cell transfusion to reduce the amount of hemoglobin S to less than 30% to reduce the risk of cerebral edema (George, 2019).

Reproductive Disorders

The adverse effects of SCD on sexual function have become more evident as patients with the disease are living longer. Hypogonadism with associated low testosterone levels, delayed puberty, low libido, erectile dysfunction, and infertility occur frequently in men with SCD (Huang & Muneyyirci-Delale, 2017). Episodes of priapism (prolonged penile erection, without sexual stimulation) also contribute to significant pain and decreased libido. Over time, repeated episodes lead to permanent damage and erectile dysfunction, thereby making priapism a medical emergency that needs early recognition and treatment to preserve normal sexual function (Field, Vemulakonda, DeBaun, et al., 2019). In addition to physical signs and symptoms, these problems can also lead to embarrassment and depression.

In young women, menarche may be delayed, but menstrual patterns are generally normal. Fertility problems in women are not well described. Contraception is important when hydroxyurea is used in SCD treatment

because of its teratogenic effects. Concerns about infertility may be associated with poor adherence to hydroxyurea therapy. Although most pregnancies complicated by maternal SCD are likely to result in live births, these pregnancies are at increased risk of obstetrical and fetal complications, as well as medical complications of SCD (Vichinsky, 2018).

Assessment and Diagnostic Findings

The patient with sickle cell trait usually has a normal hemoglobin level, normal hematocrit, and normal blood smear. Conversely, the patient with SCD has a low hematocrit and sickled cells on the blood smear. The white blood cell count and platelet count are often elevated as a result of a chronic inflammatory state (Natrajan & Kutlar, 2016). Abnormal hemoglobin is identified by hemoglobin electrophoresis.

Medical Management

Patients with SCD are typically diagnosed in childhood, with anemia often occurring in infancy and crises beginning as early as 1 or 2 years of age. Some children die in the first few years of life as a result of infection; however, outcomes have improved considerably in recent years. Average life expectancy is lower than the general population, rarely exceeding the sixth decade (Field, 2019). Young adults often experience multiple, severe complications from their disease. A subgroup of patients experiences a decrease in symptoms and complications after age 30; however, at present there is no means to predict who will fall into this group. Death is most often caused by cardiac, lung, kidney, or neurologic complications, or from infection (Field, 2019).

Treatment of SCD is the focus of continued research. In addition to aggressive management of symptoms, including pain, and complications, there are a few primary treatment modalities.

Hematopoietic Stem Cell Transplant

HSCT may cure SCD. However, this treatment modality is available to only a small subset of affected patients, either due to a lack of compatible donors or due to severe organ damage (e.g., renal, liver, lung) that may be already present in the patient (see [Chapter 12](#) for further discussion of HSCT).

Pharmacologic Therapy

For patients with SCD, hydroxyurea is a chemotherapeutic agent that is effective in increasing levels of fetal hemoglobin (i.e., hemoglobin F), which in turn decreases the formation of sickled cells. It is the only drug currently approved by the FDA for treatment of SCD. Studies have demonstrated that

patients with SCD who received hydroxyurea experienced fewer episodes of painful crisis, had a lower incidence of acute chest syndrome, and needed fewer transfusions (Matte, Zorzi, & De Franceschi, 2019). Additional studies have shown a 40% decrease in mortality in patients receiving hydroxyurea (Natrajan & Kutlar, 2016). It is unknown whether hydroxyurea can prevent or reverse organ damage. Side effects of the drug include chronic lowering of the leukocyte count, teratogenesis, and potential for later development of a malignancy. Patients' response to the drug can vary widely. The incidence and severity of side effects are variable. Adherence to the prescribed treatment regimen may be difficult for some patients.

Patients with SCD often require daily folic acid supplements to maintain the amount needed for increased erythropoiesis to counteract the effects of hemolysis. Infections are common and should be treated promptly with the appropriate antibiotics. Pneumococcal pneumonia is common in children with SCD while in adults, *Staphylococcus aureus* infection is more common, involving bones and joints (Natrajan & Kutlar, 2016). Patients should be immunized against pneumococcal infection and receive annual influenza vaccines.

Acute chest syndrome is managed by prompt treatment with antibiotics. Incentive spirometry has been shown to significantly reduce the incidence of pulmonary complications. In severe cases, bronchoscopy may be needed to identify the source of acute chest syndrome symptoms. Hydration is important but must be monitored carefully to avoid fluid overload. Corticosteroids may also be helpful. Transfusion can reduce hypoxia. Pulmonary function should be monitored carefully to detect symptoms of pulmonary hypertension as soon as possible so that therapies, including hydroxyurea and HSCT, can be of the greatest benefit.

Transfusion Therapy

RBC transfusions have been shown to be highly effective in several situations: in an acute exacerbation of anemia (e.g., aplastic crisis, severe vaso-occlusive crisis), in the prevention of severe complications from anesthesia and surgery, in improving the response to infection (when it results in exacerbated anemia), in the case of acute chest syndrome and multiple organ dysfunction syndrome (MODS), and in thwarting the cerebral edema from a stroke. Transfusions are also effective in diminishing episodes of sickle cell crisis in pregnant women, although such transfusions do not improve fetal survival. Ongoing transfusion therapy may be effective in preventing or managing complications from SCD by keeping the HbS level to less than 30% (DeBaun, 2018).

Transfusions are not without risks, so it is important to consider the risks of complications versus benefits. Complications include difficulty with venous access, which necessitates placement of a vascular access device, and the concomitant risk for access site infection and thrombosis. Additional risks

include other infections, particularly hepatitis; delayed hemolytic transfusion reactions; and iron overload that requires treatment with chelating agents.

Iron overload is very likely with long-term/ongoing transfusion therapy, causing deposition of iron in vital organs, including the liver, heart, pancreas, kidneys, and pituitary gland. It is sometimes difficult to distinguish organ damage associated with the disease process from damage associated with iron overload. Iron chelation therapy, aimed at keeping iron levels at near normal, reduces complications (see [Chapter 30](#) for further discussion of chelation therapy) (Coates & Wood, 2017). An additional complication of transfusion therapy is increased blood viscosity without reduction in the concentration of hemoglobin S. Exchange transfusion, where some of the patient's blood is removed and replaced by RBC transfusion, may reduce the risk of increasing blood viscosity (Davis, Allard, Qureshi, et al., 2017). Additionally, repeated transfusions may result in development of multiple antibodies to other blood antigens, making cross matching increasingly difficult, and lead to increased risk for hemolytic transfusion reaction. This phenomenon is referred to as alloimmunization (Davis et al., 2017). Some patients who are alloimmunized have an increased risk of avascular necrosis, end-organ damage, and death (Holmes-Maybank, Martin, & Duckett, 2017). Hemolytic transfusion reaction may mimic the signs and symptoms of sickle cell crisis. A distinguishing feature of a hemolytic reaction versus sickle cell crisis is that the patient becomes more anemic after the transfusion than before. Close observation after hemolytic transfusion reaction is needed and further transfusion should be avoided until after the hemolytic process subsides. Patients are supported with corticosteroids, such as prednisone, intravenous immunoglobulins (IVIG) and erythropoietin alfa.



For the procedural guidelines for managing immunoglobulin therapy, go to thepoint.lww.com/Brunner15e.

Supportive Therapy

Supportive care is essential for patients with SCD. Pain management is a significant problem. Acute pain is most often associated with vaso-occlusive crisis and is the frequent reason for hospitalization and emergency department visits in people with SCD. Pain may also be neuropathic in nature stemming from damage or inflammation of nerves as seen with avascular necrosis and leg ulcers (see [Fig. 29-3](#)). Chronic non-neuropathic pain may result from CNS dysfunction, including CNS sensitivity to peripheral afferent pain signals, or differences in psychosocial aspects of pain perception (Darbari & Brandow,

2017). Pain severity may interfere with ability to work, even when patients do seek assistance with pain management from health care providers.

The use of medications for acute pain relief is critical and should be appropriate for the etiology of the pain. Aspirin may be useful in patients with mild pain; it decreases inflammation and risk for potential thrombosis (because it inhibits platelet adhesion). NSAIDs are useful for moderate pain or in combination with opioid analgesics. While there is no risk of developing tolerance to NSAIDs there is a “ceiling effect” by which increased doses do not improve analgesia but increase the risk for adverse effects. NSAID use must be monitored carefully because of the risk for renal dysfunction and GI bleeding. Severe acute pain is most often treated with parenteral opioids (Okwerekwu & Skirvin, 2018). Patient-controlled analgesia is frequently used for this purpose in the acute care setting (see [Chapter 9](#) for additional information on pain management). Neuropathic pain can be effectively managed with gabapentinoids, tricyclic antidepressants, and serotonin and norepinephrine reuptake inhibitors (Sharma & Brandow, 2019). With chronic pain management, the principal goal is to maximize functioning; pain may not be completely eliminated without sacrificing function. This concept may be difficult for patients to understand and ongoing education and support is often needed. Nonpharmacologic pain management strategies are important in this setting. Such strategies include physical therapy including heat, massage and exercise; occupational therapy; cognitive and behavioral therapies, including distraction and relaxation techniques; and support groups (Okwerekwu & Skirvin, 2018).



Figure 29-3 • Chronic skin ulcers seen in a patient with sickle cell anemia. Reprinted with permission from Tkachuk, D. C., & Hirschman, J. V. (2007). *Wintrobe's atlas of clinical hematology* (Fig. 1.71, p. 36). Philadelphia, PA: Lippincott Williams & Wilkins.

Hydration is critical during a painful crisis. Oral hydration may be sufficient if the patient is able to maintain adequate intake. IV hydration may be needed if the patient is unable to consume 2 to 3 L of fluid during a crisis episode. Supplemental oxygen may also be needed.

Another significant problem for people with SCD is fatigue. Fatigue can interfere with ability to perform effectively at work and school and reduce quality of life. Its causes, as with pain, may be multifactorial. Fatigue may occur in response to hypoxia associated with low levels of normal hemoglobin and decreased capacity to carry oxygen with sickled cells. Endothelial cells in the blood vessels become inflamed as a result of hypoxia. Inflammatory cytokines are increased in patients with SCD resulting in reduced muscle strength and decreased exercise capacity, increased resting energy expenditure, and sleep disturbances, all exacerbating fatigue. Sleep disturbances and depression are common and contribute to fatigue (Ahmadi, Poormansouri, Beiranvand, et al., 2018).

Working with patients who have multiple episodes of severe pain and fatigue can be challenging. Health care providers must recognize that patients with SCD are confronted with lifelong experiences with severe pain and fatigue that impair physical and social functioning that may be associated with depression and helplessness. Patients without adequate sources of support may have more issues with coping.

NURSING PROCESS

The Patient with Sickle Cell Crisis

Assessment

The patient is asked to identify factors that precipitated previous crises and measures taken to prevent and manage crises. If a sickle cell crisis is suspected, the nurse needs to determine whether the pain currently experienced is the same as or different from the pain typically encountered in crisis. Pain levels should always be assessed (see [Chapter 9](#)). A similar assessment should be made of the patient's fatigue, including the impact of fatigue on the current lifestyle, quality of life, and the extent that the fatigue influences pain and interferes with sleep.

Because the sickling process can interrupt circulation in any organ or tissues, a thorough assessment of all body systems is needed. Particular attention should be placed on assessing pain, swelling, and fever. Careful examination of all joints for pain and swelling is necessary. The abdomen is assessed for pain and tenderness because of the possibility of splenic infarction.

The cardiovascular and respiratory systems must also be assessed carefully. These assessments include measurement of oxygen saturation, auscultation of breath sounds, and recognition of signs of cardiac failure, including the presence of dependent edema, increased size of the point of maximum impulse, and cardiomegaly (as seen on a chest x-ray). The patient is assessed for signs and symptoms of dehydration by a history of reduced fluid intake, and careful examination of mucous membranes, skin turgor, urine output, and serum creatinine and blood urea nitrogen levels.

A meticulous neurologic examination is essential to identify symptoms of cerebral hypoxia, but it is also important to recognize that evidence of ischemia may be present on magnetic resonance imaging (MRI) or Doppler studies before becoming evident on the physical examination. MRI or Doppler may be used for early diagnosis resulting in improved patient outcomes because therapy can be initiated promptly. Cognitive dysfunction is often present and may reflect reduced blood flow and oxygenation to the brain. Assessment for neurologic abnormalities is important in identifying silent cerebral ischemia or infarction.

Assessment for the presence of infectious processes is crucial as many patients with SCD are susceptible to infection. Special attention should be paid to examination of the chest, long bones, and femoral head because pneumonia and osteomyelitis are particularly common. Leg ulcers are common, frequently recurrent, occur in as many as 75% of adults with SCD, and may become infected and slow to heal (El Khatib & Hayek, 2016) (see [Fig. 29-3](#)).

The degree of anemia and ability of the bone marrow to replenish erythrocytes are assessed with hemoglobin level, hematocrit, and reticulocyte counts, and comparing these to baseline values. The patient's current and past history of medical care must also be obtained, particularly long-term transfusion therapy, hydroxyurea treatment, and prior treatment of infections.

Diagnosis

NURSING DIAGNOSES

Based on the assessment data, major nursing diagnoses may include:

- Acute pain, chronic pain, and fatigue associated with tissue hypoxia due to agglutination of sickled cells within blood vessels
- Risk for infection
- Risk for powerlessness associated with illness-induced helplessness
- Lack of knowledge regarding sickle cell crisis prevention

COLLABORATIVE PROBLEMS/POTENTIAL COMPLICATIONS

Potential complications may include the following:

- Hypoxia, ischemia, and poor wound healing leading to skin breakdown and ulcers
- Dehydration
- Cerebrovascular disease (stroke)
- Anemia
- Acute kidney injury and chronic kidney failure
- Heart failure, pulmonary hypertension, and acute chest syndrome
- Impotence and impaired fertility
- Cognitive dysfunction
- Poor adherence to therapy
- Mutual conflict and distrust between patient and health care providers due to poorly managed acute and chronic pain

Planning and Goals

The major goals for the patient are relief of pain, decreased incidence of crisis, enhanced sense of self-esteem and power, and absence of complications.

Nursing Interventions

MANAGING PAIN

Acute pain during a sickle cell crisis can be unpredictable and severe. The patient's subjective description of pain rating on a pain scale is useful in directing its treatment (see [Chapter 9](#)). Swollen joints should be supported and elevated until swelling subsides. Relaxation techniques, breathing exercises, yoga, and self-hypnosis may be helpful to some patients in

coping with pain (DeBaun & Vichinsky, 2019). Following acute pain episodes, aggressive measures should be taken to preserve joint function. Physical therapy, whirlpool baths, and transcutaneous electrical nerve stimulation (TENS) are among modalities that may be used. While heat packs may be helpful, cold packs and ice should be avoided as cold may precipitate sickling (DeBaun & Vichinsky, 2019).

It is not unusual for patients to have difficulty coping with repeated episodes of acute pain and with chronic pain, making adherence to the prescribed treatment regimen difficult. Some patients with SCD develop substance use disorder although the incidence of substance abuse among people with SCD is not unlike that of patients with other chronic conditions (Natrajan & Kutlar, 2016). This can be a result of inadequate treatment of acute pain during episodes of crisis, which then leads to a lack of trust of the health care system and of health care providers. Research findings suggest that prompt treatment of pain during vaso-occlusive crises can improve patient satisfaction with care and also decrease patient length of stay or treatment times (Kim et al., 2017) (see [Chart 29-4](#) Nursing Research Profile: Acute Pain Management for Patients with Sickle Cell Disease).

MANAGING FATIGUE

Fatigue experienced with SCD may be acute or chronic. Assisting the patient to find a balance between activity and rest is important. Patients need to develop strategies to help cope with the demands on their lives while dealing with their fatigue. Maximizing nutrition, hydration, adequate sleep, and tissue perfusion can all help to minimize fatigue. Research is needed to better understand fatigue in this patient population and identify the most effective ways to relieve it. Although there are validated scales that have been used to quantify the extent of fatigue in patients with SCD, such as the PROMIS Fatigue short form®, standards for when to assess fatigue are currently lacking (Aslani, Georgios, & Maria, 2018; Hildenbrand, Quinn, Mara, et al., 2019).

PREVENTING AND MANAGING INFECTION

Nursing care focuses on monitoring patients for signs and symptoms of infection. Prescribed antibiotics should be administered as soon as possible. If oral antibiotics are prescribed at home, patients and caregivers must understand the importance of completing the entire course of antibiotics. Patients should be encouraged to seek immunizations per the latest guidelines (see [Chapter 3, Table 3-3](#)), particularly the pneumonia and influenza vaccines.

PROMOTING COPING SKILLS

SCD may cause patients to feel powerless and lacking in self-worth because of the health problems associated with repeated crises and chronic health conditions. These feelings can be exacerbated when pain and fatigue

are not well controlled. Optimizing management of pain and fatigue are critical in helping patients to cope with their illness. Listening to and advocating for the needs of patients is important for building a therapeutic relationship based on mutual respect and trust. Nursing care that focuses on patients' strengths and not their deficits aids in promoting effective coping. Providing patients with opportunities to make decisions about their care can help foster autonomy and a sense of control. Supportive guidance can help patients understand the importance of adhering to their therapeutic regimen.

Chart 29-4



NURSING RESEARCH PROFILE

Acute Pain Management for Patients with Sickle Cell Disease

Kim, S., Brathwaite, R., & Kim, O. (2017). Evidence-based practice standard care for acute pain management in adults with sickle cell disease in an urgent care center. *Quality Management in Healthcare*, 26(2), 108–115.

Purpose

Vaso-occlusive episodes (VOEs) are the most common reason patients with sickle cell disease (SCD) seek emergency or urgent care services. Evidence-based guidelines specify that patients with SCD who seek urgent care for treatment of VOE should receive analgesics quickly. However, these guidelines are not followed by many clinicians, resulting in poorly managed pain in this patient population. The purpose of this study was to find whether implementing a VOE analgesic care algorithm in an urgent care (UC) center would decrease patient time to receipt of analgesics, improve patient satisfaction with care, and decrease length of treatment time.

Design

The setting for this study was an urban tertiary care UC center. Eligible participants were adults at least 18 years of age who sought care at the UC center for VOE from SCD. A Quality Improvement (QI) best practice VOE analgesic intervention was conducted with UC center staff so that all were educated to follow the algorithm. Data were collected over 6 months. Time to administration of first analgesic medication for participants postintervention ($n = 63$) was compared with historical controls preintervention ($n = 61$), as were participant reports of satisfaction with care and their length of stay in the UC center.

Findings

The mean time to administration of analgesics decreased significantly from pre- to postintervention, from 92 minutes to 62 minutes ($p = 0.001$). Likewise, participant satisfaction with care improved from pre- to postintervention ($p = 0.002$) and mean time in the UC center decreased significantly from pre- to postintervention, from 283 minutes to 256 minutes ($p = 0.01$).

Nursing Implications

Findings from this study suggest that administering analgesics quicker to patients with SCD complicated with VOE not only mitigates their pain, but may also improve their satisfaction with care, and decrease their time in treatment. This may indirectly help to foster patient trust of the health care system and of providers. Nurses can leverage findings from this study to replicate this best practice algorithm and improve the care of patients with SCD complicated with VOE.

MINIMIZING KNOWLEDGE DEFICITS

Patients with SCD benefit greatly from understanding the circumstances that may precipitate a sickle cell crisis and the steps they can take to prevent or diminish the symptoms they may experience during a crisis. Keeping warm, reducing risks for infection, and maintaining adequate hydration can be effective in reducing the occurrence and severity of crises.

When hydroxyurea is prescribed for women of childbearing age, they should be informed that the drug can cause harm to an unborn fetus and advised that pregnancy should be avoided.

MONITORING AND MANAGING POTENTIAL COMPLICATIONS

Many of the measures for managing potential complications have already been described. Other measures follow.

Leg Ulcers. Leg ulcers require careful management and protection from trauma and contamination. Referral to a wound-ostomy-continence nurse or other wound care specialist may facilitate healing and promote prevention. If leg ulcers fail to heal, skin grafting may be needed (El Khatib & Hayek, 2016). Meticulous aseptic technique during wound care is needed to reduce risk for hospital-acquired wound infections.

Priapism and Impotence. Male patients may experience sudden, painful erection known as priapism. Initial management can include warm compresses or warm bath, and mild to moderate exercise, oral hydration, and masturbation with ejaculation (Field et al., 2019). If the priapism persists longer than 3 hours the patient should seek medical attention; treatment may consist of IV hydration, administration of analgesics, and possible aspiration of blood from the corpus cavernosa with or without injection of a sympathomimetic drug (Al-Qudah, 2016; Field et al., 2019). Repeated episodes of priapism may lead to extensive vascular damage resulting in impotence.

PROMOTING HOME, COMMUNITY-BASED, AND TRANSITIONAL CARE



Educating Patients About Self-Care. Because patients with SCD are typically diagnosed during childhood, their parents typically participate in the initial education. As the child ages, educational interventions prepare the child to assume more responsibility for self-care. Most families can learn about vascular access device management and chelation therapy. Nurses in outpatient facilities or home health nurses may need to provide follow-up care for patients with vascular access devices.

Continuing and Transitional Care. The illness trajectory of SCD is highly variable, often with unpredictable episodes of complications or crises. Care is frequently on an emergency basis, especially for some patients with pain management problems. All health care providers who offer services to patients with SCD and their families must communicate regularly with each

other. Alternative methods of care delivery including day hospitals for acute symptom management and patient-centered medical homes, where multidisciplinary care is emphasized, are available in some regions. Nurses play an important role in serving as coordinators and facilitators of care by communicating with health care providers in a variety of settings to optimize the care of patients. Patient education about which parameters are important to monitor and how to monitor them is also a critical role for nurses. Making certain that patients understand when to seek urgent care for acute problems is essential.

Evaluation

Expected patient outcomes may include the following:

1. Control of pain and fatigue
 - a. Uses analgesic agents appropriately to relieve pain
 - b. Uses nonpharmacologic strategies to help relieve pain and fatigue, such as relaxation techniques, breathing exercises, and guided imagery
2. Absence of infection
 - a. Is afebrile
 - b. Maintains leukocyte count within normal baseline ($4500/\text{mm}^3$ to $11,000/\text{mm}^3$)
 - c. Identifies importance of completing antibiotics as prescribed
 - d. Demonstrates measures to prevent infection (i.e., obtains recommended immunizations)
3. Expresses improved sense of control
 - a. Participates in goal setting, planning, and implementing daily activities
 - b. Participates in making decisions about care
 - c. Adheres to prescribed medical therapy
4. Increases knowledge about disease process
 - a. Identifies situations and factors that can precipitate sickle cell crisis
 - b. Describes lifestyle changes needed to prevent crisis
 - c. Describes the importance of warmth, adequate hydration, and prevention of infection in preventing crisis
5. Absence of complications

Thalassemias

The thalassemias are a group of hereditary anemias characterized by **hypochromia** (an abnormal decrease in the hemoglobin content of erythrocytes), extreme **microcytosis** (smaller than normal size erythrocytes),

hemolysis, and variable degrees of anemia. The thalassemias occur worldwide, but the highest prevalence is found in people of Mediterranean, African, and Southeast Asian ancestry (Weatherall, 2016).

Thalassemias are associated with impaired hemoglobin synthesis so that one or more globulin chains in the hemoglobin molecule are reduced. When this occurs, the imbalance in the configuration of the hemoglobin molecule causes it to precipitate in premature or mature erythrocytes. This increases the rigidity of erythrocytes, leading to premature cell destruction.

Thalassemias are classified into two major groups according to which hemoglobin chain is affected, alpha or beta. The alpha-thalassemias occur mainly in people of Southeast Asian and eastern Mediterranean descent (i.e., Middle Eastern), and the beta-thalassemias are most prevalent in those of African descent. Thalassemias are not limited to any geographic region because of extensive immigration (Weatherall, 2016). Symptoms of the alpha-thalassemias are typically less severe than those of beta-thalassemias. In alpha-thalassemias, erythrocytes are often quite microcytic but anemia, when present, is usually mild.

The severity of beta-thalassemia varies depending on the extent to which the hemoglobin chains are affected. Patients with mild forms have microcytosis and mild anemia. When untreated, severe beta-thalassemia (i.e., thalassemia major or Cooley's anemia) can be fatal within the first few years of life. HSCT offers a chance of cure. When this is not possible, treatment consists of PRBC transfusion and iron chelation therapy, as needed (Fibach & Rachmilewitz, 2017). Patient education for adolescents and young adults should include preconception counseling about the risk of thalassemia major in offspring (see [Chapter 6](#) for discussion about genetic counseling and evaluation services).

Thalassemia major is characterized by severe anemia, profound hemolysis, and ineffective erythropoiesis. With early initiation of regular transfusions with PRBCs, growth and development through childhood is supported. Iron overload that can result from multiple transfusions can lead to organ dysfunction. Regular chelation therapy can reduce complications associated with iron overload and prolong life in those with thalassemia major. Long-term survivors of beta thalassemia may experience neurologic complications including cognitive dysfunction, peripheral neuropathy, and cerebrovascular disease (Fibach & Rachmilewitz, 2017).

Glucose-6-Phosphate Dehydrogenase Deficiency

The Glucose-6-Phosphate Dehydrogenase (G-6-PD) gene is responsible for the abnormality seen in this disorder. The gene produces an enzyme within the erythrocyte that is necessary to stabilize the cell membrane. Some patients produce an enzyme so defective that they have chronic hemolytic anemia;

however, the most common type of defect only results in hemolysis when cells are under certain types of stress, associated with fever and certain types of medications. G-6-PD deficiency is one of the most common X-linked genetic blood disorders in the world, affecting more than 400 million people (see [Chapter 6](#) for discussion of X-linked disorders). However, women may also develop the disease because one of the X chromosomes is inactivated in each cell of the female embryo; thus, a female who is heterozygous for the deficiency would have one half normal red blood cells and one half with the deficiency. While the deficient cells are at risk for hemolysis, symptoms are generally milder in affected women because normal cells are not subject to hemolysis. In the United States, African Americans and people of Mediterranean descent are most likely to be affected with G-6-PD (Anderle, Bancone, Domingo, et al., 2018). The type of deficiency found in person with Mediterranean ancestry is typically more severe than that in African Americans; it results in more hemolysis and sometimes life-threatening hemolytic anemia.

Oxidant drugs have hemolytic effects for people with G-6-PD deficiency, particularly some antibiotics including sulfadiazine, nitrofurantoin, trimethoprim-sulfamethoxazole, moxifloxacin, and chloramphenicol, as well as antimalarial agents including chloroquine, primaquine, and dapsone. Other medications associated with hemolysis include phenazopyridine, rasburicase, methylthioninium, tolonium chloride, tamsulosin, glyburide, nonsteroidal anti-inflammatory drugs, and the street drug amyl nitrate (van Solinge & van Wijk, 2016). A severe hemolytic episode can also occur in affected people after ingesting fava beans, menthol, tonic water, and some Chinese herbs.

Clinical Manifestations

Patients are typically asymptomatic and have normal hemoglobin levels and reticulocyte counts. However, within several days after exposure to an offending agent, pallor, jaundice, and hemoglobinuria develop. The reticulocyte count increases, and symptoms of hemolysis develop. Special stains of peripheral blood often show Heinz bodies (degraded hemoglobin) within the erythrocytes. Hemolysis may be mild and self-limited; however, in more severe cases, usually in the Mediterranean type of the disease, spontaneous recovery does not occur.

Assessment and Diagnostic Findings

The diagnosis is made by a screening test for the deficiency or by quantitative assay of G-6-PD.

Medical Management

Treatment requires discontinuation of the offending agent. Transfusion is not usually necessary unless severe hemolysis is present, as may be seen in the Mediterranean variety of G-6-PD deficiency.

Nursing Management

Patients should be educated about the disease and provided with a list of medications and other substances to be avoided. Patients with G-6-PD deficiency should always seek medical advice before taking any new medication or supplement. The G-6-PD Deficiency organization Web site (see Resources) is an excellent source of information. If hemolysis occurs, nursing interventions are the same as for hemolysis with other conditions. Patients should be advised to wear Medic-Alert bracelets that identify that they have G-6-PD deficiency. Genetic counseling may also be indicated (see [Chapter 6](#)).

Immune Hemolytic Anemias

Immune hemolytic anemias can result from exposure of erythrocytes to antibodies. Alloantibodies (antibodies against the host or “self”) occur as a result of immunization of a person to foreign antigens (e.g., the immunization of an Rh-negative person with Rh-positive blood). Alloantibodies tend to be of the immunoglobulin G (IgG) type and cause immediate destruction of sensitized erythrocytes either within the blood vessels (intravascular) or the liver. Hemolysis and anemia associated with hemolytic transfusion reaction is an example of alloimmune hemolytic anemia.

Autoantibodies may develop for a number of reasons. In some circumstances, the person’s immune system is dysfunctional and falsely identifies its own erythrocytes as foreign and produces antibodies against them. This may be seen in people with chronic lymphocytic leukemia (CLL) (see [Chapter 30](#)). Another cause of autoimmune hemolytic anemia is a deficiency of suppressor lymphocytes, which normally prevents antibody production against the patient’s own antigens. Erythrocytes are then sequestered in the spleen and destroyed by macrophages outside of blood vessels (extravascular hemolysis) (Phillips & Henderson, 2018).

Autoimmune hemolytic anemias may be classified based on the body temperature involved when the antibodies react with the RBC antigen. Warm-body antibodies are the most common (80%) and bind to erythrocytes most actively in warm-body conditions (37°C [98.6°F]); cold-body antibodies react in cold conditions (0°C [32°F]) (Packman, 2016). Autoimmune hemolytic anemia is associated with other disorders in most cases (e.g., medication exposure, lymphoma, CLL, other malignancies, collagen vascular diseases, autoimmune diseases, infection). In idiopathic autoimmune hemolytic states, the cause for antibody production is unknown. This primary form affects

people of all ages and genders equally, while secondary forms occur more frequently in females and in people over the age of 45 years (Packman, 2016).

Clinical Manifestations

Clinical signs and symptoms vary and often reflect the severity of anemia. The hemolysis may range from very mild, with the patient's bone marrow able to compensate adequately with few or no symptoms, to severe, with life-threatening anemia. Most patients complain of fatigue and dizziness. Splenomegaly, with associated abdominal discomfort, is a common finding; hepatomegaly, lymphadenopathy, and jaundice are also frequently seen.

Assessment and Diagnostic Findings

Laboratory tests show a low hemoglobin level and hematocrit, usually associated with an elevated reticulocyte count. Erythrocytes appear abnormal; **spherocytes** (small, spherically shaped erythrocytes) are often seen on the peripheral blood smear. The serum bilirubin level is elevated, and if the hemolysis is severe, the haptoglobin level is low or absent. The Coombs test (also known as the direct antiglobulin test), which detects antibodies on the surface of the erythrocytes, is typically positive.

Medical Management

Any possible contributing medication should be immediately discontinued. Treatment most often consists of high doses of corticosteroids until hemolysis decreases; this is especially beneficial when treating warm-antibody-induced hemolysis (Packman, 2016). Corticosteroids have several actions including suppressing antibody production, reducing the affinity of antibodies for the erythrocytes, and reducing destruction of erythrocytes by macrophages in the spleen (Go, Winters, & Kay, 2017). If the hemoglobin levels return to normal, often within a few weeks, the corticosteroid dose can be gradually reduced, and in some cases be tapered and eventually discontinued. However, treatment with corticosteroids does not produce lasting effects. In severe cases, transfusions with PRBCs are needed to maintain adequate levels of hemoglobin until the hemolytic process can be reduced. The antibodies may react to donor cells, making careful typing and cross matching essential. Transfusions are given slowly and cautiously with careful monitoring for transfusion reaction. Folic acid supplementation should be given when hemolysis is severe, because the bone marrow will attempt to compensate by increasing hematopoietic activity (Hill, Stamps, Massey, et al., 2017).

If corticosteroids do not result in remission, splenectomy (removal of the spleen) may be necessary to remove a major site of erythrocyte destruction. If

neither corticosteroids nor splenectomy are successful, immunosuppressive medications may be given (Hill et al., 2017). Immunosuppressive drugs used include cyclophosphamide and azathioprine. Cyclophosphamide has a rapid onset of action but is associated with significant toxicity. Azathioprine has a slower onset of action but less toxicity. Danazol, a synthetic androgen, may be beneficial for some patients, especially when used in combination with corticosteroids. Immunosuppressive drugs and corticosteroids must be tapered slowly over several months to avoid a flare of the immune system leading to an exacerbation of hemolysis. Monoclonal antibodies, including rituximab, can be effective in some patients and may offer long-term control of symptoms (Hill et al., 2017).



Quality and Safety Nursing Alert

Cross-matching blood when antibodies are present can be difficult. If imperfectly cross-matched PRBCs must be transfused, the nurse should begin the infusion very slowly (10 to 15 mL over 20 to 30 minutes) and monitor the patient very carefully for signs and symptoms of a hemolytic transfusion reaction.

For patients with cold-antibody hemolytic anemia, no treatment may be needed, other than to advise the patient to keep warm. Relocation to a warmer climate may be advisable in some cases. In other situations, where hemolysis is more severe, more aggressive interventions as previously described may be needed.

Nursing Management

Patients may have difficulty understanding the complex nature of their illness and may need repeated explanations in terms they can understand. Patients who have had splenectomy should receive the pneumococcal pneumonia vaccine and annual influenza vaccine and be informed that they are permanently at increased risk for infection. Patients receiving long-term corticosteroid therapy, particularly those with diabetes or hypertension, need careful monitoring. They must understand the need for their medications and avoid abruptly discontinuing them. A written explanation and a tapering schedule should be provided, emphasizing adjustments based on hemoglobin levels. Similar information should be provided when immunosuppressive agents are used. Corticosteroid therapy is associated with risks and patients should be monitored frequently for complications (see [Chapter 45, Table 45-3, Corticosteroid therapy and implications for nursing practice](#)).

Hereditary Hemochromatosis

Hereditary hemochromatosis is a genetic condition characterized by excess iron absorption from the GI tract. Normally, the GI tract absorbs 1 to 2 mg of iron daily, but in those with hereditary hemochromatosis, this rate is significantly increased. The excess iron is deposited in various organs, especially the liver, skin, and pancreas; and less frequently, the heart, testes, and thyroid gland. Eventually, affected organs become dysfunctional. Although hereditary hemochromatosis is diagnosed in 1% to 6% of the U.S. population, the actual prevalence is unknown because it is not always recognized. The genetic defect associated with hemochromatosis is most commonly seen as a specific mutation (C282Y homozygosity) of the *HFE* gene. Despite the high prevalence of the genetic mutation, the actual expression of the disease is much lower; the reason for this discrepancy is not clear. The prevalence of hemochromatosis is lower in Asian Americans, African Americans, Latinos, and Pacific Islanders and higher in people of European descent (Kowdley, Brown, Ahn, et al., 2019). Women are less often affected than men because women lose iron through menses.

Clinical Manifestations

Tissue damage is seldom evident until middle age because the accumulation of iron in body organs occurs gradually. Symptoms of weakness, lethargy, arthralgia, and weight loss are common and occur earlier in the course of the disease. The skin may appear hyperpigmented or bronze in color from melanin deposits and **hemosiderin**, an iron-containing pigment. Cardiac arrhythmias and cardiomyopathy can occur, with resulting dyspnea and edema. Endocrine dysfunction can be manifested as hypothyroidism, diabetes, and hypogonadism with testicular atrophy, diminished libido, and impotence. Cirrhosis is common in later stages of the disease, shortens life expectancy, and is a risk factor for hepatocellular carcinoma (Kowdley et al., 2019).

Assessment and Diagnostic Findings

Diagnostic laboratory findings include an elevated serum ferritin and high serum transferrin saturation. CBC values are often normal. The definitive diagnostic test for hemochromatosis was formerly a liver biopsy but that test has been replaced by testing for the associated genetic mutation. While the prevalence of the genetic mutation is high (1 in 200 to 300 in persons of Northern European descent) few people with the gene will actually develop sufficient iron overload to cause symptoms and organ dysfunction (Bacon, 2019).

Medical Management

Therapy often involves the removal of excess iron with therapeutic phlebotomy (removal of whole blood via venipuncture). Each unit of blood removed results in a decrease of 200 to 250 mg of iron. Initial treatment typically involves weekly removal of one unit of whole blood. As the ferritin level decreases, the frequency of phlebotomy can be decreased. The goal is to maintain an iron saturation between 10% and 50% and a serum ferritin level of less than 100 mcg/L (Ganz, 2016). Evaluation of iron studies should be repeated regularly and phlebotomy resumed when the ferritin level rises. CBCs and iron panel tests should be performed at regular intervals during treatment to ensure that the patient is not becoming anemic. If moderate anemia occurs, a delay in phlebotomy is often adequate to correct the problem. Aggressive removal of excess iron can prevent organ dysfunction and the complications associated with organ damage. Fatigue, skin pigmentation changes, and fibrosis are partially reversed by achieving and maintaining normal ferritin levels. Screening for hepatocellular carcinoma includes monitoring alpha-fetoprotein levels and serial abdominal ultrasounds (Kowdley et al., 2019).

Nursing Management

Patients with hemochromatosis frequently limit their iron intake; however, this is not typically effective as lone therapy. They should be advised to avoid taking additional iron supplements. Vitamin C supplementation should also be limited because it enhances iron absorption. Patients with hemochromatosis must be careful to avoid substances that might impair liver function including excessive alcohol ingestion. Other body systems should be monitored for evidence of organ dysfunction, particularly the endocrine and cardiac systems, so that appropriate interventions can be initiated without delay. Children of patients who are homozygous for the *HFE* gene mutation should be screened for the mutation. Patients who are heterozygous for the gene do not develop the disease but should be advised that they may transmit the gene to their children.

POLYCYTHEMIA

Polycythemia refers to an increased volume of RBCs. The term is used when the hematocrit is elevated (more than 55% in males and 50% in females). Dehydration can cause elevated hematocrit but not usually to the level seen with polycythemia. Polycythemia is classified as either primary or secondary. Primary polycythemia, also known as polycythemia vera, is a myeloproliferative neoplasm that is discussed in Chapter 30.

Secondary Polycythemia

Secondary polycythemia is caused by excessive production of erythropoietin. This may occur in response to a reduced amount of oxygen, which acts as a stimulus for production. Heavy smoking, obstructive sleep apnea (OSA), chronic obstructive pulmonary disease (COPD), severe heart disease, or conditions such as living at high altitudes or exposure to low levels of carbon monoxide may be responsible for increased erythropoietin production. Certain hemoglobinopathies (e.g., hemoglobin Chesapeake), in which the hemoglobin has a high affinity for oxygen, or genetic mutations that cause abnormally high erythropoietin levels may also increase erythropoiesis (Prchal, 2016b). Secondary polycythemia can also occur from certain neoplasms that stimulate erythropoietin production (e.g., renal cell carcinoma), excessive use of exogenous erythropoietin, and androgen use.

Management

When secondary polycythemia is mild, treatment may not be necessary. When treatment is necessary, however, it involves treating the primary condition. If the cause cannot be corrected (e.g., treatment of OSA or improving function with smoking cessation), therapeutic phlebotomy may be needed for symptom management and to reduce blood viscosity and volume. Therapeutic phlebotomy is not indicated when the cause for the elevated RBC count is an appropriate response to tissue hypoxia (Prchal, 2016b).

Neutropenia

Neutropenia is defined as a neutrophil count less than $2,000/\text{mm}^3$. It is the result of decreased production of neutrophils or increased destruction of cells (see [Chart 29-5](#)). Neutrophils are essential in preventing and limiting bacterial infection. A patient with neutropenia is at increased risk for infection from both exogenous and endogenous sources (the GI tract and skin are common endogenous sources). The risk for infection is based not only on the severity of the neutropenia but also on its duration. The actual number of neutrophils, known as the **absolute neutrophil count (ANC)**, is determined by a simple mathematical calculation using information from the CBC and differential (see [Chapter 12](#) for further discussion of the ANC). The risk for infection increases proportionately with a decrease in the neutrophil count. The risk is low when the ANC is greater than $1000/\text{mm}^3$, and high when less than $500/\text{mm}^3$ and greatest when less than $100/\text{mm}^3$ (Dale & Welte, 2016). The duration of neutropenia is another risk factor for developing infection as is the underlying etiology (see [Chart 29-6](#)).

Chart 29-5

Causes of Neutropenia

Decreased Production of Neutrophils

- Aplastic anemia, due to medications or toxins
- Chemotherapy
- Metastatic cancer, lymphoma, leukemia
- Myelodysplastic syndromes
- Radiation therapy

Ineffective Granulocytopoiesis

- Megaloblastic anemia

Increased Destruction of Neutrophils

- Bacterial infections
- Hypersplenism
- Immunologic disorders (e.g., systemic lupus erythematosus)
- Medication induced^a
- Viral disease (e.g., infectious hepatitis, mononucleosis)

^aFormation of antibody to medication, leading to a rapid decrease in neutrophils.

Adapted from Dale, D. C., & Welte, K. (2016). Neutropenia and neutrophilia. In K. Kaushansky, M. A. Lichtman, J. T. Prchal, et al. (Eds.). *Williams hematology* (9th ed.). New York: McGraw-Hill Medical.

Clinical Manifestations

There are no definite symptoms of neutropenia until the patient develops an infection. A routine CBC with differential can reveal neutropenia before the onset of infection.

Chart 29-6



RISK FACTORS

Development of Infection and Bleeding in Patients with Hematologic Disorders

Risk for Infection	Risk for Bleeding
<ul style="list-style-type: none"> • <i>Severity of neutropenia:</i> Risk for infection is proportional to severity of neutropenia. • <i>Duration of neutropenia:</i> Increased duration of neutropenia leads to increased risk for infection. • <i>Nutritional status:</i> Decreased protein stores lead to decreased immune response and anergy. • <i>Deconditioning:</i> Decreased mobility leads to decreased respiratory effort, leading to increased pooling of secretions. • <i>Lymphocytopenia; disorders of lymphoid system (chronic lymphocytic leukemia, lymphoma, and myeloma):</i> Decreased cell-mediated and humoral immunity. • <i>Invasive procedures:</i> Breaks in skin integrity create increased opportunities for organisms to enter blood system. • <i>Hypogammaglobinemia:</i> Decreased antibody formation. 	<ul style="list-style-type: none"> • <i>Severity of thrombocytopenia:</i> Risk increases when platelet count decreases; usually not a significant risk until platelet count drops below $10,000/\text{mm}^3$, or less than $50,000/\text{mm}^3$ with trauma or when an invasion procedure is performed. • <i>Duration of thrombocytopenia:</i> Risk increases when duration increases (e.g., risk is less when duration is transient as after chemotherapy than when duration is prolonged as with decreased cell production by bone marrow). • <i>Sepsis:</i> Mechanism unclear; appears to cause increased platelet consumption. • <i>Increased intracranial pressure:</i> Increased blood pressure leads to rupture of blood vessels. • <i>Liver dysfunction:</i> Decreased synthesis of multiple clotting factors. • <i>Renal dysfunction:</i> Decreased platelet function. • <i>Dysproteinemia:</i> Protein coats surface of platelet, leading to decreased platelet function; protein causes increased blood viscosity, which leads to stretching of capillaries an increased risk for rupture and bleeding. • <i>Alcohol abuse:</i> Suppressive effect on bone marrow results in decreased platelet production and impaired platelet function; impaired liver function results in decreased production of clotting factors.

- *Poor hygiene*: Increased organisms on skin and mucous membranes, including perineum.
- *Poor dentition; mucositis*: Decreased endothelial integrity leads to increased opportunity for organisms to enter blood system.
- *Antibiotic therapy*: Increased risk for superinfection, often fungal.
- *Certain medications*: See text.

Adapted from Dale, D. C., & Welte, K. (2016). Neutropenia and neutrophilia. In K. Kaushansky, M. A. Lichtman, J. T. Prchal, et al. (Eds.). *Williams hematology* (9th ed.). New York: McGraw-Hill Medical; Diz-Kucukkaya, R., & Lopez, J. (2016). Thrombocytopenia. In K. Kaushansky, M. A. Lichtman, J. T. Prchal, et al. (Eds.). *Williams hematology* (9th ed.). New York: McGraw-Hill Medical; Vasu, S., & Caligiuri, M. A. (2016). Lymphocytosis and lymphopenia. In K. Kaushansky, M. A. Lichtman, J. T. Prchal, et al. (Eds.). *Williams hematology* (9th ed.). New York: McGraw-Hill Medical.



Quality and Safety Nursing Alert

Patients with neutropenia do not always exhibit classic signs of infection. Fever is the most common indicator of infection, but is not always present, particularly if the patient is taking corticosteroids or is an older adult.

Medical Management

Treatment of neutropenia varies depending on its etiology. If the neutropenia is medication induced, the offending agent should be discontinued immediately whenever possible. Treatment of an underlying neoplasm can temporarily

make the neutropenia worse, but after bone marrow recovery, treatment may improve it. Corticosteroids may be used if the neutropenia is caused by an immunologic disorder. The use of growth factors such as granulocyte colony-stimulating factor or granulocyte-macrophage colony-stimulating factor can be effective in increasing neutrophil production when the cause is reduced cell production. Withholding or reducing the dose of chemotherapy or radiation therapy may be necessary when the neutropenia is caused by these cancer treatments; however, when treatment is potentially curative, administration of growth factors is preferable so that the maximum antitumor effect of the cancer treatment can be achieved (Lyman, 2019).

If the neutropenia is associated with fever, it is assumed that the patient has an infection. Cultures of blood, urine, and sputum, as well as a chest x-ray are obtained. Broad-spectrum antibiotics are initiated immediately after cultures are obtained to ensure adequate treatment of infectious organisms. After culture and sensitivity results are obtained, the antibiotic regimen may be changed.

Nursing Management

Nurses in all settings can play a crucial role in assessing the severity of neutropenia and in preventing and managing complications, which most often include infections. Knowledge of risk factors for developing infection is an integral part of nursing care, particularly for those who work with patients who have cancer. Patient education is equally important, particularly at the time of discharge from the hospital or in the outpatient setting so that the patient can put an appropriate self-care plan into effect, including knowing when to seek medical attention (see [Chart 29-7](#)). Patients at risk for neutropenia should have blood drawn for a CBC with differential; the frequency is based on the suspected duration and severity of the neutropenia. To assess the severity of neutropenia and risk for infection, nurses must assess the ANC (see [Chapter 12](#) for formula). Nursing interventions related to neutropenia are delineated in Chapters 12 and 30.

Lymphopenia

Lymphopenia is defined as a lymphocyte count less than $1500/\text{mm}^3$. It may occur as a result of exposure to ionizing radiation, long-term use of corticosteroids, uremia, infections (particularly viral infections), neoplasms (breast and lung cancer and advanced Hodgkin disease), and some protein-losing enteropathies which may cause lymphocytes from the GI tract to be lost (Vasu & Caligiuri, 2016). When lymphopenia is mild, there are no serious sequelae, but when it is severe, it can result in bacterial infections (due to

reduced B lymphocytes) or in opportunistic infections (due to reduced T lymphocytes). T-lymphocyte depletion is frequently associated with viral infections, including human immune deficiency virus (HIV). Excessive or prolonged use of alcohol can also impair lymphocyte production; lymphocyte counts can improve when alcohol intake is discontinued (Vasu & Caligiuri, 2016).

Bleeding Disorders

The failure of normal hemostatic mechanisms can result in bleeding which may be severe. Bleeding is commonly provoked by trauma; however, in certain circumstances, it can occur spontaneously. The causes of bleeding disorders can be categorized based upon whether there is a deficiency of platelets or a defect in the platelets, or based upon whether there is an inherited or acquired coagulation factor abnormality, or based upon a defect in the vasculature. When the cause is platelet or coagulation factor abnormalities, bleeding can occur anywhere in the body. When the source is a vascular abnormality the site of bleeding is more localized. Some patients may have simultaneous defects in more than one hemostatic mechanism.

Chart 29-7



HOME CARE CHECKLIST

The Patient at Risk for Infection

At the completion of education, the patient and/or caregiver will be able to:

- State the impact of alterations in neutrophils, lymphocytes, immunoglobulins on physiologic functioning, ADLs, IADLs, roles, relationships, and spirituality.
- State changes in lifestyle (e.g., diet, activity) or home environment necessary to decrease risk for infection.
 - Maintain good hand hygiene technique, oral hygiene, total body hygiene, and skin integrity.
 - Avoid cleaning birdcages and litter boxes; consider avoiding garden work (soil) and fresh flowers in stagnant water.
 - Maintain a high-calorie, high-protein diet, with fluid intake of 3000 mL daily (unless fluids are restricted).
 - Avoid people with infections and crowds.
 - Perform deep breathing; use incentive spirometer every 4 hours while awake if mobility is restricted.
 - Provide adequate lubrication with gentle vaginal manipulation during penile-vaginal intercourse; avoid anal intercourse.
- Identify signs and symptoms of infection to report to the primary provider, such as fever; chills; wet or dry cough; breathing problems; white patches in the mouth; swollen glands; nausea; vomiting; persistent abdominal pain; persistent diarrhea; problems with urination or changes in the character of the urine; red, swollen, or draining wounds; sores or lesions on the body; persistent vaginal discharge with or without itching; and severe fatigue.
- Demonstrate how to monitor for signs of infection.
- Describe to whom, how, and when to report signs of infection.
- Describe appropriate actions to take should infection occur.

ADLs, activities of daily living; IADLs, instrumental activities of daily living.

The bone marrow may be stimulated to increase platelet production. This can be a reactive response to significant bleeding, or a more general response to increased hematopoiesis, as in iron deficiency anemia. Sometimes an increase in platelets does not result from increased platelet production, but from a loss of platelet pooling in the spleen. The spleen typically holds about one third of circulating platelets at any time. If the spleen is absent (e.g., after splenectomy) the platelet reservoir is lost, and an abnormally high number of platelets enter the circulation. Eventually the rate of platelet production slows to reestablish a more normal platelet level.

Clinical Manifestations

Signs and symptoms of bleeding disorders vary according to the type of defect. A careful history and physical examination can be useful in determining the source of the hemostatic defect. Abnormalities of the vascular system are sources of localized bleeding, usually into the skin. Because platelets are primarily responsible for stopping bleeding from small vessels, patients with decreased platelets develop **petechiae**, often in clusters. These lesions can be seen on the skin and mucous membranes and occur throughout the body (see Fig. 29-4). Bleeding from platelet disorders can be severe, but most often, bleeding from platelet disorders can be controlled when pressure is applied.

In contrast, coagulation factor defects do not tend to cause superficial bleeding because the primary hemostatic mechanisms are still intact. Instead, bleeding occurs deeper within the body (e.g., subcutaneous or intramuscular hematomas, hemorrhage into joint spaces). External bleeding diminishes very slowly when local pressure is applied; it frequently recurs several hours after pressure is removed. An example of this would be severe bleeding that occurs several hours after tooth extraction. Risk factors for bleeding are listed in Chart 29-6.



Figure 29-4 • Petechiae. Reprinted with permission from *Wintrobe's clinical hematology* (10th ed). (1999). Color plate 62.4. Philadelphia, PA: Lippincott Williams & Wilkins.

Medical Management

Management varies based on the underlying bleeding disorder. If bleeding is significant, transfusion of blood products may be indicated. The specific blood product used is determined by the underlying defect and the extent of blood loss. If fibrinolysis is excessive, hemostatic agents such as aminocaproic acid can be useful to inhibit the process, but this agent must be used cautiously because excessive inhibition of fibrinolysis can lead to thrombosis. A patient scheduled for an invasive procedure may need to have transfusions of select blood products to reduce risk for excessive bleeding.

Nursing Management

Patients who have bleeding disorders or who have the potential for development of such disorders as a result of disease or therapeutic agents must be educated to monitor themselves frequently and carefully for signs of bleeding (see [Chart 29-8](#)). They should understand the importance of avoiding activities that increase the risk for bleeding, such as contact sports. The skin should be examined for evidence of bleeding, including petechiae and ecchymoses (bruises) and the nose and gums should also be examined for bleeding. When bleeding disorders are severe, patients who are hospitalized are monitored for bleeding by testing all drainage and excreta (feces, urine, emesis, and, gastric drainage) for obvious and occult blood.

Chart 29-8



HOME CARE CHECKLIST

The Patient at Risk for Bleeding

At the completion of education, the patient and/or caregiver will be able to:

- Describe the source and function of platelets and clotting factors.
- State the impact of an alteration in platelets on physiologic functioning, ADLs, IADLs, roles, relationships, and spirituality.
- State changes in lifestyle (e.g., diet, activity) or home environment necessary to decrease risk of bleeding.
 - Avoid the use of suppositories, enemas, and tampons
 - Avoid constipation
 - Avoid vigorous sexual intercourse and anal sex
 - Avoid contact sports
 - Avoid or limit aggressive manual labor
 - Use an electric razor for shaving and a soft-bristled toothbrush for teeth brushing
 - Notify health care professional before having dental work or other invasive procedures
- Identify medications and other substances to avoid (e.g., aspirin-containing medications, alcohol).
- Identify signs and symptoms of bleeding.
- Demonstrate how to monitor for signs of bleeding.
- Describe to whom, how, and when to report signs of bleeding.
- Demonstrate appropriate actions to take should bleeding occur.

ADLs, activities of daily living; IADLs, instrumental activities of daily living.

TABLE 29-3 Causes and Management of Thrombocytopenia

Cause	Management
Decreased Platelet Production	
Hematologic malignancy; especially acute leukemia	Treat leukemia, platelet transfusion
MDS	Treat MDS, platelet transfusion
Bone marrow metastases from solid tumors	Treat solid tumor
Aplastic anemia	Treat underlying condition
Megaloblastic anemia	Treat underlying anemia
Toxins	Remove toxin
Medications (e.g., sulfa drugs, methotrexate)	Discontinue medication
Infection (especially sepsis, viral infections, tuberculosis, chronic hepatitis C)	Treat underlying infection
Chronic alcohol abuse	Refrain from alcohol, refer for substance use disorder
Chemotherapy	Delay or decrease dose, platelet transfusion
Chronic liver disease	Treat underlying disorder
Radiation (e.g., pelvic irradiation)	Platelet transfusion
Delayed engraftment after stem cell transplantation	Platelet transfusion
Increased Platelet Destruction	
Due to antibodies:	Treat underlying condition
ITP	
SLE	
Malignant lymphoma	
CLL	Treat CLL and/or treat as ITP
Medications	Discontinue medication
Due to infection: Bacteremia/sepsis; post-viral infection	Treat infection
Sequestration of platelets in spleen	If severe, splenectomy may be needed
Increased Platelet Consumption	
DIC	Treat underlying condition triggering DIC; refer to text for indicated treatments
Major bleeding	Transfusion support, surgery if appropriate
Severe pulmonary embolism/severe thrombosis	Treat clot
Intravascular devices (intra-aortic balloon pump, cardiac assist devices)	Transfusion support as needed
Extracorporeal circulation (hemofiltration, extracorporeal lung assist)	Transfusion support as needed

CLL, chronic lymphocytic leukemia; DIC, disseminated intravascular coagulation; ITP, idiopathic thrombocytopenic purpura; MDS, myelodysplastic syndrome; SLE, systemic lupus erythematosus.

Thrombocytopenia

Thrombocytopenia (low platelet level) can result from a variety of factors, including reduced production of platelets in the bone marrow, increased destruction of platelets, or increased consumption of platelets (e.g., the use of platelets for clot formation). Causes and treatments are summarized in [Table 29-3](#).

Clinical Manifestations

Bleeding and petechiae rarely occur with platelet counts greater than $50,000/\text{mm}^3$, but excessive bleeding can occur after surgery or other trauma. When platelet counts fall to $20,000/\text{mm}^3$ or less, petechiae may occur. Additionally, nasal and gingival bleeding, excessive menstrual bleeding, and excessive bleeding from surgery or dental extractions can occur. Spontaneous and potentially fatal bleeding in the CNS or GI tract can occur when platelet counts fall to less than $5000/\text{mm}^3$. If platelet function is abnormal as a result of disease (e.g., MDS) or medications (e.g., aspirin) the risk of bleeding may be much greater even when the platelet count is mildly reduced.

Assessment and Diagnostic Findings

Bone marrow aspiration and biopsy are used to identify platelet deficiency associated with decreased production. A number of genetic causes of thrombocytopenia have been identified. Autosomal dominant, autosomal recessive, and X-linked mutations are among such disorders. When platelet destruction is the cause of thrombocytopenia, the bone marrow shows increased megakaryocytes and normal or increased platelet production as the body attempts to compensate for the decreased platelets in the circulation. Screening for hepatitis B or C, which can cause thrombocytopenia, should be done.

An important cause to exclude is pseudothrombocytopenia. Platelets aggregate and clump in the presence of ethylenediaminetetraacetic acid (EDTA), the anticoagulant present in the tube used for CBC collection. This clumping can be seen 0.8% to 1.25% of the population. Manual examination of the peripheral smear can easily detect platelet clumping as the cause of thrombocytopenia. Redrawing the blood in a tube anticoagulated with citrate rather than EDTA, followed by rapid analysis of the platelet count can provide a more accurate count.

Medical Management

Secondary thrombocytopenia is usually managed with treatment of the underlying disease. If platelet production is impaired, platelet transfusion may be needed to increase the platelet count and stop bleeding or prevent spontaneous hemorrhage. If excessive platelet destruction occurs, transfused platelets may also be destroyed. The most common cause of increased platelet destruction is immune thrombocytopenic purpura (ITP) (see the following discussion). In some circumstances, splenectomy may be a therapeutic intervention, but it is not always feasible. For example, when an enlarged spleen is associated with portal hypertension related to cirrhosis, splenectomy may cause further issues with bleeding.

Nursing Management

When determining nursing interventions, the nurse considers the cause of the thrombocytopenia, the likely duration, and overall condition of the patient. Education is an important intervention to promote safety and should include fall prevention, particularly for older adults and those who are frail. Interventions for patients with secondary thrombocytopenia are the same as those for a patient with cancer who is at risk for bleeding (see [Chapter 12](#)).

Immune Thrombocytopenic Purpura

ITP is a condition that affects people of all ages but is most common in children and young women. This disorder is also referred to as idiopathic thrombocytopenic purpura, and immune thrombocytopenia. Primary ITP occurs as an isolated disorder while secondary ITP is associated with other disorders including autoimmune disorders (e.g., antiphospholipid antibody syndrome), viral infections (e.g., hepatitis C, HIV), and some drugs (e.g., cephalosporins, sulfonamides, furosemide). A platelet count less than $100,000/\text{mm}^3$ with no explicable cause is the primary criterion for the diagnosis (Nomura, 2016).

Pathophysiology

Primary ITP is an acquired immune disorder characterized by thrombocytopenia that results from pathologic antiplatelet antibodies, impaired production of megakaryocytes, and T-cell-mediated destruction of platelets. Secondary ITP is associated with other underlying disorders, including autoimmune disease (systemic lupus erythematosus or rheumatoid arthritis), HIV infection, *Helicobacter pylori* infection, or underlying immune dysregulation syndromes, such as common variable immunodeficiency. The

majority of adults with ITP (approximately 80%) have primary ITP. With both types of ITP, antiplatelet antibodies develop and bind to the patient's platelets. The antibody-bound platelets are then destroyed by the reticuloendothelial system (RES) and tissue macrophages. The body attempts to compensate for the platelet destruction by increasing platelet production within the bone marrow (Lambert & Gernsheimer, 2017).

Clinical Manifestations

ITP is often asymptomatic; the low platelet count frequently is an incidental finding. Platelet counts of less than $30,000/\text{mm}^3$ are not uncommon. Common signs of thrombocytopenia include easy bruising, heavy menses, and petechiae on the extremities or trunk (see Fig. 29-4). Patients who experience only bruising and petechiae tend to have fewer complications from bleeding than those with bleeding from mucosal surfaces, such as the GI tract and respiratory system (sometimes described as "wet purpura"). Patients with wet purpura have a greater risk of life-threatening bleeding which requires immediate aggressive treatment to reduce complications (Diz-Kucukkaya & Lopez, 2016). Severe thrombocytopenia, characterized by platelet count less than $20,000/\text{mm}^3$, a prior history of minor bleeding episodes, and advanced age, is a risk factor for severe bleeding. Despite low platelet counts, platelets are typically immature yet very functional, with the ability to adhere to endothelial surfaces and each other. This may explain why spontaneous bleeding does not always occur. Treatment is not necessary unless bleeding becomes severe or if surgery or another invasive procedure is required (Diz-Kucukkaya & Lopez, 2016).

Assessment and Diagnostic Findings

A careful history and physical examination are essential to aid in excluding other causes of thrombocytopenia and identify sites of bleeding. Patients should be tested for hepatitis C and HIV, if not previously done to rule them out as potential causes. Bone marrow aspirate may reveal an increased number of megakaryocytes. The severity of the thrombocytopenia is highly variable.

H. pylori infection is associated with ITP, and treatment to eradicate the infection may improve the platelet count. The correlation between *H. pylori* infection and ITP is not clear; it is postulated that the presence of the *H. pylori* organism may stimulate an autoimmune reaction (Aljarad, Alhamid, Tarabishi, et al., 2018).

Medical Management

The primary goal of treatment is to achieve a platelet count high enough to maintain hemostasis. Because the risk for bleeding does not typically increase until the platelet count is less than 30,000/mm³, a patient whose platelet count exceeds 30,000/mm³ to 50,000/mm³ may be carefully monitored without immediate intervention. However, if the platelet count is less than 30,000/mm³ or if bleeding occurs, the goal is to improve the patient's platelet count and not to cure the disease. The decision to treat is made based upon the severity of bleeding (if any) and not solely on the platelet count. Potential treatment side effects, the patient's lifestyle, activity level, concurrent use of medications, and treatment preferences are also considered. A person with a sedentary lifestyle can tolerate a low platelet count more safely than a more active person; however, increasing age is also associated with increased risk for bleeding and mortality (Diz-Kucukkaya & Lopez, 2016).

Treatment for ITP usually involves several approaches. If the patient is taking a medication known to be associated with ITP (e.g., quinine, sulfonamides), then that medication should be discontinued. Transfusions are often ineffective because antiplatelet antibodies bind with transfused platelets, causing them to be destroyed. Platelet counts may drop even further after platelet transfusion. Thus, despite extremely low platelet counts, platelet transfusions may result in catastrophic bleeding in patients with wet purpura. Aminocaproic acid, a fibrinolytic enzyme inhibitor that slows the dissolution of blood clots, may be useful for patients with significant mucosal bleeding that is resistant to other treatments.

The mainstay of short-term therapy is the use of immunosuppressive agents. These agents block the binding receptors on macrophages to reduce platelet destruction. The American Society of Hematology recommends dexamethasone or prednisone in adults with newly diagnosed ITP as the types of corticosteroids that might be selected for initial therapy. Continuous long-term use of corticosteroids is not recommended because of the risk for side effects (Neunert, Terrell, Arnold, et al., 2019). Platelet counts typically begin to rise within a few days after initiating treatment with corticosteroids. The platelet count tends to decrease once the corticosteroid dose is tapered but may remain sufficiently adequate to prevent bleeding.

IVIG is commonly used to treat ITP. It renders its effect by binding to the receptors on macrophages. However, the need for high doses of IVIG and its high cost are disadvantages.



For the procedural guidelines for managing immunoglobulin therapy, go to thepoint.lww.com/Brunner15e.

The effects of treatment are transient in most cases. Another approach to treatment of chronic ITP is the use of anti-D immunoglobulin in patients who are Rh (D) positive. The exact mechanism of action is unknown, but it is theorized that the anti-D binds to the patient's erythrocytes, which are in turn destroyed by the body's macrophages. The receptors in the RES may become flooded with sensitized erythrocytes, which then reduce the number of antibody-coated platelets. This then results in a transient reduction of hematocrit and an increased number of platelets in some patients with ITP (Neunert et al., 2019).

Eventually, the platelet count again declines and additional therapy is needed. Second-line treatment options should take the patient's individual needs and the potential treatment-related side effects into account.

Splenectomy is an alternative treatment and typically results in a sustained increase in platelets. Many patients can maintain a "safe" platelet count of more than 30,000/mm³ after splenectomy; however, many patients may have a recurrence of thrombocytopenia months or years later (Neunert et al., 2019). Patients who undergo splenectomy are permanently at risk for serious infection and should receive pneumococcal, influenzae, and meningococcal vaccines approximately 2 weeks prior to splenectomy, or 2 to 3 weeks postoperatively if splenectomy is performed emergently (Bonanni, Grazzini, Niccolai, et al., 2017) (see [Chapter 19](#) for information on pneumonia vaccine).

Other management strategies include use of monoclonal antibodies, such as rituximab. Patients may have long lasting effects with increased platelet counts for up to 1 year after treatment. Unfortunately, when the response dwindles, platelets may fall to unsafe levels, making additional treatment necessary (Neunert et al., 2019).

Two thrombopoietin receptor agonists are available for treatment of refractory ITP. These include romiplostim and eltromopag. Romiplostim is given as a weekly subcutaneous injection and eltromopag is given orally. The response varies widely, and treatment must be continued indefinitely (Depré, Aboud, Ringel, et al., 2016).

Nursing Management

Nursing care includes a thorough assessment of the patient's lifestyle to determine risks for bleeding associated with activities. A careful medication history should also be obtained, including use of over-the-counter (OTC) medications, herbs, and nutritional supplements. The nurse must be alert to sulfa-containing medications and others that may interfere with platelet function (e.g., aspirin, NSAIDs). The nurse must assess for a history of recent viral illness and reports of headache, visual disturbances, and other symptoms that may indicate intracranial bleeding. Patients admitted to the hospital with wet purpura and low platelet counts should have neurologic assessment

included with their vital sign measurements. Injections and rectal medications should be avoided. Rectal temperature measurements should also be avoided because they may cause trauma to the rectal mucosa and stimulate bleeding.

There is evidence that patients with ITP experience an increase in fatigue when compared to those without the disease that is not associated with the duration of the disease, corticosteroid use, bleeding, or low platelet counts (Diz-Kucukkaya & Lopez, 2016). Assessment of the extent of the patient's fatigue can be beneficial in helping the patient to identify coping strategies.

Patient and family education should address signs of exacerbation (e.g., petechiae and ecchymoses), how to contact appropriate health care personnel, the name and type of medications inducing ITP (if appropriate) current medical treatment (name of medications, side effects, tapering schedule, if indicated), frequency of monitoring for the platelet count, and follow-up appointments.

The patient should be instructed to avoid all agents that interfere with platelet function, including herbal therapies and OTC medications. The patient should avoid constipation, straining, and vigorous flossing of the teeth. Electric razors should be used for shaving and soft-bristled toothbrushes should be used for dental hygiene. Patients and their partners should be counseled to avoid vigorous sexual intercourse when platelet counts are low. Patients who are receiving long-term corticosteroids should understand that they are at increased risk for complications including osteoporosis, proximal muscle wasting, cataract formation, and dental caries (see [Chapter 45, Table 45-3](#)). Bone mineral density should be monitored, and patients may benefit from supplemental calcium, vitamin D, and bisphosphonate to reduce risk for significant bone disease.

Platelet Defects

Quantitative platelet defects (i.e., thrombocytopenia, thrombocytosis) are not uncommon, however qualitative defects may also occur. Despite normal platelet counts, when qualitative defects are present, platelets do not function normally. A platelet function analyzer is used to evaluate platelet function. This technique is valuable for rapid screening. Examination of platelet morphology with the peripheral blood smear in the laboratory can also identify possible qualitative defects. Platelet morphology is frequently hypogranular and pale and may also be larger than normal (Coutre, 2018).

Aspirin may induce a platelet disorder. Even small amounts of aspirin can reduce normal platelet aggregation and increase bleeding time for several days after ingestion. Although this typically does not cause bleeding in most people, patients with thrombocytopenia and coagulation disorders such as hemophilia

can experience significant bleeding after ingestion of aspirin, especially in conjunction with trauma and invasive procedures.

Chart 29-9 PHARMACOLOGY

Medications and Substances That Impair Platelet Function

Medications

Angiotensin-converting enzyme inhibitors
Angiotensin receptor blockers
Antibiotics
Beta-lactams
Cephalosporins
Penicillins
Beta-blockers
Calcium channel blockers
Chemotherapeutic agents
Mithramycin
Vincristine
Diuretics
Ethacrynic acid
Furosemide
HMG-CoA reductase inhibitors (i.e., "statins")
 Atorvastatin
 Simvastatin
Methylxanthines
 Aminophylline
 Theophylline
Milrinone
Misoprostol
Nitrates
 Isosorbide
 Nitroglycerin
Phosphodiesterase inhibitors
Pentoxyfilline
Sildanafil
Tadalafil
Protease inhibitors
Ritonavir
Tipranavir
Phenytoin
Selective serotonin reuptake inhibitors
 Fluoxetine
 Fluvoxamine
 Paroxetine
 Sertraline
Tricyclic antidepressants
 Doxepin
 Imipramine

Tyrosine kinase inhibitors
Dasatinib
Imatanib
Valproic acid

Food and Food Additives

Caffeine
Ethanol (Alcohol)
Fish oils
Garlic
Ginger
Grape juice

Over-the-Counter and Herbal Supplements

Ginkgo biloba
Ginseng
Saw palmetto
Vitamin C
Vitamin E

Adapted from Comerford, K. C., & Durkin, M. T. (2020). *Nursing 2020 drug handbook*. Philadelphia, PA: Wolters Kluwer; Coutre, S. (2019). Congenital and acquired disorders of platelet function. *UpToDate*. Retrieved on 1/1/2020 at: www.uptodate.com/contents/congenital-and-acquired-disorders-of-platelet-function; Nagalla, S., & Bray, P. F. (2017). Hematology: Drug-induced platelet dysfunction. Cancer Therapy Advisor. Retrieved on 1/1/2020 at: www.cancertherapyadvisor.com/home/decision-support-in-medicine/hematology/drug-induced-platelet-dysfunction/

NSAIDs can also impair platelet function, but the effects are not as prolonged as with aspirin (4 days vs. 7 to 10 days). Other causes of platelet dysfunction include end-stage renal disease, MDS, multiple myeloma, cardiopulmonary bypass, herbal remedies, and other medications (see [Chart 29-9](#)).

Clinical Manifestations

Bleeding can range from mild to severe. The severity does not necessarily correlate with the platelet count or with tests that measure coagulation (prothrombin time [PT], activated partial thromboplastin time [aPTT]). However, results from these tests may be useful in determining the etiology of the bleeding disorder when abnormalities are present (Levi, Seligsohn, & Kaushansky, 2016). For example, an elevated PT in the setting of a normal aPTT and platelet count may suggest factor VII deficiency, whereas an elevated aPTT in the setting of a normal PT and platelet count is suggestive of

von Willebrand disease (vWD) or hemophilia. Ecchymoses, particularly on the extremities, are frequently evident. Patients with platelet dysfunction are at increased risk for bleeding after trauma or invasive procedures (e.g., dental extraction, biopsy).

Medical Management

Platelet dysfunction that is associated with a medication requires stopping the medication when possible, especially when bleeding occurs. If platelet dysfunction is present, bleeding may be prevented by transfusion of platelets prior to an invasive procedure. Antifibrinolytic agents (e.g., aminocaproic acid) may be needed to prevent significant bleeding after procedures; desmopressin, a synthetic vasopressin analogue, can reduce the duration of bleeding and improve hemostasis for some patients (Levi et al., 2016).

Nursing Management

Patients with platelet dysfunction should be instructed to avoid substances that can interfere with platelet function. These include OTC medications such as aspirin and NSAIDs, as well as some herbal preparations, nutritional supplements, and alcohol. Patients should notify all health care providers, including dentists, of their underlying condition before undergoing any invasive procedure so that measures to reduce risk for bleeding can be implemented. Maintaining good oral hygiene is important to promote good dental health and reduce risk for gingival bleeding.

Inherited Bleeding Disorders

Two of the more commonplace inherited bleeding disorders include hemophilia and vWD. Each of these is discussed in the sections that follow.

Hemophilia

There are two forms of hemophilia: hemophilia A and hemophilia B. Both are clinically similar but are distinguishable by laboratory tests. Hemophilia A is caused by a genetic defect that results in deficient or defective factor VIII. Hemophilia B, also known as Christmas disease, is due to a genetic defect that causes a deficiency or defect in factor IX. Hemophilia is a relatively common disease, with hemophilia A occurring in 1 of every 5000 to 7000 births. Hemophilia A is five times more common than hemophilia B (Escobar & Key, 2016). Both hemophilia A and hemophilia B are inherited as X-linked traits, making both conditions much more common in males than in females.

Females can be carriers of the gene but are typically asymptomatic. It is estimated that one third of cases result from spontaneous mutations rather than familial transmission (National Hemophilia Foundation, 2019).

The tendency for developing bleeding is the basis for the classification of hemophilia (Escobar & Key, 2016):

- Severe disease is defined by a plasma factor activity level of less than 1 IU/dL, or less than 1% normal factor VIII levels.
- Moderate disease reflects a level of 1 to 5 IU/dL or factor VIII level between 1% and 5% of normal.
- Mild disease reflects a level above 5 IU/dL or factor VIII level above 5%.

Hemophilia is often recognized in early childhood, usually in the toddler period. However, patients with mild hemophilia may not be diagnosed until they experience severe trauma or surgery.

Clinical Manifestations

Hemophilia is manifested by hemorrhages into various parts of the body; hemorrhages can be severe and can occur even with minimal trauma. The frequency and severity of bleeding depend on the degree of factor deficiency and the severity of the precipitating trauma. Those with mild factor deficiency rarely develop spontaneous bleeding; hemorrhage is usually associated with trauma. In contrast, spontaneous bleeding, including hemarthroses and hematomas, occur frequently in patients with severe factor deficiency (Escobar & Key, 2016).

About 75% of bleeding in patients with hemophilia occurs in the joints. Joints most frequently affected include the knees, elbows, ankles, shoulders, wrists, and hips. Pain is often noticed prior to the presence of swelling and limitations in movement. Recurrent joint hemorrhages can lead to joint arthropathy that causes ankylosis and chronic pain (see Fig. 29-5). Patients with severe factor deficiency may become disabled due to joint damage early in life. Bleeding may be superficial as hematomas or as deep hemorrhages into muscle and subcutaneous tissue. With severe factor VIII deficiency, hematomas can occur without trauma and extend into the surrounding tissue. Hematomas in the muscles, particularly in the extremities, may cause peripheral nerve compression with impaired sensation. Over time, nerve compression may lead to weakness and atrophy of the affected area.



Figure 29-5 • Hemophilic arthropathy: Sequelae of recurrent joint bleeding. Reprinted with permission from *Wintrobe's clinical hematology* (10th ed). (1999). Color plate 68. Philadelphia, PA: Lippincott Williams & Wilkins.

Bleeding is not limited to joints and muscles. Dental procedures, including extractions, are associated with bleeding. Spontaneous hematuria and GI bleeding may also occur. Bleeding is also common in other mucous membranes, including the nasal passages and conjunctivae as well as soft tissue. Falls in adults are particularly dangerous. Intracranial and extracranial hemorrhages are the most serious sites of bleeding. Any head trauma requires immediate evaluation and treatment. Surgical procedures often result in excessive bleeding at the surgical site. Clot formation and wound healing are often poor.

Medical Management

Recombinant forms of factor VIII and IX concentrates are available and decrease the need for using plasma-derived factor concentrates and fresh-frozen plasma. Concentrates are used when patients are actively bleeding; it is important that treatment is initiated as soon as possible to reduce risk for bleeding complications. Factors should be administered prophylactically prior to traumatic procedures to prevent excessive bleeding (Escobar & Key, 2016). Children frequently receive prophylactic treatment three to four times per week to reduce risk for joint complications. The cost and challenges with adhering to the prescribed regimen may limit the effectiveness of this approach.

(Thornburg & Duncan, 2017). Initiating prophylactic treatment in adolescents and young adults can also lead to positive outcomes by reducing joint complications, pain, and disability and improving quality of life (Reding, 2018).

Development of neutralizing antibodies (inhibitors) to factor concentrates is a significant complication of factor replacement therapy. Up to 33% of patients with hemophilia A and 3% of patients with hemophilia B develop antibodies to factor concentrates (Reding, 2018). The presence of these inhibitors may be transient; however, the effects may be significant and lead to partial or complete refractoriness to factor replacement, leading to increased risk for bleeding. Ideally, antibody titers should remain low. It is important to identify rising antibody titers as soon as possible. To reduce the impact of inhibitors, inducing immune tolerance is critical. Immunosuppressive therapy in the form of corticosteroids, IVIG or cyclophosphamide may be used to remove inhibitors. Emicizumab is a new bispecific humanized monoclonal antibody that is effective in preventing bleeding in patients with hemophilia A. Initially indicated as effective therapy for patients with inhibitors, it is now also indicated for patients without inhibitors (Franchini, Marano, Pati, et al., 2019; Young, Liesner, Chang, et al., 2019). Patients with severe factor deficiency should be screened for antibodies, particularly prior to invasive procedures, so that appropriate therapy aimed at reducing risk for bleeding complications can be started. Other therapeutic options include administration of recombinant factor VIIa or activated prothrombin complex concentrates (Reding, 2018).

Aminocaproic acid inhibits fibrinolysis and subsequently stabilizes blood clots. It can be very effective as an adjunctive measure to treat mucosal bleeding after oral surgery. Desmopressin induces a significant but short-lived increase in factor VIII levels; the mechanism of this response is unclear. In patients with mild forms of hemophilia A, desmopressin is very useful and can significantly reduce the requirement for blood products (Mannucci, 2018).

Nursing Management

Most adult patients with hemophilia are diagnosed during childhood. They frequently need assistance in coping with the disease because it is chronic and imposes restrictions on their lifestyle. Additionally, the disease is inherited and can be passed to future generations. Helping patients cope with their condition, assisting them to identify positive aspects of their lives, and encouraging independence and self-sufficiency are important nursing activities. This must be balanced with promoting safety and preventing trauma that can result in acute bleeding. As patients mature, they can be encouraged to work through their feelings, progressing toward acceptance, and assuming greater responsibility for maintaining an optimal state of health.

Patients with mild factor deficiency may not be diagnosed until they reach adulthood if they do not have surgery or significant trauma during childhood. The nurse must provide these patients with extensive education to understand activity restrictions and self-care strategies to reduce risk for hemorrhage and complications associated with bleeding. Safety at home and at work should be emphasized.

Patients and family caregivers need to learn how to administer factor concentrate at home at the earliest signs of bleeding to minimize bleeding and reduce complications. Prophylactic factor replacement can be beneficial in reducing morbidity associated with repeated episodes of bleeding. This method requires factor administration several times a week, making adherence to the regimen difficult. Nurses can help patients and families understand the potential benefits of prophylactic therapy while helping them to minimize the disadvantages. Patients with hemophilia are also instructed to avoid agents that can interfere with platelet aggregation that can add additional risk for bleeding. Aspirin, NSAIDs, some herbal and nutritional supplements (e.g., nettle, chamomile, alfalfa), and alcohol should be avoided. Oral hygiene is an important measure to reduce gingival bleeding, and good dental health should be promoted to reduce the need for extractions over the long term. While application of pressure may be helpful in controlling bleeding from minor injuries in patients with factor deficiency, it is inadequate in the presence of severe factor deficiency. Nasal packing for epistaxis should be avoided because bleeding often resumes when packing is removed. Splints and other orthopedic devices may be beneficial in supporting and immobilizing joints and muscles affected by hemorrhage. All injections should be avoided; invasive procedures (e.g., endoscopy, lumbar puncture) should be avoided or performed after administration of appropriate factor replacement. Patients with hemophilia should carry or wear medical identification (e.g., Medic-Alert bracelets). Additionally, patients and families should have a written emergency plan that includes measures to be taken in specific situations along with names and telephone numbers for emergency contacts.

During bleeding episodes, the extent of bleeding must be carefully assessed. Patients at risk for significant complications (e.g., bleeding into the respiratory tract or CNS) require close observation, specifically assessing for respiratory distress and altered levels of consciousness. Patients who have had recent surgery need careful monitoring to assess for bleeding from surgical sites. Frequent monitoring of vital signs, drains, and dressings is necessary to identify postoperative bleeding.

Significant pain requiring analgesics is often associated with hematomas and joint hemorrhage. Warm baths can be helpful in relieving pain, promoting relaxation, and improving mobility. During bleeding episodes, heat should be avoided because it may exacerbate bleeding; applications of cold are more efficacious.

Factor concentrates used since 1985 are free of viruses, including hepatitis C and HIV; however, patients treated prior to that time were exposed to these viruses (Escobar & Key, 2016). Patients who have acquired HIV and other viral infections may need assistance in coping with these additional diagnoses and the consequences of infection.

Genetic testing and counseling should be offered to female carriers so they can make informed decisions regarding childbearing and managing pregnancy (see [Chapter 6](#)).

Gerontologic Considerations

Advances in treatment have led to extended lifespans for patients with hemophilia, causing unique challenges for older patients with this disorder. Older adult patients with hemophilia are likely to have been managed with blood component transfusion and plasma-derived clotting factors prior to the advent of universal screening, at least early in life. For this reason, HIV and hepatitis B and C infections are not uncommon in this population; these infections carry significant risk for liver cancer and other liver diseases (Mannucci, 2019). Intracranial hemorrhage is the third most common cause of death after HIV and hepatitis and result from trauma. The likelihood of acquiring inhibitors increases with age.

Cardiovascular disease among adults with hemophilia can be difficult to manage. Antiplatelet therapy (including aspirin) can be challenging for patients with severe hemophilia. Stent placement and coronary artery bypass graft surgery are accompanied by significant risk but aggressive factor replacement therapy can make these therapeutic treatments possible (Kanelloupolou & Nomikou, 2018). Close collaboration and coordination of care with the patient's hematologist are required to improve outcomes.

Arthropathy is a major cause of morbidity in older patients with hemophilia and can result in reduced range of motion, impaired functioning, and chronic pain. However, quality of life can improve with arthroplasty and multidisciplinary rehabilitation tailored to address the special needs of older adults with hemophilia (Mannucci, 2019).

von Willebrand Disease

vWD is an inherited bleeding disorder characterized by a deficiency in von Willebrand factor (vWF), which is necessary for factor VIII activation. The disease is characterized primarily by mucosa-associated bleeding and bleeding following surgery and trauma. vWD is the most common inherited bleeding disorder, affecting up to 1% of the general population. It typically has an autosomal dominant inheritance pattern, affecting both genders equally (Rick, 2019). vWD is divided into types 1, 2, and 3. Type 1 accounts for 70% to 80%

of cases, and is characterized by a quantitative deficiency of vWF. Type 2, accounting for approximately 20% of cases, is caused by dysfunctional vWF. Type 2 is further subdivided on the basis of certain phenotypic characteristics. Type 3 vWD is rare and accounts for fewer than 5% of cases. It is the most severe form, and is caused by the absence of circulating vWF (Leebeek, & Eikenboom, 2016). [Figure 29-6](#) illustrates the differences in clotting found with hemophilia and vWD.

Clinical Manifestations

Bleeding most often involves the mucous membranes. Nosebleeds, heavy menses, easy bruising, and prolonged bleeding from cuts and surgical sites are common. Soft tissue and joint hemorrhages are not seen often, unless the patient has type 3 vWD. As laboratory values fluctuate, so does bleeding. For example, postoperative bleeding may be minor with one procedure but significant with another (Rick, 2019).

Assessment and Diagnostic Findings

vWD may be suspected based upon a personal or family history of bleeding that may then be confirmed by laboratory evidence of abnormalities in vWF, factor VIII, or both. The diagnosis of vWD is based on measurements of vWF antigen; the level of vWF-dependent platelet adhesion, measured with the use of the vWF–ristocetin cofactor activity assay; and the coagulant activity of factor VIII. Type 3 vWD is diagnosed when vWF antigen is undetectable (or the level is less than 5 IU/dL). These results are variable with individual patients over time, making it important to review laboratory values over time and not rely on single measurements (Rick, 2019).

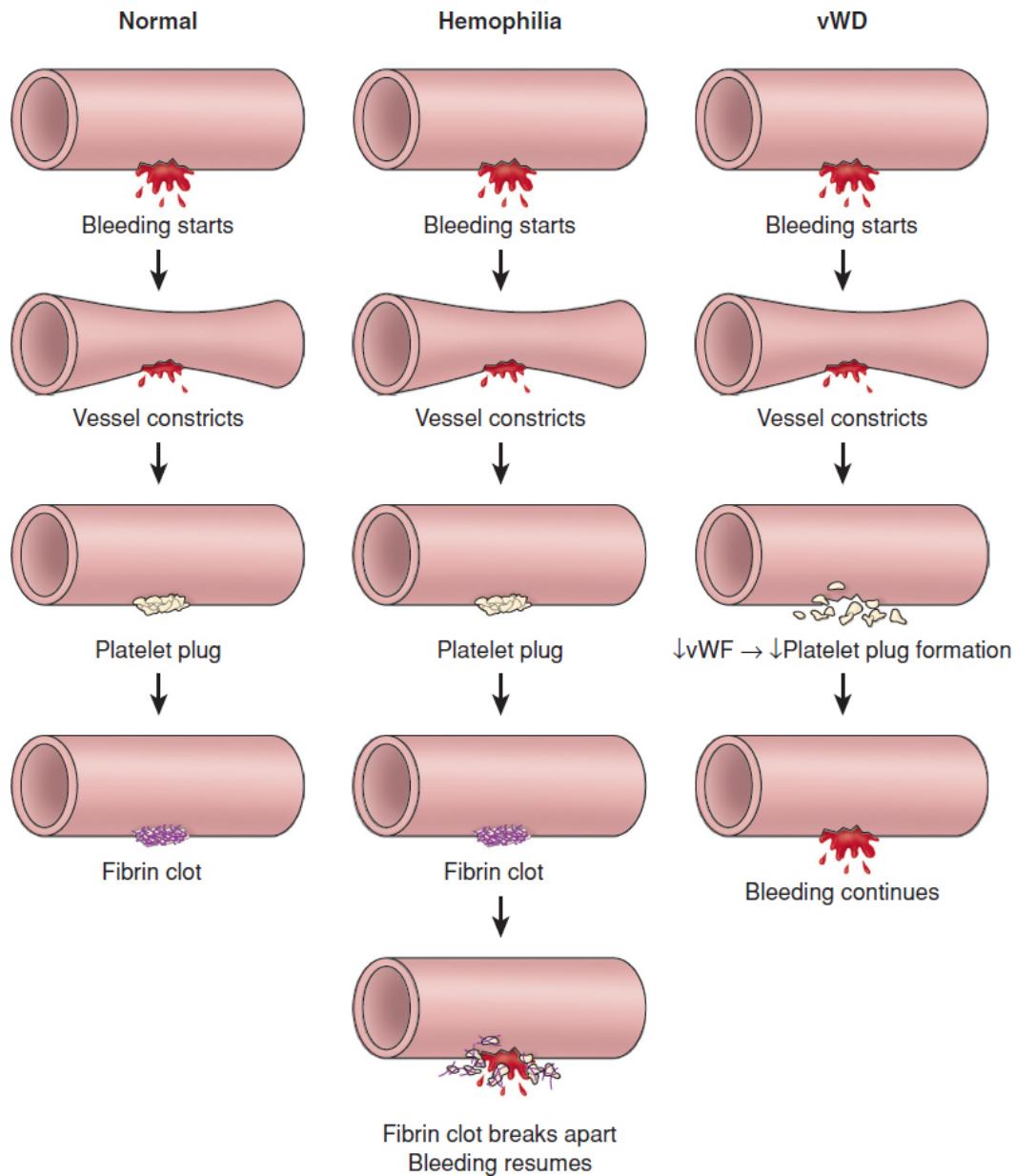


Figure 29-6 • Differences in bleeding. Normal, hemophilia, and von Willebrand disease (vWD). Reprinted with permission from Thomas, M., & Morrow, K. *Veterans Administration Palo Alto Health Care System*. Palo Alto: CA.

Management

The goal of treatment is to replace the deficient protein (e.g., vWF or factor VIII) at the time of spontaneous bleeding or prior to an invasive procedure to prevent subsequent bleeding. Desmopressin is often used to prevent bleeding associated with dental and surgical procedures or to manage mild bleeding after surgery in patients with mild vWD; it is often not effective in treating

those with type 3 vWD (Leebeek, & Eikenboom, 2016). Desmopressin provides a transient increase in factor VIII coagulant activity and may also correct bleeding time. Desmopressin can be given as an IV infusion or intranasally. IV administration is preferred for invasive procedures, including surgery. Hyponatremia and seizures may occur after repeated doses; therefore, treatment longer than 3 consecutive days is not typically indicated.

Factor replacement concentrates of vWF and factor VIII are the treatments of choice for patients with type 3 vWD and most patients with type 2. The dosage and frequency of administration of these agents depend on the patient's factor VIII level and extent of bleeding. Treatment may be needed for up to 7 to 10 days after a surgical procedure and 3 to 4 days postpartum. In patients with type 3 vWD, prophylactic use of replacement agents is often successful in preventing or limiting spontaneous bleeding. Formation of antibodies to these agents is most likely to occur in patients with type 3 vWD receiving high doses.

Other agents are also effective in controlling bleeding. Aminocaproic acid is useful in managing mild mucosal bleeding because it inhibits dissolution of the thrombus at the site of bleeding. Topical agents that augment thrombin formation at the site of application help to achieve hemostasis in dental procedures. Estrogen-progesterone compounds may reduce bleeding associated with menses. Platelet transfusions are useful when there is significant bleeding. Cryoprecipitate, which is rich in vWF and factor VIII, typically is used only in emergencies due to risk for iatrogenic transmission of viruses. Herbs and medications that interfere with platelet function should be avoided (Leebeek & Eikenboom, 2016).

Acquired Bleeding Disorders

There are a plethora of acquired bleeding disorders. Common causes include liver disease, vitamin K deficiency, and heparin-induced thrombocytopenia (HIT).

Liver Disease

Excluding factor VIII, most blood coagulation factors are synthesized in the liver. Therefore, liver dysfunction (due to cirrhosis, hepatitis, and tumor) can lead to reduced amounts of the factors needed for coagulation and hemostasis (see [Chapter 43](#)). Prolongation of the PT may indicate severe hepatic dysfunction, unless associated with vitamin K deficiency. Patients may experience minor bleeding (e.g., ecchymoses) but are also at risk for significant bleeding, especially after surgery or trauma. Transfusion of fresh-frozen plasma may be needed to replace clotting factors and prevent or stop

bleeding. Life-threatening hemorrhage associated with peptic ulcer or esophageal varices may occur. In the event of significant hemorrhage, transfusion of fresh-frozen plasma, PRBCs, and platelets is often necessary.

Vitamin K Deficiency

Vitamin K is an essential element for synthesis of many coagulation factors. Vitamin K deficiency is often seen in patients who are malnourished. Prolonged use of some antibiotics can reduce the intestinal flora that produce vitamin K, causing depletion of vitamin K stores. Correction of the deficiency can be achieved with oral or subcutaneous administration of vitamin K (phytonadione). Adequate synthesis of coagulation factors is reflected in normalization of the PT.

Heparin-Induced Thrombocytopenia

HIT is a serious complication of heparin-based therapy, a medication commonly prescribed for its anticoagulant effects (see [Chapter 26](#) for description of indications for heparin). HIT involves the formation of antibodies against the heparin–platelet complex. HIT may occur in as many as 5% of patients receiving heparin (Brien, 2019). The type of heparin used, the duration of therapy (4 to 14 days), and surgery (especially if cardiopulmonary bypass is used) appear to be risk factors for developing HIT. Bovine heparin preparations are more likely to lead to HIT than porcine preparations; even low-molecular-weight heparins (LMWHs) carry risk for HIT. Neither the dose nor the route of administration of heparin is a risk factor. Women appear to be at higher risk and young adults are at low risk for developing this condition. A decline in the platelet count is the hallmark sign that most often develops 5 to 10 days after heparin therapy is initiated; therefore, monitoring the platelet count in patients receiving heparin therapy is essential. The platelet count can drop significantly, typically by 50% of the baseline over a period of 1 to 3 days. Autoantibodies develop that may activate platelets, causing thromboses. After patients with HIT are successfully managed, these autoantibodies typically disappear in 2 to 3 months.

Affected patients are at increased risk for thrombosis, either venous, arterial, or both, with thromboses that may manifest as deep vein thrombosis (DVT), acute coronary syndrome (ACS), stroke, or thrombosis to major vessels in an extremity, leading to amputation. Venous thromboembolism (VTE) is the most common manifestation of thrombosis secondary to HIT (i.e., DVT or pulmonary embolism [PE]) (Brien, 2019).

Treatment for HIT includes immediate cessation of heparin (including heparin-coated catheters) and initiation of another form of anticoagulation. If the heparin is discontinued without providing an alternative form of

anticoagulation, the patient is at increased risk of developing new thrombi. Argatroban, a thrombin inhibitor, is an FDA-approved anticoagulant for the treatment of HIT. Oral anticoagulation with warfarin is contraindicated because it initially promotes thrombosis in the microvasculature by depletion of protein C. This can lead to tissue ischemia and gangrenous limbs, ultimately resulting in amputation if untreated (Arepally, 2017). Patients who develop thrombosis in the presence of HIT should receive anticoagulation for 3 to 6 months; in the absence of thrombosis, treatment may be shorter. Patients must be aware that the condition may be reactivated with re-exposure to heparin, even in small amounts, within 3 to 4 months of the diagnosis (Arepally, 2017).



Disseminated Intravascular Coagulation

Disseminated intravascular coagulation (DIC) is a systemic syndrome that is characterized by microthromboses and bleeding. DIC may be precipitated by sepsis, trauma, cancer, shock, abruptio placentae, allergic reactions, and other conditions. Most cases are associated with infection or malignancy (Levi & Seligsohn, 2016). The severity of DIC varies but it is potentially life-threatening.

Pathophysiology

Normal hemostatic mechanisms are altered in DIC. The inflammatory response generated by the underlying disease initiates the process of inflammation and coagulation within the vasculature. The normal anticoagulation pathways in the body are impaired, and fibrinolysis is suppressed allowing numerous small clots to form in the microcirculation. Coagulation time is initially normal; however, when platelets and clotting factors form microthrombi, coagulation fails. The result of these processes leads to both excessive clotting and bleeding (see Fig. 29-7).

The clinical manifestations of DIC are primarily reflected in compromised organ function or failure. Decline in organ function is usually a result of excessive clot formation (with resultant ischemia to all or part of the organ) or, less often, of bleeding. The excessive clotting triggers the fibrinolytic system to release fibrin degradation products, which are potent anticoagulants, furthering the bleeding. The bleeding is characterized by low platelet and fibrinogen levels; prolonged PT, aPTT, and thrombin time; and elevated fibrin degradation products and D-dimers.

The mortality rate can exceed 80% in patients who develop severe DIC with ischemic thrombosis, frank hemorrhage, and MODS. Identification of patients who are at risk for DIC and recognition of the early clinical

manifestations of this syndrome can result in prompt medical intervention, which may improve the prognosis. However, the primary prognostic factor is the ability to treat the underlying condition that precipitated DIC (Levi & Seligsohn, 2016).

Clinical Manifestations

During the initial process of DIC, the patient may have no new symptoms—the only manifestation being a progressive decrease in the platelet count. As the thrombosis becomes more extensive, the patient exhibits signs and symptoms of thrombosis in the organs involved. Then, as the clotting factors and platelets are consumed to form these thrombi, bleeding occurs. Initially, the bleeding is subtle, but it can develop into frank hemorrhage. Signs and symptoms depend on the organs involved and are listed in [Chart 29-10](#). Patients with frank DIC may exhibit bleeding from mucous membranes and venipuncture sites as well as the GI and urinary tracts. Bleeding may range from minimal, occult internal bleeding to copious bleeding from multiple orifices.

Physiology/Pathophysiology

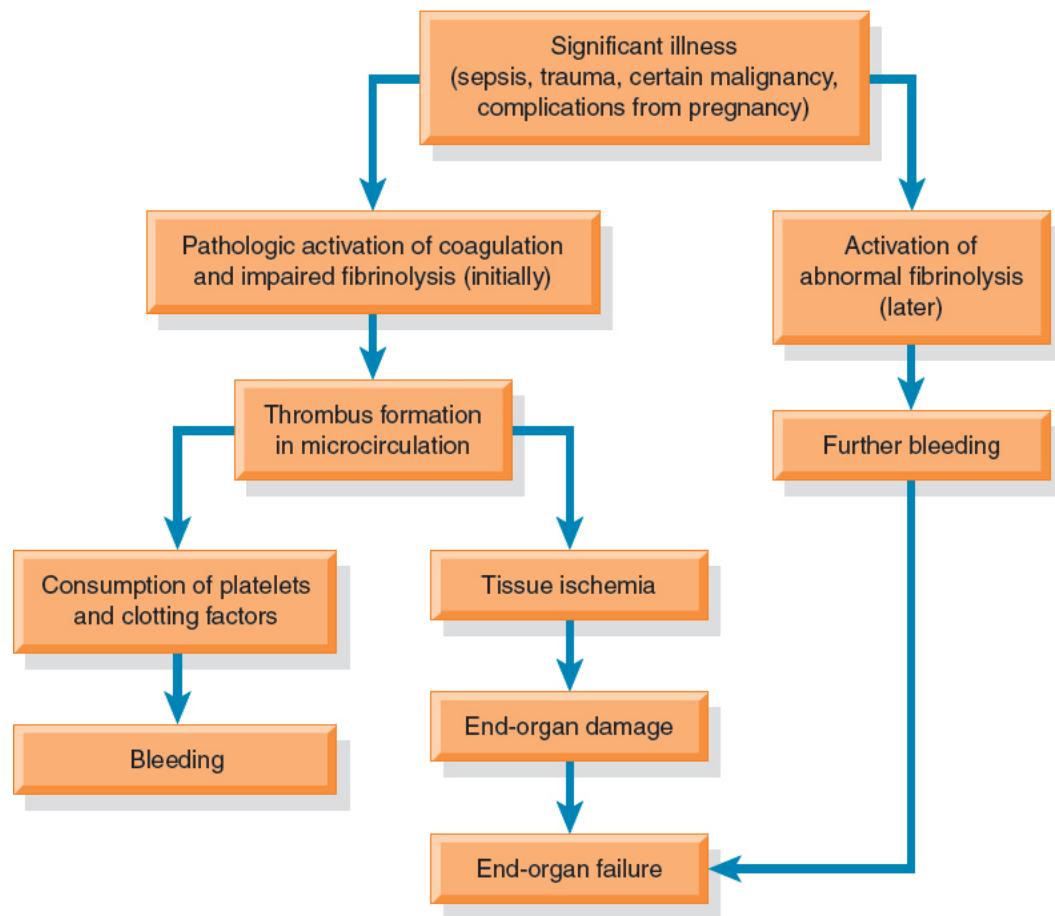


Figure 29-7 • Pathophysiology of disseminated intravascular coagulation.

Chart 29-10 ASSESSMENT

Assessing for Thrombosis and Bleeding in Disseminated Intravascular Coagulation

System	Signs and Symptoms of Microvascular Thrombosis	Signs and Symptoms of Microvascular and Frank Bleeding
Integumentary	↓ Temperature, sensation; ↑ pain; cyanosis in extremities, nose, earlobes; focal ischemia, superficial gangrene	Petechiae, including periorbital and oral mucosa; bleeding: gums, oozing from wounds, previous injection sites, around catheters (IVs, tracheostomies); epistaxis; diffuse ecchymoses; subcutaneous hemorrhage; joint pain
Circulatory	↓ Pulses; capillary filling time >3 seconds	Tachycardia
Respiratory	Hypoxia (secondary to clot in lung); dyspnea; chest pain with deep inspiration; ↓ breath sounds over areas of large embolism	High-pitched bronchial breath sounds; tachypnea; ↑ consolidation; signs and symptoms of acute respiratory distress syndrome
Gastrointestinal	Gastric pain; “heartburn”	Hematemesis (heme⊕ nasogastric output); melena (heme⊕ stools → tarry stools → bright-red blood from rectum); retroperitoneal bleeding (abdomen firm, distended, and tender to palpation; ↑ abdominal girth)
Renal	↓ Urine output; ↑ creatinine, ↑ blood urea nitrogen	Hematuria
Neurologic	↓ Alertness and orientation; ↓ pupillary reaction; ↓ response to commands; ↓ strength and mobility	Anxiety; restlessness; ↓ mentation, altered level of consciousness; headache; visual disturbances; conjunctival hemorrhage

↓, decreased; ↑, increased; heme⊕, positive for hemoglobin; IV, intravenous.

Note: Signs of microvascular thrombosis are the result of an inappropriate activation of the coagulation system, causing thrombotic occlusion of small vessels within all body organs. As the clotting factors and platelets are consumed, signs of microvascular bleeding appear. This bleeding can quickly worsen, becoming frank hemorrhage. Treatment must be aimed at the underlying disorder so that the stimulus for the syndrome is diminished or arrested.

Adapted from Levi, M., & Seligsohn, U. (2016). Disseminated intravascular coagulation. In K. Kaushansky, M. A. Lichtman, J. T. Prchal, et al. (Eds.). *Williams hematology* (9th ed.). New York: McGraw-Hill Medical.

Assessment and Diagnostic Findings

The diagnosis of DIC is frequently made based on laboratory tests that demonstrate the consumption of platelets and clotting factors (see [Table 29-4](#)). Although each test is useful in establishing the diagnosis of DIC, the specificity of each individual test is lacking. The International Society of Thrombosis and Haemostasis developed a highly sensitive and specific scoring system using platelet count, fibrin degradation products, PT, and fibrinogen level to diagnose DIC (Levi & Seligsohn, 2016) (see [Table 29-5](#)). Additionally, this system is useful in predicting the severity of the disease and subsequent mortality. Additional tests, such as thromboelastography, can be performed at the bedside and can effectively assess platelet function and fibrinolytic activity. Studies suggest that assessment of the status of the coagulation system at the bedside of critically ill patients is more useful than using conventional laboratory tests (Afzal & Syed, 2017).

TABLE 29-4 Laboratory Values Commonly Found in Disseminated Intravascular Coagulation^a

Test	Function Evaluated	Normal Range	Changes in DIC
Platelet count	Platelet number	150,000–450,000/mm ³	↓
Prothrombin time (PT)	Extrinsic pathway	11–12.5 s	↑
Partial thromboplastin time (activated)(aPTT)	Intrinsic pathway	23–35 s	↑
Thrombin time (TT)	Clot formation	8–11 s	↑
Fibrinogen	Amount available for coagulation	170–340 mg/dL	↓
D-dimer	Local fibrinolysis	0–250 ng/mL	↑
Fibrin degradation products (FDPs)	Fibrinolysis	0–5 mcg/mL	↑
Euglobulin clot lysis	Fibrinolytic activity	≥2 h	≤1 h

^aBecause DIC is a dynamic condition, the laboratory values measured will change over time. Therefore, a progressive increase or decrease in a given laboratory value is likely to be more important than the actual value of a test at a single point in time.

↓, decreased; ↑, increased; DIC, disseminated intravascular coagulation.

Adapted from Fischbach, F. T., & Fischbach, M. A. (2018). *A manual of laboratory and diagnostic tests* (10th ed.). Philadelphia, PA: Wolters Kluwer.

TABLE 29-5 Scoring System for Disseminated Intravascular Coagulation

Laboratory Test	0	1	2	3
Platelet count	>100,000/mm ³	>50,000/mm ³ , <100,000/mm ³	<50,000/mm ³	
Fibrin degradation products	No increase		Moderate increase	Strong increase
Prothrombin time (upper limit of normal)	<3 s	>3 s, <6 s	>6 s	
Fibrinogen	>100 mg/dL	<100 mg/dL		

Note: 5 or more is compatible with overt disseminated intravascular coagulation.

Adapted from Taylor, F. B., Toh, C. H., Hoeks, W. K., et al. (2007). Towards a definition, clinical and laboratory criteria, and a scoring system for DIC. *Journal of Thrombosis and Haemostasis*, 5(3), 445–459.

Medical Management

The most critical factor in managing DIC is treatment of the underlying cause; until the cause is controlled, DIC will continue. Correcting the secondary effects of tissue ischemia by increasing tissue oxygenation, replacing fluids, correcting electrolyte abnormalities, and administering vasopressor medications is also important. When serious hemorrhage is present, depleted coagulation factors and platelets are replaced to promote normal hemostasis and reduce bleeding. The extent of hemorrhage and need for any invasive procedure are important considerations in determining the decision to provide transfusion support. Cryoprecipitate is given to replace fibrinogen and factors V and VII (Levi & Seligsohn, 2016).

The use of a heparin infusion to interrupt the thrombosis process is a controversial treatment strategy. Heparin may inhibit the formation of microthrombi and allow improved tissue perfusion to vital organs. Traditionally, heparin has been used in patients with predominantly thrombotic manifestations or in those in whom blood component replacement failed to reduce hemorrhage or increased fibrinogen and other clotting levels. When bleeding is absent, LMWH can be used to prevent VTE, while therapeutic doses may be used when severe thrombosis is predominant. Normalization of plasma fibrinogen and diminished signs of bleeding serve as evidence of heparin's effectiveness. Fibrinolytic inhibitors, such as aminocaproic acid, are not routinely used as they block the lysis of fibrin that is necessary to preserve tissue perfusion. If bleeding is profuse and there is evidence of extensive fibrinolysis, fibrinolytic inhibitors are used along with continuous infusion of IV heparin (Levi & Seligsohn, 2016).

Recombinant forms of thrombomodulin were believed to inactivate thrombin, the main culprit in inciting the coagulopathy that undergirds DIC. However, a systematic review of clinical trials found no improvement in mortality rates with patients with DIC who were prescribed recombinant thrombomodulin (Murao & Yamakawa, 2019). All management strategies must be individualized to the specific patient, underlying cause of DIC, and response to interventions.

Nursing Management

Nurses need to identify patients at risk for DIC (see previous discussion on precipitating factors). It is important to assess patients frequently and thoroughly for signs and symptoms of thrombi and bleeding and monitor for progression of these signs (see [Chart 29-10](#)). Laboratory values must be monitored frequently to assess for trends over time as well as for changes in values.

[Chart 29-11](#) describes care of the patient with DIC. Assessment and interventions should target potential sites of end-organ damage. As organs become ischemic from microthrombi, organ function diminishes; the kidneys, lungs, brain, and skin are particularly vulnerable. Lack of renal perfusion may result in acute tubular necrosis and kidney injury, sometimes requiring dialysis. Placement of a large-bore dialysis catheter is extremely hazardous for this patient population and should be accompanied by adequate platelet and plasma transfusions. Hepatic dysfunction is also relatively common, reflected in altered liver function tests, depleted albumin stores, and diminished synthesis of clotting factors. Respiratory function warrants careful monitoring and aggressive measures to diminish alveolar compromise. Suctioning should be performed as gently as possible to diminish the risk of additional bleeding. CNS involvement can be manifested as headache, visual changes, and alteration in level of consciousness.

Secondary Thrombocytosis

Increased platelet production is the primary mechanism of secondary or reactive **thrombocytosis**, characterized by an elevation in the platelet count. However, these elevations are rarely above 1 million/mm³. This is in contrast to essential thrombocytosis which is a chronic myeloproliferative disease (see [Chapter 30](#)). In secondary thrombocytosis, platelet function and survival are typically normal; therefore, hemorrhage and thrombosis are rare (Kaushansky, 2016). A number of disorders are associated with a reactive increase in platelets, including infection, iron deficiency anemia, chronic inflammatory disorders, malignancy, acute hemorrhage, and splenectomy. Treatment is directed at the underlying disorder. When managed successfully, the platelet count often returns to normal.

THROMBOTIC DISORDERS

Several conditions can affect the balance of normal hemostasis, causing excessive thrombosis that can alter arterial or venous circulation. Arterial thrombosis is caused by platelet aggregation, while venous thrombosis is a result of accumulation of platelets, red blood cells, and thrombin. Abnormalities that predispose a person to thrombotic events include decreased clotting inhibitors in the circulation, impaired liver function, lack of fibrinolytic enzymes, and vascular abnormalities that promote platelet aggregation. Thrombosis may also occur as the initial manifestation of an occult malignancy or as a complication of a previously diagnosed cancer. In some cases, more than one precipitating factor exists. There are several inherited or acquired disorders, including hyperhomocysteinemia, antithrombin (AT) deficiency, protein C deficiency, protein S deficiency, activated protein C (APC) resistance, and factor V Leiden deficiency that can predispose patients to repeated episodes of thrombosis. These are also referred to as hypercoagulable states or thrombophilia. Inherited disorders should prompt a referral for familial genetic testing. Genetic testing is not indicated with acquired disorders.

Chart 29-11**PLAN OF NURSING CARE****The Patient with Disseminated Intravascular Coagulation**

NURSING DIAGNOSIS: Risk for hypovolaemia associated with bleeding

GOAL: Hemodynamic status maintained; urine output $\geq 0.5 \text{ mL/kg/h}$ over 6 hours or $<400 \text{ mL}$ in 24 hours

Nursing Interventions	Rationale	Expected Outcomes
<ol style="list-style-type: none">1. Avoid procedures/activities that can increase intracranial pressure (e.g., coughing, straining to have a bowel movement).2. Monitor vital signs closely, including neurologic checks:<ol style="list-style-type: none">a. Monitor hemodynamics.b. Monitor abdominal girth.c. Monitor urine output.3. Avoid medications that interfere with platelet function if possible (e.g., aspirin, nonsteroidal anti-inflammatory drugs, beta-lactam antibiotics).4. Avoid rectal probes, rectal medications.5. Avoid intramuscular injections.6. Monitor amount of external bleeding carefully:<ol style="list-style-type: none">a. Monitor number of dressings, percentage of dressing saturated; time to saturate a dressing is more	<ol style="list-style-type: none">1. Prevents intracranial bleeding2. Identifies signs of hemorrhage/shock as soon as possible3. Decreases problems with platelet aggregation and adhesion4. Decreases risk of rectal bleeding5. Decreases risk of intramuscular bleeding6.<ol style="list-style-type: none">a. Provides accurate, objective assessment of extent of bleeding	<ul style="list-style-type: none">• Level of consciousness (LOC) stable• Central venous pressure 5–12 cm H₂O, systolic blood pressure $\geq 70 \text{ mm Hg}$• Urine output $\geq 0.5 \text{ mL/kg/h}$• Decreased bleeding• Decreased oozing• Decreased ecchymoses• Amenorrhea• Absence of oral and bronchial bleeding• Oral mucosa clean, moist, intact

- objective than “dressing saturated a moderate amount.”
- b. Assess suction output, all excreta for frank or occult blood.
 - c. Monitor pad counts in women with vaginal bleeding.
 - d. Women may receive progesterone to prevent menses.
7. Use low pressure for any necessary suctioning.
8. Administer oral hygiene carefully.
- a. Avoid lemon-glycerin swabs, hydrogen peroxide, commercial mouthwashes.
 - b. Use sponge-tipped swabs, salt/baking soda (bicarbonate of soda) mouth rinses.
9. Avoid dislodging any clots, including those around IV sites and injection sites.
- b. Identifies presence of or quantifies extent of bleeding
- c. Quantifies extent of bleeding
- d. Decreases risk of bleeding from gynecologic source
7. Prevents excessive trauma that can cause additional bleeding
8. Prevents excessive trauma that can cause bleeding. Glycerin and alcohol (in commercial mouthwashes) dry the mucosa, increasing risk for bleeding.
9. Reduces risk for excessive bleeding from sites

NURSING DIAGNOSIS: Risk for impaired skin integrity associated with ischemia or bleeding

GOAL: Skin integrity remains intact; oral mucosa remains intact

Nursing Interventions Rationale

Expected Outcomes

- | | | |
|--|---|--|
| 1. Assess skin, with particular attention to bony prominences, skin folds. | 1. Prompt identification of any area of risk for skin breakdown or showing early signs of breakdown can prompt early intervention and reduce complications. | • Skin integrity remains intact; skin is warm, and of normal color.
• Oral mucosa is intact, pink, moist, without bleeding. |
| 2. Reposition carefully; use pressure-reducing mattress. Perform careful skin care every 2 hours, emphasizing dependent areas, all bony prominences, and perineum. | 2–4. Meticulous skin care and use of measures to prevent pressure on bony prominences decreases risk of skin trauma. | |
| 4. Use lamb's wool between digits, around ears, as needed. | | |
| 5. Use prolonged pressure (at least 5 minutes) after injection or procedure when such measures must be performed. | 5. Initial platelet plug is very unstable and can be easily dislodged, which can lead to increased bleeding. | |
| 6. Perform oral hygiene carefully (see previous discussion). | 6. Meticulous care is needed to decrease trauma, bleeding, and risk of infection. | |

NURSING DIAGNOSIS: Fluid imbalance associated with excessive blood and/or factor component replacement

GOAL: Absence of edema; absence of crackles; intake not greater than output

Nursing Interventions	Rationale	Expected Outcomes
1. Auscultate breath sounds every 2–4 hours.	1. Crackles can develop quickly.	• Breath sounds clear

- | | | |
|--|--|--|
| <ol style="list-style-type: none"> 2. Monitor extent of edema. 3. Monitor volume of IV fluids, blood products; decrease volume of IV medications if indicated. 4. Administer diuretics as prescribed. | <ol style="list-style-type: none"> 2. Fluid may extend beyond intravascular space. 3. Helps prevent fluid overload 4. Decreases excess fluid volume | <ul style="list-style-type: none"> • Absence of edema • Intake does not exceed output • Weight stable |
|--|--|--|

NURSING DIAGNOSIS: Risk for injury associated with microthrombi

GOAL: Neurologic status remains intact; absence of hypoxemia; peripheral pulses remain intact; skin integrity remains intact; urine output remains ≥ 0.5 mL/kg/h over 6 hours and >400 mL in 24 hours

Nursing Interventions	Rationale	Expected Outcomes
<ol style="list-style-type: none"> 1. Assess neurologic, pulmonary, integumentary systems. 2. Monitor response to heparin therapy. 3. Assess extent of bleeding. 4. Monitor fibrinogen levels. 5. Stop aminocaproic acid, if prescribed, if symptoms of thrombosis occur. 	<ol style="list-style-type: none"> 1. Initial signs of thrombosis may be subtle. 2. Assure anticoagulation effectiveness that may prevent formation of additional thromboses. 3. Objective measurements of all sites of bleeding are crucial to accurately assess extent of blood loss. 4. Response to heparin is most accurately reflected in fibrinogen level. 5. Aminocaproic acid should be used only in the setting of extensive hemorrhage not 	<ul style="list-style-type: none"> • Arterial blood gases, O_2 saturation, pulse oximetry, LOC within normal limits • Breath sounds clear • Absence of edema • Intake does not exceed output • Weight stable

responding to replacement therapy.

NURSING DIAGNOSIS: Anxiety associated with uncertain prognosis and risk for death

GOAL: Feelings identified/verbalized; realistic hope maintained

Nursing Interventions	Rationale	Expected Outcomes
<ol style="list-style-type: none">1. Identify previous coping mechanisms, if possible; encourage patient to use them as appropriate.2. Explain all procedures and their rationale in terms that the patient and family/significant others can understand.3. Assist family in supporting patient.4. Use services from behavioral health, chaplain as needed.	<ol style="list-style-type: none">1. Identifying previous stressful situations can aid in recall of successful coping mechanisms.2. Decreased knowledge and uncertainty can increase anxiety.3. Family/significant others can be valuable in assisting the patient to use coping strategies and to maintain hope.4. An interdisciplinary approach may be warranted, particularly when coping strategies are maladaptive or ineffective. The spiritual dimension of care may be especially important in a crisis.	<ul style="list-style-type: none">• Previously used coping strategies are identified and utilized, to the extent the patient is able to do so.• Patient and family indicate understanding of procedures as situation permits.

LOC, level of consciousness.

Thrombotic disorders require anticoagulation therapy; the duration of therapy varies with the location and extent of thrombosis, precipitating events (e.g., trauma, immobility), and any concurrent risk factors (e.g., use of oral

contraceptives, obesity, tobacco use, integrity of blood vessels, previous thrombotic events; see [Table 29-6](#)). Conditions that may result from thrombosis include ACS (see [Chapter 23](#)), ischemic stroke (see [Chapter 62](#)), and occlusive peripheral arterial disease (see [Chapter 26](#)). With some conditions, or with repeated thrombosis, lifelong anticoagulation may be required.

TABLE 29-6



Risk Factors for Thrombosis

Acquired	Inherited	Mixed/Unknown
Advanced age	Antithrombin deficiency	Activated protein C resistance
Antiphospholipid antibody syndrome	Factor V Leiden	↑ Factor VII
Atrial fibrillation	Factor XII deficiency	↑ Factor VIII
Diabetes	Protein C deficiency	↑ Factor IX
Drugs (e.g., cocaine, ergot)	Protein S deficiency	↑ Factor XI
Estrogen therapy	Prothrombin 20210 ^a	↓ Fibrinolytic activity ↑ Homocysteine
Hypertension		
Inflammatory bowel disease		
Immobility		
Lupus anticoagulant		
Major surgery		
Myeloproliferative disease		
Nephrotic syndrome		
Obesity		
Paralysis		
Pregnancy/postpartum period		
Prior stroke		
Prior superficial vein thrombosis		
Smoking		
Trauma/fracture		
Vascular access devices		

Note: Risk factors for first, unprovoked venous thromboembolism. Note that the factor levels that are increased are procoagulant proteins.

↑, increased; ↓, decreased.

Adapted from Koupenova, M., Kehrel, B. E., Corkerey, H. A., & Freedman, J. E. (2016). Thrombosis and platelets: An update. *European Heart Journal*, 38(11), 785–791.

Hyperhomocysteinemia

Homocysteine is known to promote platelet aggregation. When hyperhomocysteinemia is present, the endothelial lining of blood vessels are denuded, which can lead to thrombus formation, specifically VTE (e.g., DVT, PE) and arterial thrombosis (e.g., ischemic stroke, ACS); however, the evidence available does not clearly identify homocysteine as a causal factor.

Research suggests that the mechanisms through which hyperhomocysteinemia causes vascular disease are more complex than an increase in homocysteine alone (Ospina-Romero, Cannegieter, den Heijer, et al., 2018).

Hyperhomocysteinemia can be hereditary but may also occur as a result of folate deficiency, and to a lesser degree, deficiency of vitamins B₆ and B₁₂. These nutrients are cofactors in homocysteine metabolism. Additionally, for reasons that are unclear, older adults and those with kidney injury may also have elevated homocysteine levels without vitamin deficiency (Ostrakhovich & Tabibzadeh, 2019). While a fasting measurement of plasma homocysteine can be useful for screening in some cases, levels may be normal or slightly elevated in people with inherited hyperhomocysteinemia or those with vitamin B₆ deficiency. A more sensitive method of measurement involves obtaining a second measurement 4 hours after consumption of methionine; hyperhomocysteinemia is found more often using this method. Supplemental use of folic acid, vitamin B₁₂, or vitamin B₆ has not been shown to be effective in reducing the recurrence of venous or arterial thromboemboli (Middeldorp & Coppens, 2016). Smoking is associated with reduced levels of vitamin B₆, vitamin B₁₂, and folate, making smoking cessation an important goal for patients with known hyperhomocysteinemia.

Antithrombin Deficiency

AT is a protein that inhibits thrombin and certain coagulation factors. It may also play a role in reducing inflammation within the endothelium of blood vessels. AT deficiency can be acquired by four mechanisms: accelerated consumption of AT (as in DIC); decreased synthesis of AT (as in hepatic dysfunction); increased excretion of AT (as in nephrotic syndrome); and medication induced (e.g., estrogens) (Bunn & Bauer, 2017). However, AT deficiency is most often an inherited condition that can lead to venous thrombosis, especially when AT levels are less than 60% of normal. The most common sites of thrombosis are the deep veins in the legs and within the mesentery. Recurrent thrombosis can occur, particularly as patients age. Patients with AT deficiency may exhibit heparin resistance and therefore require greater doses of heparin to achieve adequate anticoagulation. Patients with AT deficiency should encourage their family members to be tested for the condition.

Protein C Deficiency

Protein C is a vitamin K-dependent enzyme synthesized in the liver that, when activated, inhibits coagulation. When protein C levels are low, the risk for

thrombosis increases and thrombosis may occur spontaneously. People with protein C deficiency are often asymptomatic until they reach adulthood; the risk for thrombosis then increases with age. A rare but important complication for patients with protein C deficiency receiving warfarin for anticoagulation is warfarin-induced skin necrosis. This condition is believed to be a result of progressive thrombosis of capillaries in the skin. The degree of necrosis can be quite extensive (Bunn & Bauer, 2017). Prompt recognition of the problem with immediate cessation of the warfarin, along with treatment with vitamin K, heparin, and fresh-frozen plasma infusions are needed to arrest the pathophysiologic process and reverse the effects of warfarin. Treatment with purified protein C concentrate may be necessary.

Protein S Deficiency

Protein S is another natural anticoagulant normally produced by the liver. APC requires protein S to inactivate certain clotting factors. When the level of protein S is deficient, this inactivation process is diminished and the risk of thrombosis increases. As with protein C deficiency, patients with protein S deficiency have a greater risk for recurrent venous thrombosis early in life, including risk for PE (Bunn & Bauer, 2017).

Thromboses frequently occur in axillary, mesenteric, and cerebral veins. Warfarin-induced skin necrosis is also possible with protein S deficiency. A number of conditions may lead to acquired protein S deficiency including pregnancy, DIC, liver disease, nephritic syndrome, HIV infection, and the use of L-asparaginase.

Activated Protein C Resistance and Factor V Leiden Mutation

APC resistance is a common condition that can occur with other hypercoagulable states. APC is an anticoagulant, and resistance to APC increases risk for venous thrombosis. A defect in the factor V gene has been identified in 90% of patients with APC resistance. This factor V Leiden mutation is the most common cause of inherited hypercoagulability in Caucasians; its incidence appears to be much lower in other ethnic groups (Bunn & Bauer, 2017; Middeldorp & Coppens, 2016). The risk of thrombosis significantly increases when factor V Leiden mutation is paired with other risk factors (e.g., increased age, use of oral contraceptives, hyperhomocysteinemia). People who are homozygous for factor V Leiden mutation are at extreme risk for thrombosis and therefore require lifelong anticoagulation. In contrast, those who are heterozygous for the mutation have

a lower risk for developing a thrombus. The duration of anticoagulation is based on the coexistence of other risk factors for thrombus formation.

Antiphospholipid Antibody Syndrome

Antibodies to phospholipids are common causes of thrombophilia; up to 5% of the general population may have this disorder. These antibodies reduce levels of annexin V, a protein that binds to phospholipids and has anticoagulant activity. The most common of the antiphospholipid antibodies are lupus and anticardiolipin antibodies, or an antibody to beta-2 glycoprotein (Rand & Wolgast, 2016). Antiphospholipid antibody syndromes are classified as primary or secondary, with a reaction secondary to a preexisting autoimmune disease, with systemic lupus erythematosus being most frequently implicated. Primary antiphospholipid antibody syndrome is associated with a number of infections including hepatitis C, HIV, syphilis and malaria as well as certain medications (e.g., antibiotics, quinine, hydralazine, procainamide); a genetic predisposition to this syndrome has been postulated but has not been proven. Antiphospholipid antibodies are associated with multiple miscarriages and are strongly associated with stroke (Heuser & Branch, 2019). Most thromboses are venous, but arterial thrombosis is also possible in up to one third of patients with this syndrome. Recurrent thromboses tend to occur in the same fashion, with recurrent venous thrombosis after an initial venous presentation and recurrent arterial thromboses after an initial arterial thrombosis. Thrombi typically occur in large vessels. Therapy varies depending on the type of syndrome (e.g., secondary forms caused by autoimmune disorders may be treated with immunosuppressive therapy), history of prior thrombosis, and location of the thrombus (venous or arterial). Arterial thrombosis is often treated by adding low-dose aspirin to some form of heparin therapy (see later discussion).

Malignancy

Cancers, particularly stomach, pancreatic, lung, and ovarian cancers, are often associated with thrombophilia with significant risk for VTE. VTE contributes to morbidity and mortality of patients with cancer, with a fatal PE being three times more common in patients with cancer than in those without cancer. Patients with cancer have a five- to sevenfold increased risk of developing VTE, and those who develop VTE at diagnosis of cancer or within a year of diagnosis tend to have a significantly worse prognosis than patients with cancer without VTE. A diagnosis of VTE is a serious complication of cancer that adversely affects a patient's quality of life and reduces overall survival.

Anticoagulation may be difficult to manage and thromboses can progress despite adequate doses of anticoagulants. LMWH may be more effective than warfarin in treating this group of patients (Razak, Jones, Bhandari, et al., 2018).

Medical Management

The primary treatment for thrombotic disorders is anticoagulation. However, when to treat and how long to treat with anticoagulant medications is controversial. Anticoagulation therapy is not without risk, with the most significant risk of bleeding. Anticoagulant medications used to treat a variety of thromboses are discussed in Chapter 26.

Nursing Management

Patients with thrombotic disorders should be counseled to avoid activities that lead to circulatory stasis (e.g., immobility, crossed legs). Exercise, especially ambulation, should be performed frequently throughout the day, especially during long trips by car or plane. Anti-embolism stockings may be prescribed and patients often need instruction in how to use them properly. Surgery increases risk for thrombosis significantly.

Medications that alter platelet aggregation, such as low-dose aspirin or clopidogrel, may be prescribed. Some patients require lifelong anticoagulation therapy.

Patients with thrombotic disorders, particularly those with thrombophilia, should be evaluated for concurrent risk factors for thrombosis and should avoid them whenever possible. For example, products containing tobacco and nicotine should be avoided, blood pressure should be controlled, and alcohol consumption limited. In some instances, younger patients with thrombophilia may not need prophylactic anticoagulation, but when concomitant risk factors (e.g., pregnancy), increasing age, or subsequent thrombotic events are present, prophylactic or long-term anticoagulation therapy may be needed. Being able to provide the health care provider with an accurate health history can be extremely useful and help in guiding the selection of the appropriate interventions. Patients need to be aware of risk factors for thrombosis and how they can be reduced or eliminated, such as avoiding tobacco, using alternative forms of contraception, avoiding immobility, and maintaining a healthy weight. Patients with hereditary disorders should encourage their siblings and children to be tested for the disorder.

When a patient with a thrombotic disorder is hospitalized, frequent assessment should be performed to promote early recognition of signs and symptoms of thrombus formation, particularly in the legs (DVT) and lungs (PE). Ambulation or range-of-motion exercises as well as anti-embolism

stockings or sequential compression devices are used to decrease venous stasis.

CRITICAL THINKING EXERCISES

1 pq A 72-year-old man presents to the emergency department complaining of acute shortness of breath and chest pain. He reports increasing fatigue, exertional dyspnea, dull abdominal pain, and weight loss over the last few months. His CBC reveals a normal WBC count and platelet count; however, the hemoglobin is 7.2 mg/dL and the hematocrit is 22.3%. The MCV is reduced. Iron deficiency anemia is suspected. What are your priority interventions targeted at relieving the patient's symptoms? What other medical interventions do you anticipate might be prescribed? What additional laboratory tests do you anticipate for this patient?

2 ipc A 23-year-old female patient with sickle cell disease tells you during a routine office visit that she would like to become pregnant. Her condition has been well controlled with hydroxyurea. She takes ibuprofen on a regular basis for chronic pain. What additional information should you collect in the patient history? What challenges do you anticipate in caring for this patient? What other members of the interdisciplinary team do you think should be consulted to be part of the patient's prenatal care?

3 ebp Your 44-year-old female neighbor tells you that her brother has been "nagging her" to get tested for hemochromatosis since he was diagnosed with this disease a few months ago. Her brother has periodic therapeutic phlebotomies to treat his disease, and she feels her lifestyle is too busy to support these types of treatments. She tells you that she "feels fine" and wonders how likely it is that she has hemochromatosis, and if she does, whether treatment would be needed. What are the risks for hemochromatosis? If your neighbor does have hemochromatosis, what is the strength of the evidence for best treatment options for her?

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*Asterisk indicates nursing research.

**Double asterisk indicates classic reference.

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Resources

- American Association of Blood Banks (AABB), www.aabb.org
 American Hemochromatosis Society, www.americanhs.org
 American Red Cross, www.redcross.org
 American Society for Transplantation and Cellular Therapy, www.asbmt.org/home
 Aplastic Anemia and MDS International Foundation, www.aamds.org
 APS Foundation of America (antiphospholipid syndrome), www.apsfa.org
 G6PD Deficiency, www.g6pd.org
 National Heart, Lung, and Blood Institute, www.nhlbi.nih.gov

National Marrow Donor Program, www.bethematch.org

Platelet Disorder Support Association (PDSA), www.pdsa.org

Sickle Cell Disease Association of America (SCDAA), www.sicklecelldisease.org

30 Management of Patients with Hematologic Neoplasms

LEARNING OUTCOMES

On completion of this chapter, the learner will be able to:

1. Compare and contrast the different types of leukemias in terms of their incidence, physiologic alterations, clinical manifestations, complications, and medical and nursing management.
2. Use the nursing process as a framework for care of the patient with acute leukemia.
3. Explain the differences between the various myeloproliferative disorders in terms of their incidence, physiologic alterations, clinical manifestations, complications, and medical and nursing management.
4. Compare and contrast Hodgkin and non-Hodgkin lymphomas in terms of their incidence, physiologic alterations, clinical manifestations, complications, and medical and nursing management.
5. Discuss medical and nursing care of the patient with multiple myeloma.

NURSING CONCEPTS

Cellular Regulation
Clotting

GLOSSARY

absolute neutrophil count (ANC): a calculation of the number of circulating neutrophils, derived from the total white blood cells (WBCs) and the percentage of neutrophils counted in a microscope's visual field

angiogenesis: formation of new blood vessels

apoptosis: programmed cell death

blast cells: immature leukocytes

clone: proliferation from same cell of origin so that descendent cells are identical to the cell of origin

cytokines: proteins produced by leukocytes that are vital to regulation of hematopoiesis, apoptosis, and immune responses; also called biochemical or inflammatory mediators

erythrocyte sedimentation rate (ESR): laboratory test that measures the rate of settling of red blood cells (RBCs); elevation is indicative of inflammation; also called the sed rate

erythromelalgia: a burning, painful sensation and erythema in the fingers or toes

hematopoiesis: complex process of the formation and maturation of blood cells

indolent: when in reference to a neoplasm refers to a slow-growing cancer that often remains localized or causes few symptoms

leukemia: uncontrolled proliferation of WBCs, often immature

lymphadenopathy: enlargement of a lymph node or lymph nodes

lymphoid: pertaining to lymphocytes

myeloid: pertaining to nonlymphoid blood cells that differentiate into RBCs, platelets, macrophages, mast cells, and various WBCs

neutropenia: lower-than-normal number of neutrophils

pancytopenia: abnormal decrease in WBCs, RBCs, and platelets

petechiae: tiny capillary hemorrhages

phagocytosis: process of cellular ingestion and digestion of foreign bodies

reticulocytes: slightly immature RBCs, usually only 1% of total circulating RBCs

splenomegaly: enlargement of the spleen

stem cell: primitive cell, capable of self-replication and differentiation into myeloid or lymphoid stem cell

thrombocythemia: higher-than-normal platelet count that occurs without a known cause

thrombocytopenia: lower-than-normal platelet count

thrombocytosis: higher-than-normal platelet count that results because of a disease or disorder

Hematopoiesis is the process by which all blood cells develop, differentiate, and mature. This process starts with the hematopoietic stem cells (HSC) in the bone marrow. As these **stem cells** divide, they are delineated into one of two cell pathways, to become lymphoid or myeloid progenitor cells. The myeloid stem cells then differentiate into red blood cells, white blood cells (WBCs), and platelets, while the lymphoid stem cells differentiate into B and T lymphocytes. Normally, the differentiation of these progenitor cells is regulated according to the body's need. However, when the mechanisms that control the production of these cells is disrupted or impaired, the cells can proliferate uncontrollably, leading to the development of a hematologic malignancy. The pathophysiologic processes for the development of hematologic malignancies are complex. Understanding these processes and the rationale for treatments is important so that nurses may appropriately assess, monitor, educate, and intervene with patients with hematologic neoplasms.

Hematopoietic malignancies are classified by the specific blood cells involved. **Leukemia** is a neoplastic proliferation of a particular cell type (granulocytes, lymphocytes, or infrequently erythrocytes or megakaryocytes). This proliferation leads to an overcrowding in the bone marrow resulting in impaired hematopoietic cell function and can affect other organs in the body (i.e., lymph nodes, skin, and spleen) (Leukemia & Lymphoma Society, 2018b). The defect originates in the HSC, the myeloid, or the lymphoid stem cell. Lymphomas are neoplasms of lymphoid tissue, usually derived from B lymphocytes. Multiple myeloma is a malignancy of the most mature form of B lymphocyte—the plasma cell.

CLONAL STEM CELL DISORDERS

A key feature of hematologic malignancies is the increased proliferation of blood cells from an abnormal single HSC, known as clonal hematopoiesis. Despite this increase in proliferation, the clonal HSCs continue to differentiate, leading to increased myeloid cells, erythroid cells, and platelets in the peripheral blood as well as hyperplasia in the bone marrow (Leukemia & Lymphoma Society, 2018b). Figure 30-1 illustrates how hematopoietic malignancies develop and whether they are derived from the myeloid or lymphoid stem cells (Leukemia & Lymphoma Society, 2019f).

LEUKEMIA

The term *leukocytosis* refers to an increase of leukocytes (WBCs) in the circulation. Typically, only one specific cell type is increased. Because the proportions of several types of leukocytes (e.g., eosinophils, basophils, monocytes) are small, an increase in other types can be great enough to elevate the total leukocyte count, particularly the neutrophils or lymphocytes. Although leukocytosis can be a normal response to increased need (e.g., in acute infection), the elevation in leukocytes should decrease as the physiologic need decreases. A prolonged or progressively increasing elevation in leukocytes is abnormal and should be evaluated. A significant cause of persistent leukocytosis is a hematologic malignancy (i.e., leukemia).

The common feature of the leukemias is an unregulated proliferation of leukocytes in the bone marrow. In acute forms (or late stages of chronic forms), the proliferation of leukemic cells leaves little room for normal cell production. There can also be a proliferation of cells in the liver and spleen (extramedullary hematopoiesis). With acute forms, there can be infiltration of leukemic cells in other organs, such as the meninges, lymph nodes, gums, and skin. The cause of leukemia is not fully known, but exposure to radiation or chemicals, certain genetic disorders, and viral infections are known to be risk factors for certain types of leukemia. Bone marrow damage from pelvic radiation or certain types of chemotherapy drugs can cause acute leukemia, typically occurring years after treatment for another malignancy (Leukemia & Lymphoma Society, 2018b).

The leukemias are commonly classified according to the stem cell line involved, either **lymphoid** (referring to stem cells that produce lymphocytes) or **myeloid** (referring to stem cells that produce nonlymphoid blood cells). They are also classified as either acute or chronic, based on the time it takes for symptoms to evolve and the phase of cell development that is halted (i.e., with few leukocytes differentiating beyond that phase).

In acute leukemia, the onset of symptoms is abrupt, often occurring within a few weeks. Leukocyte development is halted at the blast phase, and thus most leukocytes are undifferentiated cells or blasts. Acute leukemia can progress rapidly, with death occurring within weeks to months without aggressive treatment.

In chronic leukemia, symptoms evolve over a period of months to years, and the majority of leukocytes produced are mature. Chronic leukemia progresses more slowly; the disease trajectory can extend for years.

Acute Myeloid Leukemia

Acute myeloid leukemia (AML) originates due to a series of genetic mutations in the myeloid HSC leading to clonal development of abnormal blast cells (National Comprehensive Cancer Network [NCCN], 2019a). As these **blast**

cells (i.e., immature leukocytes) continue to proliferate, they crowd out normal bone marrow production resulting in anemia, **thrombocytopenia** (i.e., low platelet count), and either low or elevated WBC counts (rarely, the WBC may be within normal range). There is also impaired development of all myeloid cells: monocytes, granulocytes (i.e., neutrophils, basophils, eosinophils), erythrocytes, and platelets.

AML is the most common form of leukemia, as well as most common cause of death from all leukemias. AML can affect any age group. However, the incidence of this disease increases with age, with the median age at time of diagnosis being about 68 years (Leukemia & Lymphoma Society, 2019a). On an annual basis, AML accounts for approximately 1% of all cancer-related deaths (NCCN, 2019a).

The exact cause of AML is unclear, but there are several known risk factors. In addition to increasing age, males have a higher incidence than females. Other risks include having been exposed to chemicals such as benzene or pesticides or exposed to ionizing radiation; and a history of prior treatment with chemotherapeutic drugs, such as alkylating agents or topoisomerase inhibitors, tobacco smoking, other blood disorders (e.g., myeloproliferative diseases), and several genetic disorders (e.g., Down syndrome, Trisomy 8, or Fanconi anemia) (Leukemia & Lymphoma Society, 2019a).

Blood cancers can develop in many different places within normal blood cell formation.

The type of blood cancer that results has to do with where normal cell development is blocked. This picture shows the cell type where different blood cancers arise.

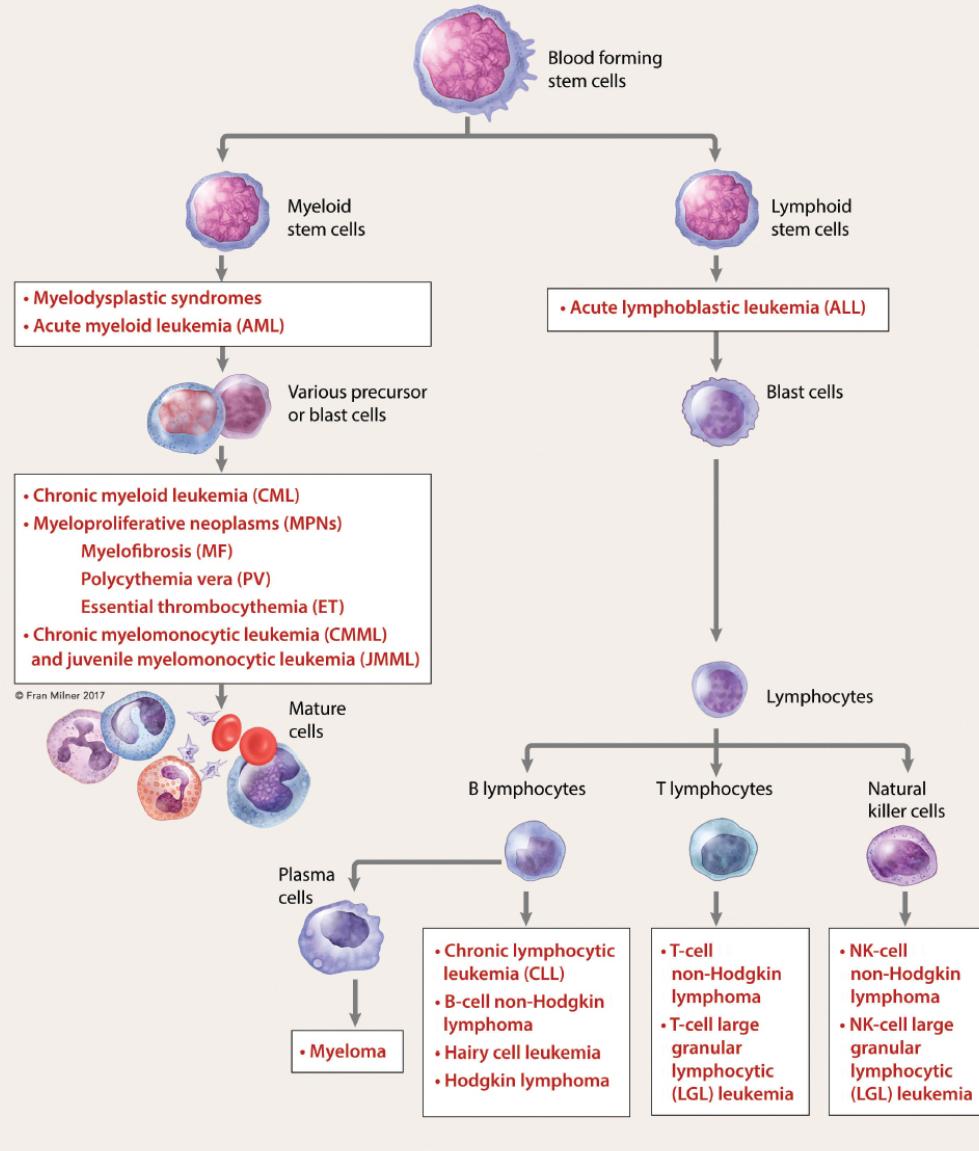


Figure 30-1 • The development of myeloid and lymphoid neoplasms. Hematologic malignancies can occur when normal cell development is inhibited. © Fran Milner 2017.

The prognosis and survival rates are highly variable. Factors influencing a more positive outcome are younger age at diagnosis, more favorable cytogenetic alterations (which are strongly associated with younger age), and few concurrent (or mild) health problems. In contrast, patients with significant comorbidities, of older age, with cytogenetic features deemed to be adverse, or who are frail, are more likely to have a poor prognosis. AML evolving from a

preexisting clonal myeloid disease or from prior cytotoxic therapy for another malignancy or immune disease is associated with a poorer prognosis and less favorable outcomes (NCCN, 2019a).



Figure 30-2 • Gingival infiltration of leukemic cells in a patient with acute myeloid leukemia. Reprinted with permission from Greer, J. P., Foerster, J., Rodgers, G. M., et al. (2009). *Wintrobe's clinical hematology* (12th ed., Fig. 72.8, p. 1680). Philadelphia, PA: Lippincott Williams & Wilkins.

Clinical Manifestations

AML often presents, initially, as nonspecific complaints that can abruptly occur or gradually worsen over time. The signs and symptoms result from inadequate production of normal blood cells, especially as the leukemic cells increasingly crowd out the bone marrow. Symptoms due to **neutropenia** (low neutrophil count) include fever and infection. Symptoms related to anemia include pallor, fatigue, weakness, dyspnea on exertion, and dizziness. Symptoms reflective of thrombocytopenia include ecchymoses (bruises), **petechiae** (pinpoint red or purple hemorrhagic spots on the skin), epistaxis (nosebleeds), and gingival bleeding. The proliferation of leukemic cells within organs leads to a variety of additional symptoms: pain from an enlarged liver or spleen, hyperplasia of the gums, and bone pain from expansion of marrow (see Fig. 30-2). Petechiae or ecchymoses are common on the skin (see Chapter 29, Fig. 29-4); occasionally, leukemic infiltrates are also seen (see Fig. 30-3). Leukemic cells can also infiltrate the gingiva or synovial spaces of joints. **Lymphadenopathy** (enlargement of lymph nodes) or **splenomegaly**

(enlargement of the spleen) is rare. Fevers may occur and are not always due to infection.

Assessment and Diagnostic Findings

To confirm the diagnosis of AML, laboratory studies need to be performed. The complete blood count (CBC) commonly shows a decrease in both erythrocytes and platelets. Although the total leukocyte count can be low, normal, or high, the percentage of normal cells is usually vastly decreased. A bone marrow analysis shows an excess (more than 20%) of blast cells (Arber, Orazi, Hasserjian, et al., 2016); this is the hallmark of the diagnosis.

AML can be further classified into seven different subgroups, based on cytogenetics, histology, and morphology of the blasts, as well as the presence of genetic mutations. The actual prognosis varies somewhat between subgroups and with the extent of cytogenetic abnormalities and genetic mutations, yet the clinical course and treatment differ substantially with only one subtype. That is, patients with the specific AML subtype acute promyelocytic leukemia (APL, or AML-M3) have higher potential for fatal coagulopathies; however, the potential to cure this form of AML is high (NCCN, 2019a).



Figure 30-3 • Leukemia cutis. Infiltration of leukemic cells in skin on extensor surface of forearms. Reproduced with permission from Stedman's Medical Dictionary. Copyright 2008 Lippincott Williams & Wilkins.

Medical Management

The overall objective of treatment for AML is to achieve complete remission of the disease, in which there is no residual leukemic cells in the bone marrow or peripheral blood. To obtain remission, chemotherapy treatment is administered in two parts: *induction* and *consolidation*. The choice of agents for induction therapy is based on the patient's age, physical status, and history of prior antineoplastic treatment. Induction therapy typically involves high doses of cytarabine and either daunorubicin, idarubicin, or mitoxantrone; etoposide is occasionally added to the regimen. Older patients (especially those older than 70 years) or those unable to tolerate standard therapy (in poor health) may receive lower-intensity therapy (using hypomethylating agents, low doses of cytarabine, or hydroxyurea), which may extend survival without a significant increase in toxicity beyond that of the underlying disease (NCCN, 2019a).

During induction therapy, chemotherapy not only destroys leukemic cells, but also healthy cells, requiring patients to be hospitalized for several weeks (typically 4 to 6 weeks) due to severe and potentially life-threatening side effects, such as neutropenia. For some patients, an **absolute neutrophil count (ANC)**; a calculation of the number of circulating neutrophils, derived from the total WBCs and the percentage of neutrophils counted in a microscope's visual field) of zero is not uncommon (see [Chapter 12](#) for formula used to calculate the ANC). Anemia, and severe thrombocytopenia (a platelet count of less than 5000/mm³), is also common. During this time, the patient is typically very ill, with bacterial, fungal, and occasionally viral infections; bleeding; and severe mucositis, which cause pain, diarrhea, and an inability to maintain adequate nutrition. Management consists of administering blood products (packed red blood cells [PRBCs] and platelets) and promptly treating infections. The use of granulocytic growth factors, either granulocyte colony-stimulating factor (G-CSF; filgrastim) or granulocyte-macrophage colony-stimulating factor (GM-CSF; sargramostim), may be used during the induction phase only for patients who have a life-threatening infection in order to shorten the neutropenic period (NCCN, 2019a). Patients are discharged to home once blood counts recover and the risk of infection are diminished.

When the patient has recovered from the induction therapy (i.e., the neutrophil and platelet counts have returned to normal and any infection has resolved), consolidation therapy is given to eliminate any residual leukemic cells that are not clinically detectable and to reduce the chance for recurrence of leukemia. Multiple treatment cycles of various agents are used, usually containing some form of cytarabine. Frequently, the patient receives one cycle of treatment that is almost the same as, if not identical to, the induction treatment but at lower dosages.

Allogeneic stem cell transplant is the most common form of hematopoietic stem cell transplant (HSCT) used in the treatment of AML (see [Chapter 12](#) for discussion of HSCT). HSCT is routinely done following induction and consolidation therapy. However, in certain instances (e.g., aggressive disease), HSCT may be performed following induction. The process of HSCT requires that patients begin by receiving high-dose, aggressive chemotherapy, sometimes in tandem with radiation therapy, to destroy the hematopoietic functioning in the bone marrow and to kill any residual leukemic cells. This process is called *conditioning therapy*. Then, the patient is given human leukocyte antigen (HLA-matched) donor stems cells via intravenous (IV) infusion to reestablish bone marrow functioning and to create a new immune system (Leukemia & Lymphoma Society, 2019a). The most appropriate use and timing of HSCT remain unclear. Patients with a poorer prognosis may benefit from early HSCT; those with a good prognosis may not ever require HSCT.

While most patients with AML achieve remission after these treatments, some patients have refractory or relapsed disease, even after aggressive therapy. Approximately 10% to 40% of patients do not obtain a complete remission following induction therapy (Leukemia & Lymphoma Society, 2019a). There are several other treatment options. The induction regimen might be repeated until remission or relapse occurs. Other approaches may include treatment with enasidenib, a cytarabine-based regimen, along with other agents (e.g., cladribine, fludarabine, mitoxantrone, etoposide); palliative care; or use of a hypomethylating agent (e.g., azacitidine or decitabine).

Supportive care may be the best treatment option to consider if the patient has significant comorbidity, such as extremely poor cardiac, pulmonary, renal, or hepatic function; is older and frail; or both. In such cases, the aggressive antileukemia therapy options previously described are not indicated; occasionally, hydroxyurea or hypomethylating agents such as azacitidine may be used briefly to control the increase of blast cells. The patient's symptoms may be mitigated with antimicrobial therapy and transfusions as needed. This treatment approach provides the patient with some additional time outside the hospital; however, death frequently occurs within months, typically from infection or bleeding (refer to [Chapter 13](#) for a discussion of palliative and end-of-life care).

Complications

Complications of AML include bleeding and infection, which are the major causes of death. The risk of bleeding correlates with the level and duration of platelet deficiency. The low platelet count can cause ecchymoses and petechiae. Major hemorrhages also may develop when the platelet count drops to less than $10,000/\text{mm}^3$. The most common bleeding sources include gastrointestinal (GI), pulmonary, vaginal, and intracranial. For undetermined reasons, fever and infection also increase the likelihood of bleeding. Disseminated intravascular coagulation (DIC) is common, particularly in patients with the APL subtype (NCCN, 2019a) (see [Chapter 29](#) for further discussion of DIC). A very high WBC count (greater than $100,000/\text{mm}^3$) can cause stasis within the cerebral or pulmonary circulation.

Because of the lack of mature and normal granulocytes that help fight infection, patients with leukemia are prone to infection. The likelihood of infection increases with the degree and duration of neutropenia; neutrophil counts that persist at less than $100/\text{mm}^3$ dramatically increase the risk of systemic infections. While bacterial infections commonly occur in patients with AML who are neutropenic, the risk of developing a fungal infection also increases. Fungal infections remain difficult to treat; in many cases, patients are given antifungal agents prophylactically. Granulocytic growth factors, either granulocyte colony-stimulating factor (G-CSF; filgrastim) or

granulocyte-macrophage colony-stimulating factor (GM-CSF) are used to stimulate the bone marrow to produce leukocytes, thereby shortening the period of neutropenia. These growth factors are not recommended for use in patients with APL, as differentiation syndrome (formerly known as retinoic acid syndrome), a life-threatening complication with symptoms such as unexplained fever, weight gain, hypotension, respiratory distress, and acute kidney injury can occur (NCCN, 2019a).

Massive leukemic cell destruction from chemotherapy results in the release of intracellular electrolytes and fluids into the systemic circulation. Increases in uric acid levels, potassium, and phosphate are seen; this process is referred to as tumor lysis syndrome (see [Chapter 12](#) for further discussion of tumor lysis syndrome). The increased uric acid and phosphorus levels make the patient vulnerable to renal stone formation and renal colic, which can progress to acute kidney injury. Hyperkalemia and hypocalcemia can lead to cardiac arrhythmias; hypotension; neuromuscular effects such as muscle cramps, weakness, and spasm/tetany; and confusion; and seizures may also develop (Olsen, LeFebvre, & Brassil, 2019). Patients require a high fluid intake, and prophylaxis with allopurinol or rasburicase to prevent crystallization of uric acid and subsequent stone formation.

GI problems may result from the infiltration of abnormal leukocytes into the abdominal organs and from the toxicity of the chemotherapeutic agents. Anorexia, nausea, vomiting, diarrhea, and severe mucositis are common. Because of the profound myelosuppressive effects of chemotherapy, significant neutropenia and thrombocytopenia typically result in serious infection and increased risk of bleeding.

Nursing Management

Nursing management of the patient with acute leukemia, including AML, is presented at the end of the discussion of leukemia in this chapter.

Chronic Myeloid Leukemia

Chronic myeloid leukemia (CML) arises from a mutation in the myeloid stem cell. Normal myeloid cells continue to be produced, but there is a pathologic increase in the production of forms of blast cells. Therefore, a wide spectrum of cell types exists within the blood, from blast forms to mature neutrophils. Because there is an uncontrolled proliferation of cells, the marrow expands into the cavities of long bones, such as the femur, and cells are also formed in the liver and spleen (extramedullary hematopoiesis), resulting in enlargement of these organs that is sometimes painful.

CML results from a chromosomal translocation, where a section of deoxyribonucleic acid (DNA) is shifted from chromosome 22 to chromosome 9, forming what is known as a “fusion gene” that is abnormal. The specific fused gene found in all patients with CML is the *BCR-ABL* gene, which occurs when the *BCR* gene from chromosome 22 switches places with the *ABL* gene from chromosome 9 (Leukemia & Lymphoma Society, 2019b). Normally, the *ABL* gene signals the cells when to make tyrosine kinase; however, the abnormal *BCR-ABL* gene (known as the Philadelphia chromosome) signals cells to produce too many leukocytes and is responsible for converting normal cells into leukemic cells.

CML accounts for 15% of all new cases of leukemia (NCCN, 2019b). The average age of a patient at time of diagnosis is 67 years, but CML can occur at any age. Risk factors include increasing age, being male, having a history of smoking, and being exposed to high doses of radiation (e.g., atomic bomb survivors).

Clinical Manifestations

The clinical picture of CML varies, based upon phase of disease. There are three stages in CML that include chronic, accelerated, and blast crisis (Leukemia & Lymphoma Society, 2019b). During the chronic phase, patients have few symptoms, leukocytosis is detected by a CBC performed for some other reason, and complications from the disease itself are rare.

The accelerated phase can be insidious or rapid; it marks the process of evolution (or transformation) to the acute form of leukemia (blast crisis). In the accelerated phase of disease, blood counts begin to worsen, new chromosomal changes may be seen on analysis, and symptoms consistent with leukemia may start to appear, such as fatigue, anemia, splenomegaly, or dyspnea (NCCN, 2019b). The patient may complain of bone pain and may report fevers (without any obvious sign of infection) and weight loss.

Blast crisis or blast phase of CML is the most advanced phase. Patients in this phase exhibit signs and symptoms that are more like AML than a chronic disease. Some patients present with leukocytosis, with the WBC count exceeding $100,000/\text{mm}^3$ (NCCN, 2019b). Patients with extremely high leukocyte counts may be dyspneic or slightly confused because of decreased perfusion to the lungs and brain from leukostasis (the excessive volume of leukocytes inhibits blood flow through the capillaries). The patient may have an enlarged, tender spleen, and occasionally the liver may also be enlarged and tender. Some patients have insidious symptoms, such as malaise, anorexia, and weight loss. Lymphadenopathy is uncommon, but if present, indicates late disease and a poor prognosis (NCCN, 2019b).

Medical Management

The goal of treatment for CML is to control the disease, either by obtaining remission or by keeping the patient in the chronic phase for as long as possible. CML is not considered to be curable among older adults despite advances in understanding the pathophysiology of the disease and the advent of new agents. However, the use of tyrosine kinase inhibitors (TKIs) has significantly improved treatment and long-term survival for patients with CML (Leukemia & Lymphoma Society, 2019b). Medical management is based upon the patient's age, general health, calculation of risk-score (based upon stage of disease and prognosis), and phase of disease.

TKIs work by blocking the signals within the leukemic cells that express the *BCR-ABL* protein. This inhibition prevents a series of chemical reactions that cause the cells to grow and divide, thus inducing complete remission at the cellular level. The TKI imatinib mesylate is considered to be standard of care for patients with CML. Newer, alternative TKIs approved for first-line (primary) therapy for patients in the chronic phase of CML include dasatinib or nilotinib (NCCN, 2019b). Each of these TKIs has a different toxicity profile. For example, periorbital edema is common with long-term use of imatinib; dasatinib is very myelosuppressive, and its use carries a significant risk for pleural effusion and for causing a prolonged QT interval; and nilotinib has cardiotoxic effects. Other TKIs approved for second-line therapy (when patients do not respond satisfactorily to the first-line agents) are bosutinib and ponatinib. All TKIs are metabolized by the cytochrome P450 pathway, which means that drug-to-drug interactions are common. Drugs that may decrease the effects of the TKI are corticosteroids, antiseizure medications, antacids, and St. John's wort. Drugs that may increase the effects of the TKI include grapefruit juice, certain antibiotics (e.g., clarithromycin), and azole antifungals (e.g., clotrimazole, ketoconazole).

CML is a disease that can potentially be cured with allogeneic HSCT in otherwise healthy patients who are younger than 65 years. However, with the development of TKIs, the timing of transplant has come into question. Approximately 90% of patients who receive allogeneic HSCT during the chronic phase of CML are disease free for 5 years or more (Leukemia & Lymphoma Society, 2019b).

In the acute form of CML (blast crisis), treatment may resemble induction therapy for acute leukemia, using the same medications as for AML or acute lymphocytic leukemia (ALL; see later discussion). Patients whose disease evolves into a "lymphoid" blast crisis are more likely to be able to reenter a chronic phase after induction therapy. For those whose disease evolves into AML, therapy has been largely ineffective in achieving a second chronic phase. Life-threatening infections and bleeding occur frequently in this phase.

Nursing Management

Most TKIs are oral agents; therefore, their effectiveness is dependent upon the patient's ability and motivation to adhere to the prescribed treatment regimen. These drugs may cause side effects that the patient may find difficult to manage, such as fatigue, asthenia (weakness), pruritus (itching), headache, skin rash, and oropharyngeal pain. A study conducted in Germany of patients with CML treated on an outpatient basis revealed an adherence rate of 51% to oral TKIs (Hefner, Csef, & Kunzmann, 2017), which is consistent with prior studies. In this study, forgetting to take the drug or delays of 2 or more hours from the prescribed time were the most common reported reasons for decreased adherence. Another study examining challenges to oral agent adherence conducted by Gborogen and Polek (2018) reported that over half of nurse participants reported nonadherence to oral agents among their patients. Reasons for nonadherence ranged from patient forgetfulness to perceptions of inadequate support. It is extremely important for the nurse to educate the patient about the medication regimen, how to manage side effects, drug interactions, and safe handling (Olsen et al., 2019) (see Nursing Interventions in [Table 30-1](#)). The nurse should also monitor the patient for adverse signs and symptoms of therapy, such as decreased urinary output, changes in the electrocardiogram (ECG; TKIs can cause arrhythmias and prolonged QT intervals), and myelosuppression (e.g., fevers, chills, changes in the CBC).

Acute Lymphocytic Leukemia

ALL results from an uncontrolled proliferation of immature cells (lymphoblasts) derived from the lymphoid stem cell. The cell of origin is the precursor to the B lymphocyte in approximately 75% of ALL cases; T-lymphocyte ALL occurs in approximately 25% of cases. The *BCR-ABL* translocation (see previous discussion in CML section) is found in 20% of ALL blast cells (NCCN, 2019c). ALL can occur at any age, but 75% to 80% of all cases are found in children, with the median age at diagnosis being 15 years (NCCN, 2019c). Boys are affected more often than girls; the peak incidence is 4 years of age. After 15 years of age, it is relatively uncommon, until age 45 when the incidence again rises (Leukemia & Lymphoma Society, 2018a). For those over age 45, risk factors for ALL include older age (especially over 70 years), prior exposure to chemotherapy or radiation therapy, having certain genetic conditions (e.g., especially Down syndrome; also neurofibromatosis, Klinefelter syndrome, and Fanconi anemia) (NCCN, 2019c). In the last several decades, advances in understanding the pathophysiology and molecular genetics, as well as the incorporation of targeted therapy and HSCT, have resulted in improved cure rates and overall longer survival in patients with ALL.

Clinical Manifestations

For some patients with ALL, the clinical manifestations may be nonspecific while others have no symptoms initially. The disease is commonly found incidentally with routine laboratory studies or physical exam for another condition. At the time of diagnosis, the leukocyte counts may be either higher or lower than normal, with a high proportion of immature lymphoblasts. Immature lymphocytes proliferate in the marrow and impede the development of normal myeloid cells. As a result, normal hematopoiesis is inhibited, resulting in reduced numbers of granulocytes, erythrocytes, and platelets. Manifestations of leukemic cell infiltration into other organs are more common with ALL than with other forms of leukemia and include pain from an enlarged liver or spleen as well as bone pain. The central nervous system (CNS) is frequently a site for leukemic cells; thus, patients may exhibit cranial nerve palsies or headache and vomiting because of meningeal involvement. Other extranodal sites include the testes and breasts.

TABLE 30-1

Risk Factors Associated with Lower Adherence to

Oral Therapy for Chronic Myeloid Leukemia (CML)

Risk Factor Category	Risk Factor	Nursing Interventions
Patient Characteristics	Lower education level (below high school)	
	Higher self-report of functional status	
	Low self-efficacy regarding medication administration ^a	Explore with patient perceived barriers related to medication administration
	Taking medication independent of meals ^a	Develop medication administration schedule with patient; use timer/watch alarm to alert patient when to take medication
	Lack of knowledge regarding disease and treatment ^a	Provide relevant information in format understandable to patient
Social Characteristics	Living alone ^a	Evaluate need for phone follow-up, initiation of home care
	Low levels of social support	
	Low socioeconomic status	
Disease and Treatment Characteristics	Farther time from diagnosis	Monitor patient closely for side effects
	Higher rates of treatment-related side effects ^a	Monitor patient closely for complications
	Higher number of cancer-related complications ^a	Provide patient with information on clinical trial enrollment eligibility as advisable
	Not participating in a clinical trial ^a	

^aIndicates risk factor amenable to nursing intervention.

Adapted from Gborogen, R., & Polek, C. (2018). Oral agents: Challenges with self-administered medication adherence in clinical trials. *Clinical Journal of Oncology Nursing*, 22(3), 333–339; Olsen, M., LeFebvre, K., & Brassil, K. (2019). *Chemotherapy and immunotherapy guidelines and recommendations for practice*. Pittsburgh, PA; Oncology Nursing Society.

Medical Management

The goal of treatment is to obtain remission without excess toxicity and with a rapid hematologic recovery so that additional therapy can be given if needed. Because of the heterogeneity of the disease, treatment plans are based on genetic markers of the disease as well as risk factors of the patient, primarily age. Similar to treatment for AML, treatment for ALL can be grouped into induction, consolidation, and maintenance phases. Because ALL frequently invades the CNS, preventive intrathecal chemotherapy or, less frequently, cranial irradiation, are also a key part of the treatment plan (NCCN, 2019c).

Treatment protocols for ALL tend to be complex, using a wide variety of chemotherapeutic agents and complicated administration schedules. The expected outcome of treatment is complete remission. Despite its complexity, treatment can be provided in the outpatient setting in some circumstances until severe complications develop. TKIs (e.g., imatinib) are effective in patients with Philadelphia chromosome-positive ALL; these drugs can be used alone or in combination with conventional chemotherapy (Leukemia & Lymphoma Society, 2018a).

Lymphoid blast cells are typically very sensitive to corticosteroids and to vinca alkaloids; therefore, these medications are an integral part of the initial induction therapy (NCCN, 2019c). The corticosteroid dexamethasone is preferred to prednisone, as it is more toxic to lymphoid cells and has better CNS penetration. Typically, an anthracycline is included, sometimes with asparaginase. Once a patient is in remission, special testing (immunophenotyping, immunoglobulin gene rearrangements, T-cell receptor genes, molecular testing) is done to look for residual leukemic cells; these tests can detect as few as a single ALL cell among 10,000 to 100,000 normal cells. This minimal residual disease testing is useful as a prognostic indicator. Based on these results and the rapidity in which remission is achieved, a consolidation regimen ensues, using different combinations and dosages of the drugs used in induction therapy; the goal of consolidation is to improve outcomes in those patients at high risk for relapse. For patients with relapsed or refractory B-cell precursor ALL, agents such as blinatumomab or inotuzumab ozogamicin have been found to be effective (NCCN, 2019c).

Patients with ALL can experience some unique adverse effects from treatment. The use of corticosteroids to treat ALL increases the patient's susceptibility to infection; viral infections are common. Avascular necrosis can occur in patients treated with corticosteroid-based chemotherapy, as well as with transplantation. Patients treated with asparaginase are at increased risk for thrombosis. Hepatic toxicity is also common and may necessitate cessation of supportive drugs, such as proton pump inhibitors and certain antibacterial and antifungal drugs.

Allogeneic HSCT may be considered during initial remission if disease features and testing suggest the risk of relapse is high (NCCN, 2019c; Leukemia & Lymphoma Society, 2018a). The development of chimeric

antigen receptor (CAR) T cells has significantly improved treatment outcomes and overall survival in patients with ALL (NCCN, 2019c). CAR-T therapy utilizes the patient's own immune system to fight disease; the patient's own T cells are collected, modified, and reinfused back into the patient. Treatment with CAR-T can serve as a bridge prior to transplant and has qualified patients for HSCT who were formerly ineligible. In the context of average-risk disease, HSCT may be postponed until the time of relapse, should it occur. HSCT can improve long-term disease-free survival; however, this potential benefit must be weighed with the risks associated with the procedure, including death and long-term morbid complications.

Nursing Management

Nursing management of the patient with acute leukemia, including ALL, is presented at the end of the leukemia section in this chapter.

Chronic Lymphocytic Leukemia

Chronic lymphocytic leukemia (CLL) is a common malignancy of older adults, and the most prevalent type of adult leukemia in the Western world (NCCN, 2019d). The average age at diagnosis is 71 years (Leukemia & Lymphoma Society, 2019c). CLL is rarely seen in Native Americans and infrequently among people of Asian descent. Unlike other forms of leukemia, a strong familial predisposition exists with CLL; the disease can occur in 10% of those with a first- or second-degree relative with the same diagnosis. Veterans of the Vietnam War who were exposed to Agent Orange may be at risk for developing this disease (see the following section), but there is no definitive link to other pesticides or exposure to chemicals. While many patients will have a normal life expectancy, others will have a very short life expectancy due to the aggressive nature of the disease.



Veterans Considerations

Agent Orange was an herbicide used as a defoliant by the U.S. military in Vietnam from 1962 until 1975, when American involvement in the Vietnam War ended. Since that time, dioxin, a chemical used in Agent Orange, has been found to be carcinogenic. In particular, there is sufficient evidence that CLL, Hodgkin lymphoma, non-Hodgkin lymphomas (NHLs), and monoclonal gammopathy of undetermined significance (MGUS) are associated with Agent Orange exposure, while there is also evidence that suggests that Agent Orange exposure may be linked to multiple myeloma (American Cancer Society [ACS], 2020a). Approximately 3 million American veterans could have been

exposed to the harmful effects of Agent Orange related to their military service in Vietnam. The U.S. Department of Veteran Affairs (VA) has administered an *Agent Orange Registry* since 1978. Qualified veterans who enroll in the registry are eligible for health care benefits and consultations. Those veterans who develop cancers secondary to exposure to Agent Orange may be eligible for VA disability benefits (see Resources for additional information for veterans exposed to Agent Orange) (ACS, 2020a).

Pathophysiology

CLL is typically derived from a malignant clone of B lymphocytes. A **clone** proliferates from a cell of origin so that descendent cells are identical to the cell of origin. In contrast to the acute forms of leukemia, most leukemic cells in CLL are fully mature. One possible mechanism that explains this oncogenesis is that these cells can escape **apoptosis** (programmed cell death), resulting in an excessive accumulation of the cells in the marrow and circulation. CLL is characterized by the progressive accumulation of leukemic cells in the bone marrow, blood, and lymphoid tissues (NCCN, 2019d).

Because the lymphocytes are small, they can easily travel through the small capillaries within the circulation, and the pulmonary and cerebral complications of leukocytosis seen with myeloid leukemias are not typically found in CLL. However, these cells often accumulate within the lymph nodes and spleen. When it takes less than 12 months for the absolute number of lymphocytes to double (lymphocyte doubling time), a more aggressive disease course may ensue.

Immunophenotyping of the circulating B cells is critical to establish the diagnosis by identifying the presence of a malignant clone of these cells; it is also used to gauge the prognosis (NCCN, 2019d). Other special cytogenetic and molecular analyses (e.g., fluorescence in situ hybridization [FISH]) are also used to guide prognosis and therapy. Beta-2 microglobulin, a protein found on the surface of lymphocytes, can be measured in the serum; an elevated level correlates with a more advanced clinical stage and poorer prognosis.

Autoimmune complications can occur at any stage, as either autoimmune hemolytic anemia or idiopathic thrombocytopenic purpura. In the autoimmune process, the reticuloendothelial system destroys the body's own erythrocytes or platelets. Patients with CLL also have a greater risk for developing other cancers. Approximately 2% to 10% of patients with CLL will experience transformation of their disease to a very aggressive lymphoma, known as Richter's transformation (NCCN, 2019d); this transformation results in markedly increased lymphadenopathy, splenomegaly, B symptoms (see **Chart 30-1**), and survival of only a few months despite treatment. Second cancers typically involve the skin, colon, lung, breast, prostate, and kidney.

Chart 30-1 RISK FACTORS



B Symptoms

These symptoms include the following:

- Fever of at least 100.4° F (38°C) that may come and go over several weeks that is not explained by an underlying infection
- Drenching night sweats
- Unintentional loss of at least 10% body weight over the past 6 months

Overview: B symptoms:

- Are constitutional symptoms, meaning that they affect multiple systems
- Can manifest with many types of hematopoietic malignancies, including chronic lymphocytic leukemia (CLL), Hodgkin lymphoma, and non-Hodgkin lymphomas (NHLs)
- Are associated with worst prognoses in patients with CLL, Hodgkin lymphoma and NHL than in patients who do not report B symptoms

Adapted from Leukemia & Lymphoma Society. (2018c). Hodgkin lymphoma. Retrieved on 7/10/2019 at: www.lls.org/sites/default/files/file_assets/PS57_Hodgkin_Lymphoma2018.pdf

Clinical Manifestations

Many patients are asymptomatic and are diagnosed incidentally during routine physical examinations or during treatment for another disease. Lymphocytosis (an increased lymphocyte count) is always present. The erythrocyte and platelet counts may be normal or, in later stages of the illness, decreased. Lymphadenopathy is common; this can be severe and sometimes painful (see Fig. 30-4). Splenomegaly may also occur.

Patients with CLL can develop B symptoms (see **Chart 30-1**) which portends a worsening prognosis. T-cell function is impaired and may be the cause of tumor progression and increased susceptibility to second malignancies and infections. Life-threatening infections are particularly common with advanced disease, and account for over half of all deaths in this patient population. Viral infections, such as herpes zoster, can become widely

disseminated. Defects in the complement system are also seen, which results in increased risk of developing infection with encapsulated organisms (e.g., *Haemophilus influenzae*). Patients should receive an annual comprehensive skin examination (as the incidence of skin cancer is higher in this group), and screening guidelines for other cancers should be followed, such as for breast, colorectal, lung, and prostate cancer (NCCN, 2019d) (see [Chapter 12, Table 12-3](#), for cancer screening guidelines).



Figure 30-4 • Massive lymphadenopathy in a patient with chronic lymphocytic leukemia. Note the enlarged liver and spleen as well. Reprinted with permission from Tkachuk, D. C., & Hirschman, J. V. (2007). *Wintrobe's atlas of clinical hematology* (Fig. 5.1, p. 154). Philadelphia, PA: Lippincott Williams & Wilkins.

Medical Management

For patients with no symptoms at the time of diagnosis, the traditional “watch-and-wait” approach is often used until progression of disease is noted (which could be months to years). However, with the advent of newer treatment modalities (i.e., targeted therapies and immunotherapy), treatment may be initiated sooner in the illness trajectory (NCCN, 2019d). Additionally, clinical trials are ongoing to assess for an advantage in survival with newer agents. Various parameters are considered when treatment is selected, including the clinical stage of the disease, disease-associated symptoms, the functional status of the patient, genetic risk, and the extent and efficacy of any prior treatment. Functional status is a complex consideration; in this context, it incorporates the individual’s life expectancy independent of CLL (due to other health problems), the ability to tolerate aggressive therapy (e.g., creatinine clearance is particularly important), and the ability to perform activities of daily living (Leukemia & Lymphoma Society, 2019c; NCCN, 2019d). Patients with good functional status can typically tolerate aggressive therapy and often achieve a lasting complete remission. In contrast, the objective of treatment in those with more impaired physical status focuses on controlling bothersome symptoms (e.g., drenching night sweats, painful lymphadenopathy).

Treatment for CLL is variable and can consist of a single immunotherapy agent administered in combination with chemotherapeutic agents, such as an immunotherapeutic antibody against the B-lymphocyte antigen CD20 (e.g., rituximab, ofatumumab, obinutuzumab) with chemotherapeutic agents (e.g., fludarabine, cyclophosphamide, bendamustine, chlorambucil) as initial therapy. The most commonly prescribed first-line chemotherapeutic agent is fludarabine. When the disease is accompanied by a deletion of the *TP53* gene or a mutation of this gene, TKIs such as ibrutinib or idelalisib may be used as either monotherapy or in combination with other agents (NCCN, 2019d). Depending upon the age of the patient (less than or greater than 65 years of age) and whether or not the patient has comorbidities, patients with relapsed or refractory disease may also receive newer agents such as venetoclax, duvelisib, or acalabrutinib (NCCN, 2019d).

The major side effect of fludarabine is prolonged bone marrow suppression, manifested by prolonged periods of neutropenia, lymphopenia, and thrombocytopenia, which puts patients at risk for such infections as *Pneumocystis jiroveci*, *Listeria*, mycobacteria, herpes viruses, and cytomegalovirus (CMV). The monoclonal antibody (MoAb) alemtuzumab is often used in combination with other chemotherapeutic agents when the disease is refractory to fludarabine, the patient has very poor prognostic markers, or it is necessary to eradicate residual disease after initial treatment. Alemtuzumab targets the CD52 antigen commonly found on CLL cells, and it is effective in clearing the marrow and circulation of these cells without

affecting the stem cells. Because CD52 is present on both B and T lymphocytes, patients receiving alemtuzumab are at significant risk for infection; prophylactic use of antiviral agents and antibiotics (e.g., trimethoprim-sulfamethoxazole) is important and needs to continue for several months after treatment ends. CMV infection is also common with alemtuzumab, idelalisib, and duvelisib, and prophylaxis is important; among commonly prescribed antiviral agents, valacyclovir is more effective than acyclovir for treating CMV (NCCN, 2019d).

Patients receiving idelalisib or duvelisib have an increased risk of hepatotoxicity, severe diarrhea, colitis, and pneumonitis. TKIs have been found to increase the risk of cardiovascular toxicities, including hypertension, prolonged QT interval, left ventricular dysfunction, and heart failure (Olsen et al., 2019). Ongoing periodic assessment of the CBC, blood chemistries, ECG, blood pressure, and bowel habits are important parameters to monitor among patients taking these various agents.

Because of the older age of most patients with CLL, allogeneic HSCT may not be an option, particularly if significant comorbidities exist. However, allogeneic HSCT might be considered for some patients with *TP53* deletions or mutations who otherwise have a poor prognosis. Morbidity and mortality rates remain high (20%); thus, this treatment modality may be reserved for those patients with high-risk disease, younger age, and high degree of match from the donor (NCCN, 2019d).

Nursing Management

Virtually all patients with CLL have reduced levels of immunoglobulins, and bacterial infections are common, independent of treatment. IV treatment with immunoglobulin (IVIG) may be given to select patients with recurrent infection. While studies have not demonstrated improved survival, the rate of developing major infections is reduced (NCCN, 2019d). Patients with CLL should receive both pneumonia and flu vaccinations as indicated. Live vaccines should be avoided. The patient with CLL is at increased risk of a host of infections; nursing interventions focused on diminishing these risks are summarized in [Chapter 12, Chart 12-6](#).



For the procedural guidelines for managing immunoglobulin therapy, go to the-point.lww.com/Brunner15e.

NURSING PROCESS

The Patient with Acute Leukemia

Assessment

Although the clinical picture varies with the type of leukemia as well as with the treatment implemented, the health history may reveal a range of subtle symptoms reported by the patient before the problem is detectable on physical examination. If the patient is hospitalized, assessments should be performed daily, or more frequently as warranted. Because the physical findings may be subtle initially, a thorough, systematic assessment incorporating all body systems is essential. For example, a dry cough, mild dyspnea, and diminished breath sounds may indicate a pulmonary infection. However, the infection may not be seen initially on the chest x-ray; the absence of neutrophils delays the inflammatory response against the pulmonary infection, thus delaying radiographic changes. When serial assessments are performed, current findings are compared with previous findings to evaluate improvement or worsening. Specific body system assessments are delineated in the neutropenic and bleeding precautions found in [Chapter 12, Chart 12-6](#).

The nurse also must closely monitor the results of laboratory studies, including tracking the leukocyte count, ANC, hematocrit, platelet, creatinine and electrolyte levels, and coagulation and hepatic function tests. Culture results need to be reported immediately so that appropriate antimicrobial therapy can begin or be modified.

Diagnosis

NURSING DIAGNOSES

Based on the assessment data, major nursing diagnoses may include:

- Risk for infection, hemorrhaging, or both
- Impaired oral mucous membrane integrity due to changes in epithelial lining of the GI tract from chemotherapy or prolonged use of antimicrobial medications
- Impaired nutritional status associated with hypermetabolic state, anorexia, mucositis, pain, and nausea
- Acute pain associated with mucositis, leukocyte infiltration of systemic tissues, fever, and infection
- Fatigue and activity intolerance associated with anemia, infection, inadequate nutrition, and deconditioning
- Fluid imbalance associated with renal dysfunction, diarrhea, bleeding, infection, increased metabolic rate, hypoproteinemia, and need for multiple intravenous medications and blood products

- Impaired ability to perform hygiene, impaired ability to dress, and impaired self toileting due to fatigue and malaise
- Anxiety and grief due to uncertainty about future, anticipatory loss, and altered role functioning
- Risk for spiritual distress
- Lack of knowledge about disease process, treatment, complication management, and self-care measures

COLLABORATIVE PROBLEMS/POTENTIAL COMPLICATIONS

Potential complications may include the following (see [Chapter 12](#) for further discussion):

- Infection
- Bleeding/DIC
- Renal dysfunction
- Cardiac toxicity
- Infertility
- Tumor lysis syndrome

Planning and Goals

The major goals for the patient may include absence of complications and pain, attainment and maintenance of adequate nutrition, activity tolerance, ability to provide self-care and to cope with the diagnosis and prognosis, positive body image, and an understanding of the disease process and its treatment.

Nursing Interventions

PREVENTING OR MANAGING INFECTION AND BLEEDING

The nursing interventions related to diminishing the risk of infection and bleeding are delineated in [Chapter 12, Chart 12-6](#).

MANAGING MUCOSITIS

Although emphasis is placed on the oral mucosa, the entire GI mucosa can be altered, not only by the effects of chemotherapy but also from prolonged administration of antibiotics. See [Chapter 12](#) for assessment and management of mucositis.

IMPROVING NUTRITIONAL INTAKE

The disease process can increase the patient's metabolic rate and nutritional requirements. Nutritional intake is often reduced because of pain and discomfort associated with stomatitis. Encouraging or providing mouth care before and after meals and administering analgesic agents before eating can help increase intake. If oral anesthetic agents are used, the patient must be warned to chew with extreme care to avoid inadvertently biting the tongue or buccal mucosa.

Nausea should not interfere with nutritional intake, because appropriate antiemetic therapy is highly effective. However, nausea can result from antimicrobial therapy, so some antiemetic therapy may still be required after the chemotherapy has been completed.

Small, frequent feedings of foods that are soft in texture and moderate in temperature may be better tolerated. Low-microbial diets may be prescribed (avoiding uncooked fruits or vegetables and those without a peelable skin), although there is little evidence to support this intervention (Olsen et al., 2019). Nutritional supplements are frequently used. Daily body weight (as well as intake and output measurements) is useful in monitoring fluid status. Both calorie counts and more formal nutritional assessments are often useful. Parenteral nutrition may be required to maintain adequate nutrition.

EASING PAIN AND DISCOMFORT

Recurrent fevers are common in acute leukemia; at times, they are accompanied by shaking chills (rigors), which can be severe. Myalgias and arthralgias can result. Acetaminophen is typically given to decrease fever, but it also increases diaphoresis. Sponging with cool water may be useful, but cold water or ice packs should be avoided because the heat cannot dissipate from constricted blood vessels. Bedclothes need frequent changing as well. Gentle back and shoulder massage may provide comfort.

Mucositis can also cause significant discomfort. In addition to oral hygiene practices, patient-controlled analgesia can be effective in controlling the pain (see [Chapter 9](#)). With the exception of severe mucositis, less pain is associated with acute leukemia than with many other forms of cancer. However, the amount of psychological suffering that the patient endures can be immense. Patients often benefit from active listening and possible referral for professional counseling.

DECREASING FATIGUE AND ACTIVITY INTOLERANCE

Fatigue is a common and oppressive symptom. Nursing interventions should focus on assisting the patient to establish a balance between activity and rest. Patients with acute leukemia need to maintain some physical activity and exercise to prevent the deconditioning that results from inactivity. The use of a high-efficiency particulate air (HEPA) filter mask can permit the patient to ambulate outside the room despite severe neutropenia. Stationary bicycles may also be set up in the room; however, many patients lack the motivation or stamina to use them. At a minimum, patients should be encouraged to sit up in a chair while awake rather than staying in bed; even this simple activity can improve the patient's tidal volume and enhance circulation. Physical therapy can also be beneficial. Patients with acute leukemia may require hospitalization for extensive nursing care (either during induction or consolidation therapy or during

resultant complications); sleep deprivation frequently results. Nurses need to implement creative strategies that permit uninterrupted sleep for at least a few hours while still administering necessary medications on schedule (see Nursing Research Profile, [Chart 30-2](#)).

Chart 30-2



NURSING RESEARCH PROFILE

Fatigue and Sleep Disturbances in Adults with Acute Leukemia

Bryant, A., Gosselin, T., Coffman, E., et al. (2018). Symptoms, mobility, and function, and quality of life in adults with acute leukemia during initial hospitalization. *Oncology Nursing Forum*, 45(5), 653–664.

Purpose

Patients newly diagnosed with acute leukemia require hospitalization, typically for 4 to 6 weeks, for managing aggressive induction therapy and its toxicities. These symptoms can greatly impact the patient's quality of life and ability to perform activities of daily living. The purpose of this study was to evaluate global, physical, and mental health symptoms in adults with newly diagnosed acute leukemia.

Design

This was a prospective, longitudinal study with a total of 49 adult participants, including 36 males and 13 females. Data were collected at time of hospitalization (baseline), then weekly until discharge from hospital. Evaluation tools for data included: the Patient-Reported Outcomes Measurement Information System (PROMIS) to determine several self-reported quality-of-life measures such as fatigue, anxiety, depression, pain, sleep disturbances, and global physical and mental health; the Functional Assessment of Cancer Therapy-Leukemia (FACT-Leu) to measure symptom concerns that are leukemic specific; Karnofsky Performance Status Scale (KPS) to measure function; and the Timed Up and Go Test (TUG) to measure physical mobility.

Findings

This study was the largest, to date, to evaluate the symptoms and quality of life of patients newly diagnosed with acute leukemia during hospitalization. All participants had one or more comorbidities, as well as a group mean body mass index of 30.8 (SD = 6.7), indicative of being overweight or having obesity, at time of hospitalization. No significant differences were seen in global mental health, pain, or KPS during hospitalization. There were significant decreases in fatigue ($p < 0.001$), anxiety ($p < 0.001$), depression ($p = 0.004$), and sleep disturbance ($p = 0.005$) from baseline to hospital discharge. Also significant were a decrease in leukemic symptoms ($p < 0.001$), indicating improved leukemic outcomes, which is the goal of therapy.

Nursing Implications

Nurses need to be aware of factors that can impact sleep in patients with cancer, both during and following treatment. As fatigue plays a major role in sleep disturbances, the nurse needs to assess for and develop strategies to address both concerns, especially while the patient is in the hospital. Poor sleep, fatigue, and pain can all contribute to the increased

risk for falls, so safety issues should also be addressed with the patient and the patient's family. The nurse should encourage the patient to exercise and have some physical activity as part of the daily routine, to decrease fatigue while enhancing sleep. Additionally, the nurse should have a good understanding of the symptoms common to patients with leukemia and interventions to manage them as they occur.

MAINTAINING FLUID AND ELECTROLYTE BALANCE

Febrile episodes, bleeding, and inadequate or overly aggressive fluid replacement can alter the patient's fluid status. Similarly, persistent diarrhea and vomiting that occur with certain chemotherapy and immunotherapy agents, and long-term use of certain antimicrobial agents can cause significant deficits in electrolytes. Intake and output need to be measured accurately, and daily weights should also be monitored. The patient should be assessed for signs of dehydration as well as fluid overload, with particular attention to pulmonary status and the development of dependent edema. Laboratory test results, particularly electrolytes, blood urea nitrogen, creatinine, and hematocrit, should be monitored and compared with previous results. Replacement of electrolytes, particularly potassium and magnesium, is commonly required. Patients receiving amphotericin or certain antibiotics are at increased risk for electrolyte depletion.

IMPROVING SELF-CARE: BATHING, DRESSING, AND TOILETING

Because hygiene measures are so important in this patient population, they must be performed by the nurse when the patient cannot do so. However, the patient should be encouraged to do as much as possible to preserve mobility and function as well as self-esteem. Patients may have negative feelings because they can no longer care for themselves. Empathetic listening is helpful, as is realistic reassurance that these deficits are temporary. As the patient recovers, the nurse assists them to resume more self-care. Patients are usually discharged from the hospital with a vascular access device (e.g., Hickman catheter, peripherally inserted central catheter [PICC]), and coordination with appropriate home care services is needed for catheter management.

MANAGING ANXIETY AND GRIEF

Being diagnosed with acute leukemia can be extremely frightening. In many instances, the need to begin treatment is emergent, and the patient has little time to process the fact that they have the illness before making decisions about therapy. Providing emotional support and discussing the uncertain future are crucial. The nurse also needs to assess how much information the patient wants to have regarding the illness, its treatment, and potential complications. This desire should be reassessed at intervals, because needs and interest in information change throughout the course of the disease and treatment. Priorities must be identified so that procedures,

assessments, and self-care expectations are adequately explained even to those who do not wish extensive information.

Many patients exhibit depressive symptoms and begin to grieve for their losses, such as normal family functioning, professional roles and responsibilities, and social roles, as well as physical functioning. The nurse can assist the patient to identify the source of the grief and encourage them to allow time to adjust to the major life changes produced by the illness. Role restructuring, in both family and professional life, may be required. It is essential to encourage the patient to identify options and to take time in making important decisions.

The patient's physical condition can deteriorate quickly and it is not often easy to discern if the patient may recover or will die from complications. Providing emotional support to both the patient and the family is critical and equally as important as is rendering expert physical care.

Discharge from the hospital can also provoke anxiety. Although most patients are eager to go home, they may lack confidence in their ability to manage potential complications and to resume their normal activity. Close communication between nurses across care settings can reassure patients that they will not be abandoned.

ENCOURAGING SPIRITUAL WELL-BEING

Because acute leukemia is a serious, potentially life-threatening illness, the nurse may offer support to enhance the patient's spiritual well-being. The patient's spiritual and religious practices should be assessed and pastoral services offered. Throughout the patient's illness, the nurse assists the patient to maintain hope. However, that hope should be realistic and will certainly change over the course of the illness. For example, the patient may initially hope to be cured, but with repeated relapses and a change to hospice or palliative care, the same patient may hope for a quiet, dignified death. (Refer to [Chapter 13](#) for a discussion of palliative and end-of-life care.)

PROMOTING HOME, COMMUNITY-BASED, AND TRANSITIONAL CARE



Educating Patients About Self-Care. Most patients cope better when they understand what is happening to them. Based on their health literacy level, and interest, educating the patient and family should begin with a focus on the disease (including some pathophysiology), its treatment, and certainly the resulting significant risk of infection and bleeding (see [Chapter 29](#), Charts 29-7 and 29-8).

Although management of a vascular access device can be taught to most patients or family members, this care is typically performed by a home care

agency or outpatient clinic nursing staff. Patients and family members do need basic education regarding management of the vascular access device, particularly with regard to prevention of infections.

Continuing and Transitional Care. For patients who are clinically stable but require parenteral antibiotics or blood products, these procedures are most often performed in an outpatient setting. Nurses in these settings must communicate regularly. They need to inform the patient about parameters that are important to monitor, how to monitor them, and to give the patient-specific instructions about when to seek care from the physician or other health care provider.

The patient and family need to have a clear understanding of the disease, the prognosis, and how to monitor for complications or recurrence. The nurse ensures that this information is provided. Should the patient no longer respond to therapy, it is important to respect the patient's choices about treatment and end-of-life care. Advance directives or other method should be used for patients to state their end-of-life preferences (see [Chapter 13, Chart 13-5](#)). In patients with acute leukemia, death typically occurs from infection or, less frequently, from bleeding. Family members need to have information about these complications and the measures to take should either occur. Many family members cannot cope with the care required when a patient begins to bleed actively. It is important to delineate alternatives to keeping the patient at home, such as inpatient hospice units.

Evaluation

Expected patient outcomes may include:

1. Shows no evidence of infection
2. Experiences no bleeding
3. Has intact oral mucous membranes
 - a. Participates in oral hygiene regimen
 - b. Reports no discomfort in mouth
4. Attains optimal level of nutrition
 - a. Maintains weight with increased food and fluid intake
 - b. Maintains adequate protein stores (e.g., albumin, prealbumin)
5. Reports satisfaction with pain and comfort levels
6. Has less fatigue and increased activity
7. Maintains fluid and electrolyte balance
8. Participates in self-care
9. Copes with anxiety and grief
 - a. Discusses concerns and fears

- b. Uses stress management strategies appropriately
 - c. Participates in decisions regarding end-of-life care
10. Reports sense of spiritual well-being
11. Absence of complications

MYELODYSPLASTIC SYNDROMES (MDSS)

The MDSs are a group of clonal disorders of the myeloid stem cell that cause dysplasia (abnormal development) in one or more types of cell lines. These disorders commonly result in cytopenias (low blood cell counts), with the tendency to develop into acute leukemia (Sockel & Platzbecker, 2018). A common feature of MDS is anemia due to dysplasia of the erythrocytes, although leukocytes (particularly neutrophils) and platelets can also be affected. Although the bone marrow is actually hypercellular, many of the cells within it die before being released into the circulation. Therefore, the actual number of cells in the circulation is typically lower than normal. In MDS, the affected cells do not function normally. The neutrophils have diminished ability to destroy bacteria by **phagocytosis** (cellular ingestion and digestion of foreign bodies); platelets are less able to aggregate and are less adhesive than usual. The result of these defects is an increased risk of infection and bleeding, even when the actual number of circulating cells may not be excessively low.

This disease is primarily seen in older adults (median age at diagnosis is 65 to 70 years), is idiopathic in nature due to HSC damage, and occurs more often in males than females (Montalban-Bravo & Garcia-Manero, 2017; Sockel & Platzbecker, 2018). In addition, about 10% to 15% of patients will develop MDS following exposure to alkylating agents, radiotherapy, or chemicals (e.g., benzene), and/or have an inherited genetic disorder, such as Fanconi anemia or trisomy 21 (Sockel & Platzbecker, 2018). Genetic syndromes account for about 50% of cases (e.g., Down syndrome, trisomy 8 syndrome, neurofibromatosis type 1) (Leukemia & Lymphoma Society, 2019d; NCCN, 2019e).

Clinical Manifestations

The manifestations of MDS can vary widely. Some patients are asymptomatic, with the illness being discovered incidentally when a CBC is performed for other purposes. Other patients have profound symptoms and complications from the illness. Because MDS tends to occur in older adults, other concurrent chronic health conditions may exacerbate symptoms associated with the disease. Fatigue is often present, with varying levels of intensity and

frequency. Neutrophil dysfunction puts the patient at risk for recurrent pneumonias and other infections. Because platelet function can also be altered, bleeding can occur. These problems may persist in a fairly steady state for months, even years. Over time, the marrow may fail to provide enough cells despite support with transfusion or growth factors; this is called *bone marrow failure*. MDS may also progress over time; as the dysplasia evolves into a leukemic state, the complications increase in severity. However, it is important to note that the majority of patients with MDS succumb to complications from the disease itself or from other comorbidities, and not to those from acute leukemia (Leukemia & Lymphoma Society, 2019d).

Assessment and Diagnostic Findings

The CBC typically reveals a macrocytic anemia; leukocyte and platelet counts may be diminished as well. Other potential causes for cytopenia, which may include vitamin deficiencies, viral infection, GI bleeding, autoimmune disease, splenomegaly, and liver dysfunction, should be excluded. Serum erythropoietin levels may be variable and the **reticulocyte** count (immature RBCs) may be inappropriately low. The presence of blast cells on the CBC may be indicative of disease progression to acute leukemia. To help rule out other causes of anemia, other laboratory studies may include folate, serum vitamin B₁₂, ferritin, total iron-binding capacity (TIBC), iron, and thyroid-stimulating hormone (TSH).

The official diagnosis of MDS is based on the results of a bone marrow aspiration (to assess dysplasia) and biopsy (to assess characteristics of the affected cells). These tests help in determining prognosis, risk of leukemic transformation, and in some patients, the most effective therapy (Montalban-Bravo & Garcia-Manero, 2017); thus, the nurse must understand the risk stratification category of each patient. Those patients with low-risk disease have a much longer survival (as much as 10 years) compared with untreated patients with high-risk disease (where survival is usually less than 9 months) (NCCN, 2019e) (see Chapter 28 for discussion of bone marrow aspiration and biopsy).

Medical Management

Medical management strategies for MDS are based on risk stratification to determine stage of disease and prognosis. The most commonly used tool is the International Prognostic Scoring System (IPSS) that evaluates cytopenia, transfusion needs, percent of blast cells in the bone marrow, and cytogenetic characteristics (Montalban-Bravo & Garcia-Manero, 2017). Most patients with MDSs are diagnosed as having low-risk disease; for these patients, the objective of therapy is to maintain or restore quality of life, improve cytopenia,

and decrease transfusion requirements. Some patients with mild symptoms may only require periodic monitoring of laboratory studies indicative of hematologic function (e.g., CBC, reticulocyte count, folate, ferritin, iron). Approximately two thirds of patients diagnosed as low risk have cytopenic-related complications at the time of diagnosis, however, and may require blood transfusions and/or an erythropoiesis-stimulating agent.

Patients who are at low to intermediate risk and transfusion dependent are typically treated with a hypomethylating agent (e.g., azacitidine, decitabine). These agents work by inhibiting the abnormal genes regulating methylation, promoting tumor suppression genes, and permitting myeloid differentiation within the bone marrow (NCCN, 2019e). Neither drug has been shown to modify the natural trajectory of low-risk MDS; therefore, hypomethylating agents are not typically used until erythroid-stimulating agents are no longer effective in controlling transfusion dependence (NCCN, 2019e). These agents can improve cytopenia, reduce transfusion requirements, reduce the likelihood of transformation to AML, and improve overall survival.

For the patient at high risk the goals of therapy are to delay leukemic transformation and prolong life expectancy (NCCN, 2019e; Sockel & Platzbecker, 2018). Allogeneic HSCT continues to be the only potential option of cure for MDS, but is not often a viable option for most patients, as many are of advanced age with significant comorbidities. Allogeneic HSCT is recommended for patients who have hypoplastic MDS, are younger, or those who have not responded satisfactorily to other treatment options (Montalban-Bravo & Garcia-Manero, 2017; NCCN, 2019e).

Lenalidomide (a thalidomide analog) is the standard of care for patients with the chromosomal abnormality deletion 5q, are considered low risk, and are not thrombocytopenic (NCCN, 2019e). Treatment with lenalidomide may cause neutropenia and thrombocytopenia, which may necessitate treatment delays or dose reduction (NCCN, 2019e). Other immunosuppressive therapies that have shown some efficacy in the treatment of MDS are antithymocyte globulin (ATG), with or without cyclosporine, and corticosteroids. These agents are used in a subset of patients with MDS who have weakened immune responses (e.g., have neutropenia) (Montalban-Bravo & Garcia-Manero, 2017).

Patients frequently need repeated transfusions (PRBCs, platelets, or both) throughout the illness trajectory to maintain adequate hemoglobin and platelet levels (termed *transfusion dependence*). Attempts to improve anemia and decrease RBC transfusion are often successful with the use of erythroid-stimulating agents (epoetin alfa or darbopoetin alfa). Higher-than-normal doses may be required to achieve an adequate improvement in hemoglobin. Adding myeloid growth factors such as G-CSF or GM-CSF can boost responsiveness to these agents (NCCN, 2019e). The median duration of response to this therapy is 2 years; transfusion requirements typically increase by this point.

Thrombocytopenia is a challenge to manage among patients with MDS. Severe thrombocytopenia is difficult to manage because patients can quickly develop refractoriness to platelet transfusions due to alloimmunization (Leukemia & Lymphoma Society, 2019d). Moreover, bleeding can develop even when the platelet level is not excessively low, due to poor platelet function. The cause of thrombocytopenia appears to be increased apoptosis and premature marrow destruction of the platelets prior to their release into the circulation (NCCN, 2019e). The recombinant thrombopoietin receptor agonists romiplostim and eltrombopag have been developed to stimulate the proliferation and differentiation of megakaryocytes into platelets within the bone marrow. Both drugs have demonstrated the ability to significantly raise platelet counts in this population, but their duration of action may not be long. Increased rates of marrow fibrosis and AML evolution seem to be ameliorated by discontinuing the drug, but additional study is needed (NCCN, 2019e).

Iron overload is another significant problem for patients with MDS, especially in patients who routinely receive PRBC transfusions (transfusion dependent). Surplus iron is deposited in cells within the reticuloendothelial system, and later in parenchymal organs (e.g., liver). While a true cause-and-effect has not yet been established, there is significant concern that patients with transfusion-dependent MDS are at high risk for developing cardiac disorders, particularly heart failure, as well as hepatic and endocrine dysfunction (NCCN, 2019e). Excess iron, and the resultant increased oxidative stress, is also associated with pancreatic dysfunction, the development of diabetes, increased rates of infection, and decreased hematopoiesis.

To prevent or reverse the complications of iron overload, iron chelation therapy is commonly implemented. Patients with preexisting liver disease, including cirrhosis, should not receive oral iron chelators. There are studies that have found that iron overload may play a role in increased mortality and morbidity in early-stage MDS due to hepatic, cardiac, and endocrine dysfunction (NCCN, 2019e). It is recommended that all patients with MDS who have regular transfusion needs have serum ferritin levels along with the number of PRBC transfusions routinely monitored to determine iron stores and possible overload. The ferritin level should be maintained at less than 1000 mcg/L. Iron is bound to the chelating agent and then excreted in the urine. Because chelation therapy removes only a small amount of iron with each treatment, patients with chronic iron overload from RBC transfusions need to continue chelation therapy as long as the iron overload exists. Oral iron chelation with deferasirox has replaced the need for the former standard therapy, which consisted of subcutaneous infusions of deferoxamine. However, adherence remains a challenge, largely due to toxicity associated with the drug.

Infection rates are high among patients with MDS, who frequently require hospitalization. Severe neutropenia, coexisting chronic obstructive pulmonary disease (COPD) or autoimmune disease, and history of other malignancy are

associated with higher risk for developing infection, whereas the extent of thrombocytopenia, age, MDS therapy, or diabetes are not (Leukemia & Lymphoma Society, 2019d; NCCN, 2019e). Pneumonia is the most common type of infection in this patient population; bacteria (both gram negative and gram positive) are the predominant pathogens.

The administration of myeloid growth factors alone may be useful in some patients with infections and severe neutropenia, but they are not typically used to prevent infection. Prophylactic antibiotics are not routinely used so that resistant organisms do not develop, but prompt initiation of antimicrobial therapy is crucial at the onset of infection to diminish the risk of increased mortality.

Nursing Management

Caring for patients with MDS can be challenging because the illness is unpredictable. As with other hematologic disorders, some patients (especially those with no symptoms) have difficulty perceiving that they have a serious illness that can place them at risk for life-threatening complications. At the other extreme, many patients have tremendous difficulty coping with the uncertain trajectory of the illness and fear that the illness will evolve into AML. Thus, it is important for patients to understand their unique risk of the disease transforming to AML and to recognize that, for most patients, MDS is a chronic illness. It is imperative that the nurse recognizes any concurrent health problems the patient may have. This knowledge will help the nurse better plan and manage the patient's care. For example, a patient with underlying heart failure or COPD may not tolerate anemia well, nor a more rapid rate of red blood cell transfusion.

Patients with MDS need extensive education about infection risk, measures to avoid it, signs and symptoms of developing infection, and appropriate actions to take should such symptoms occur. Education should also be provided regarding the risk of bleeding. Patients need to be encouraged to serve as their own health advocate, by informing other health care providers, including dentists, that they have MDS, and their risks for infection and bleeding. Patients with MDS who are hospitalized may require neutropenic precautions.

Fatigue is often a debilitating symptom for the patient with MDS and significantly interferes with quality of life. It can impair the patient's ability to function in the work or home setting and to engage in meaningful activities, and affect the patient's overall cognitive function (Leukemia & Lymphoma Society, 2019d; NCCN, 2019e). Patients may benefit from anticipatory guidance in learning how to live with this symptom, and creative strategies may be required.

Laboratory values need to be monitored closely to anticipate the need for transfusion and to determine response to treatment with growth factors. Patients with chronic transfusion requirements often benefit from the insertion of a vascular access device for this purpose. Those patients receiving chemotherapy need extensive education regarding treatment side effects (and how to manage them) and treatment schedules. Patients receiving growth factors need education about these medications, administration schedules, and side effects.

Chelation therapy is a process that is used to remove excess iron acquired from chronic transfusions. Side effects from oral chelators commonly include diarrhea and abdominal cramping. Educating the patient to take the medication in the evening prior to dinner and gradually increasing the dosage over time may diminish these side effects. Skin rash is usually mild and rarely warrants temporarily stopping the drug. Monitoring renal function is important as a rise in serum creatinine is common. The dosage should be reduced if the serum creatinine rises by more than one third of baseline. Patients with preexisting liver disease, including cirrhosis, should not receive oral iron chelators.

MYELOPROLIFERATIVE NEOPLASMS

Myeloproliferative neoplasms originate in the HSC and are characterized by clonal proliferation of one or more myeloid cell types (Arber et al., 2016; Spivak, 2018). These Philadelphia chromosome-negative myeloproliferative disorders include polycythemia vera, essential thrombocythemia, and primary myelofibrosis.

Polycythemia Vera

Polycythemia vera (sometimes called *P vera* or primary polycythemia) is the most common of the three Philadelphia chromosome-negative myeloproliferative disorders. In polycythemia vera the bone marrow is hypercellular, and the erythrocyte, leukocyte, and platelet counts in the peripheral blood are often elevated. Erythrocyte elevation predominates; the hematocrit can exceed 60% in some cases (Tefferi & Barbui, 2019). The median age at the onset is 60 years; median survival is typically 14 to 20 years (Fowlkes, Murray, Fulford, et al., 2018a; Tefferi & Barbui, 2019).

Clinical Manifestations

Clinical manifestations are variable. Some patients at the time of initial diagnosis may be asymptomatic (Spivak, 2018). If symptoms are present, they

tend to be related to erythrocytosis, with or without leukocytosis and/or **thrombocytosis** (i.e., higher-than-normal platelet count that occurs from a disease or disorder; in this instance, the disease is polycythemia vera). This increase in blood cell mass increases blood viscosity leading to (Fowlkes et al., 2018b; Harrison, Koschmieder, Foltz, et al., 2017; Spivak, 2018):

- neurologic symptoms such as headache, dizziness, vision changes, and transient ischemic attacks (TIAs);
- abdominal symptoms such as early satiety, abdominal discomfort/pain (that can also be associated with splenomegaly);
- cardiovascular symptoms including ruddy complexion, angina, claudication, dyspnea, hypertension, and thrombophlebitis; and
- constitutional symptoms such as fatigue and night sweats.

Another common symptom is pruritus, which may be caused by histamine released from an increased number of basophils. **Erythromelalgia**, characterized by a burning, painful sensation, and erythema in the fingers or toes, may also occur. Uric acid may be elevated as well, resulting in gout and renal stones formation.

Assessment and Diagnostic Findings

Diagnosis is based upon the evaluation of clinical symptoms and laboratory findings as well as the presence of a mutation of the *JAK2* gene (Arber et al., 2016). Assessment should include palpation of the spleen, and finding if the patient has a history of thrombotic events or has ever received a blood transfusion or medications associated with causing erythrocytosis (e.g., recombinant erythropoietin), as well as assessment of cardiovascular risk factors (e.g., obesity, smoking, and poorly controlled hypertension, diabetes, or hyperlipidemia; see later discussion of thrombotic risks under Complications). Some patients with the *JAK2* mutation who do not meet the criteria for a diagnosis of polycythemia vera are identified as having “masked polycythemia vera” (McMullin, Harrison, Ali, et al., 2019; Spivak, 2018). These patients are more likely to transform to myelofibrosis (see later discussion) or AML and have a poorer overall rate of survival (McMullin et al., 2019; Spivak, 2018).

Complications

Patients with polycythemia vera are at increased risk for thromboses that may be either venous or arterial. Thrombosis can result in strokes or myocardial infarctions; thrombotic complications are the most common cause of death. Patients older than 60 years of age, those with a prior history of thrombosis, or those with an elevated platelet count (exceeding 1 million/mm³) are at greater risk for developing thrombotic complications (Tefferi & Barbui, 2019).

Patients with enlarged spleens are also at increased risk for thrombosis. Cardiovascular risk factors thought to increase thrombotic risk include obesity, smoking, and poorly controlled hypertension, diabetes, or hyperlipidemia (Barbui, Vannucchi, Carobbio, et al., 2017).

Bleeding may also be a complication of polycythemia vera and its treatment. The bleeding can be significant and can occur in the form of nosebleeds, ulcers, frank GI bleeding, hematuria, or intracranial hemorrhage. If the patient with polycythemia vera has a bleeding complication and is taking aspirin, the aspirin should be held until the bleeding is resolved (NCCN, 2019f).

Medical Management

The objectives of management are to reduce the risk of thrombosis without increasing the risk of bleeding, reduce the risk of evolution to myelofibrosis or AML, and ameliorate symptoms associated with the disease (McMullin et al., 2019) (see [Table 30-2](#)). Specific therapy is based on an established risk stratification. Patients less than age 60 and no prior history of thrombosis are considered “low risk”; those age 60 or older, or with a history of thrombosis, or both, are considered to be “high risk” (NCCN, 2019f).

TABLE 30-2 Common Constitutional Symptoms Associated with Myeloproliferative Neoplasms

Symptoms vary between the three myeloproliferative neoplasms, both in frequency and severity. Nurses should assess these patients frequently for the presence of these symptoms and initiate appropriate measures to ameliorate them.

Symptom	P Vera (%)	ET (%)	Myelofibrosis (%)
Fatigue	85	84	94
Concentration	62	58	68
Early satiety	60	56	74
Night sweats	52	47	63
Pruritus	62	46	52
Abdominal discomfort	48	48	65
Bone pain	48	45	53
Weight loss	33	28	47
Fever	19	17	24

ET, essential thrombocythemia; P vera, polycythemia vera.

Adapted from Geyer, H. L., & Mesa, R. A. (2014). Therapy for myeloproliferative neoplasms: When, which agent, and how? *Hematology American Society of Hematology Education Program*, 2014(1), 277–286.

Phlebotomy is considered the mainstay of therapy and is used to maintain the hematocrit level at less than 45% (Spivak, 2018) (see Fig. 30-5). It involves removing enough blood (initially 500 mL once or twice weekly) to reduce blood viscosity and to deplete iron stores, thereby rendering the patient iron deficient and consequently unable to continue to manufacture excessive RBCs. Low-dose aspirin prevents vascular thrombosis without increasing the risk of bleeding and is recommended for all patients with polycythemia vera, regardless of risk (Leukemia & Lymphoma Society, 2019e; NCCN, 2019f).

Cytoreductive therapy should be considered in patients at low risk who are symptomatic due to progressive splenomegaly, leukocytosis, thrombocytosis, or have poor tolerance to phlebotomy, or whose disease has progressed to myelofibrosis or AML (McMullin et al., 2019; NCCN, 2019f). In patients at high risk, cytoreductive therapy is considered first-line treatment and might be pursued in addition to or in place of phlebotomy. Hydroxyurea, also known as hydroxycarbamide, can be used to suppress bone marrow function, thereby controlling blood counts. It has also been associated with preventing thrombotic complications (Tefferi & Barbui, 2019). Interferon-alfa is another first-line cytoreductive agent that can be selected; it is indicated in patients younger than 60 years of age, or in patients who are pregnant or intolerant of hydroxyurea (NCCN, 2019e). Interferon-alfa can also reduce splenomegaly, prevent thrombosis, and decrease pruritus. However, it may be difficult for patients to tolerate because of its side effects (e.g., flulike symptoms, depression); it is also very costly.



Figure 30-5 • Phlebotomy can markedly reduce the plethora seen in polycythemia vera. This is evidenced here by a marked reduction in facial rubor in a patient with polycythemia vera. Reprinted with permission from Turgeon, M. L. (2012). *Clinical hematology: Theory & procedures* (5th ed., Fig. 21.10, p. 373). Philadelphia, PA: Lippincott Williams & Wilkins.

Ruxolitinib is a *JAK2* inhibitor; it is used in patients who are resistant or unable to tolerate hydroxyurea and for whom interferon-alfa is not indicated (e.g., patients older than 60 years of age). This drug has been shown to reduce splenomegaly, decrease symptoms, and improve quality of life (Fowlkes et al., 2018a; McMullin et al., 2019). Common side effects of ruxolitinib include dose-dependent anemia and thrombocytopenia.

Additional cytoreductive drugs, including busulfan, pipobroman, and anagrelide, have been shown to be effective in controlling blood counts; however, these agents have been linked to an increased risk for leukemic transformation and have significant side effects. These drugs are reserved for patients who are refractory to other cytoreductive agents or with limited life expectancy (McMullin et al., 2019).

Nursing Management

Fatigue is the most commonly reported symptom in patients with polycythemia vera. It is not always correlated to disease severity. The degree of fatigue may vary, but can become so debilitating that it impairs the patient's quality of life. There are many causes of fatigue, including a release of proinflammatory **cytokines** (proteins produced by leukocytes that are vital to

regulation of hematopoiesis, apoptosis, and immune responses), impaired hematopoiesis, depression, inactivity, and the effects of certain medications (e.g., antihypertensive medications, antihistamines) (Fowlkes et al., 2018b; NCCN, 2019e). Management of fatigue can include pharmacologic agents (e.g., erythropoiesis-stimulating agents, antidepressant drugs, stimulants such as caffeine or amphetamines) and nonpharmacologic treatments (e.g., exercise, yoga, and optimizing sleep).

Another common symptom in patients is pruritus, described as strong itching, stinging, or burning. The exact etiology is not known but is thought to be related to proinflammatory cytokines. Pruritus can be triggered by contact with water of any temperature. Other causes include consuming alcohol or caffeine, having dry skin, experiencing changes in temperature, and sweating after exercise (Fowlkes et al., 2018b; Tefferi & Barbui, 2019). Antihistamines, emollient lotion, and selective serotonin reuptake inhibitors (SSRIs) are not particularly effective in controlling pruritus. Interferon-alfa and narrow band ultraviolet B phototherapy (which uses ultraviolet light for a prescribed length of time to decrease symptoms) may be used in severe cases. As the efficacy of pharmacologic strategies may not be optimal, it is important to individualize therapy and monitor for effectiveness. The nurse may recommend bathing in tepid water, avoiding vigorous toweling off after bathing, and using cocoa butter or oatmeal-based lotions.

Potentially life-threatening complications from the disease are thrombosis or hemorrhage. Risk factors for thrombotic complications, particularly a prior history of thrombosis, smoking, obesity, and poorly controlled hypertension, diabetes, and hyperlipidemia should be assessed, and patients should be encouraged to modify their cardiovascular risk factors. Adopting or maintaining a healthy lifestyle should be encouraged. Patients should be educated about the signs and symptoms of thrombosis. To reduce the likelihood of deep vein thrombosis (DVT), sedentary behavior, crossing the legs, and wearing tight or restrictive clothing (particularly stockings) should be discouraged. Patients with a history of significant bleeding are usually advised to avoid high-dose aspirin and aspirin-containing medications, because these medications alter platelet function. Minimizing alcohol intake should also be emphasized to further diminish the risk of bleeding. Patients should be counseled about the signs of bleeding. The patient needs to be instructed to avoid iron supplements, including those in over-the-counter multivitamin supplements, because the iron can further stimulate RBC production.

Essential Thrombocythemia

Essential thrombocythemia, also called primary thrombocythemia, is a rare, chronic, Philadelphia chromosome-negative myeloproliferative disorder

characterized by an increased production of megakaryocytes. A marked increase in platelet production occurs, with the platelet count consistently greater than 450,000/mm³. The platelet count can exceed 1 to 2 million/mm³. Occasionally, the **thrombocythemia** (increase in platelets without a known cause) is accompanied by an increase in erythrocytes, leukocytes, or both; however, these cells are not increased to the extent they are in polycythemia vera or myelofibrosis (see later discussion).

The exact underlying cause of essential thrombocythemia is idiopathic (i.e., unknown). Approximately 50% to 60% of patients have the *JAK2* gene mutation, and 25% of patients have the *CALR* gene mutation (Fowlkes et al., 2018a; Tefferi & Barbui, 2019). This disease affects women twice as often as men and tends to occur later in life (median age at diagnosis is 65 to 70 years). Median survival is about 20 to 33 years (Haider, Gangat, Lasho, et al., 2016); overall survival does not differ from the general population. However, survival rates vary based upon the type of gene mutation present. For example, patients with the *CALR* mutation have fewer thrombotic events and higher survival rates compared to those with the *JAK2* mutation (Tefferi & Barbui, 2019).

Clinical Manifestations

Many patients with essential thrombocythemia are asymptomatic; the illness is frequently diagnosed as the result of an incidental finding of an elevated platelet count on a CBC. Symptoms occur most often when the platelet count exceeds 1 million/mm³; however, they do not always correlate with the extent to which the platelet count is elevated. When symptoms do occur, they primarily result from vascular occlusion. This occlusion can occur in large arterial vessels (cerebrovascular, coronary, or peripheral arteries) and deep veins, as well as in the microcirculation; inflammation that may occur in the vascular endothelium may result in erythromelalgia. More common forms of venous thromboembolism (VTE), including DVT and pulmonary embolism (PE), can also occur.

One of the most common neurologic symptoms of essential thrombocythemia is headaches. Other neurologic manifestations that may be related to compromised blood flow include dizziness; lightheadedness; paresthesias; visual changes, such as diplopia; and TIAs (Fowlkes et al., 2018b; Harrison et al., 2017). Other symptoms can include tinnitus and chest pain.

Because the platelets can be dysfunctional, minor or major hemorrhage may occur. Bleeding is commonly limited to recurrent minor manifestations (e.g., ecchymoses, hematomas, epistaxis, gum bleeding), although significant GI bleeding and intracranial hemorrhage are both possible and considered major hemorrhagic events. Bleeding typically does not occur unless the platelet count

exceeds 1.5 million/mm³. It results from a deficiency in von Willebrand factor as the platelet count increases (NCCN, 2019f).

Assessment and Diagnostic Findings

The diagnosis of essential thrombocythemia is made by ruling out other potential disorders—either other myeloproliferative disorders or underlying illnesses that cause a reactive or secondary thrombocytosis (see later discussion). Iron deficiency should be excluded, because a reactive increase in the platelet count often accompanies this deficiency. The diagnosis is typically based upon both an evaluation of clinical manifestations and laboratory findings. The CBC will show markedly enlarged and abnormal platelets, as well as a persistently elevated platelet count (greater than 450,000/mm³). A bone marrow examination (i.e., aspirate or biopsy) can help distinguish between true essential thrombocythemia and other myelofibrotic diseases (Tefferi & Barbui, 2019).

Complications

Complications include inappropriate formation of thrombi and hemorrhage. Patients with cardiovascular risk factors (e.g., obesity, smoking, and poorly controlled hypertension, diabetes, hyperlipidemia) are at higher risk for thrombotic complications (Tefferi & Barbui, 2019). Patients older than 60 years and those with a history of prior thrombosis are at higher risk for complications. Major bleeding tends to occur when the platelet count is very high (greater than 1.5 million/mm³) and there is a prior history of major bleeding. Cause of death in patients is often the result of thrombosis or major bleeding (collectively called thrombohemorrhagic events) or transformation to AML or myelofibrosis (Haider et al., 2016).

Medical Management

The goals of management are to minimize the risk of thrombohemorrhagic events and to control symptoms (see [Table 30-2](#)). Treatment for essential thrombocythemia is based upon a patient's risk stratification (NCCN, 2019f). Patients at low risk are less than 60 years of age, without the *JAK2* mutation, and without a prior history of thrombosis. Typical treatment for these patients includes ongoing monitoring for new thrombosis and acquired von Willebrand factor deficiency and disease-related major bleeding; management of cardiovascular risk factors (e.g., obesity, smoking, and poorly controlled hypertension, diabetes, or hyperlipidemia); and daily low-dose aspirin as long as the patient remains asymptomatic. Patients should be monitored every 3 to 6 months for signs and symptoms of disease progression. Patients at

intermediate risk are those older than age 60, without the *JAK2* mutation, and with no prior history of thrombosis. As long as the patient has not any thrombohemorrhagic events, the treatment remains the same as for low-risk patients.

A patient is deemed high risk when there is a history of thrombosis at any age or is age 60 or older or with the *JAK2* mutation. Besides use of aspirin, treatment may also include prescribing hydroxyurea, interferon-alfa, or anagrelide (see previous discussion in polycythemia vera section), all of which are effective in decreasing platelet counts to a level below 400,000/mm³ and reducing risk for developing arterial thrombosis and hemorrhage. However, the side effects of these agents may be intolerable. As previously noted, anagrelide has been associated with disease progression to myelofibrosis or AML (McMullin et al., 2019).

Patients who develop arterial or venous thrombosis require additional treatment. Anticoagulant therapy may be useful for patients with active thrombosis (see [Chapter 26](#) for further discussion of anticoagulation therapy) and platelet apheresis may be used in patients with acute life-threatening thrombosis or major bleeding (see [Chapter 28, Table 28-3](#)) (NCCN, 2019f).

Nursing Management

It is important to assess patients for a history of prior thrombohemorrhagic events, because these are the primary cause of morbidity and mortality. Patients with essential thrombocythemia should be educated on signs and symptoms of hemorrhage and thrombosis, particularly the neurologic manifestations, such as visual changes, numbness, tingling, and weakness. Patients should be encouraged about medication adherence and management of side effects. In particular, patients taking aspirin should be informed about the importance of taking this medication as well as the increased risk of bleeding. Those patients taking hydroxyurea should have their CBCs monitored regularly; the dosage is adjusted based on the platelet and WBC count. Patients taking interferon-alfa may be taught to self-administer the medication and how to manage its side effects.

Cardiovascular risk factors associated with thrombotic complications should be assessed, such as obesity, smoking, and poorly controlled hypertension, diabetes, or hyperlipidemia. Measures should be identified and encouraged to reduce these risks. Additionally, patients who are at risk for bleeding should be educated about medications (e.g., aspirin, nonsteroidal anti-inflammatory agents [NSAIDs]) and other substances (e.g., alcohol, certain herbal therapies) that can alter platelet function.

Primary Myelofibrosis

Primary myelofibrosis, also known as agnogenic myeloid metaplasia or myelofibrosis with myeloid metaplasia, is the rarest of the Philadelphia chromosome-negative myeloproliferative disorders; it arises from neoplastic transformation of an early HSC. This disease is characterized by bone marrow fibrosis or scarring, extramedullary hematopoiesis (typically involving the spleen or liver), leukocytosis, thrombocytosis, elevated lactic dehydrogenase (LDH), and anemia. Some patients have **pancytopenia** (i.e., diminished leukocyte, platelet, and erythrocyte counts). Patients with primary myelofibrosis have increased **angiogenesis** (formation of new blood vessels) within the marrow. Immature forms of blood cells, including nucleated RBCs and megakaryocyte fragments, are frequently found in the circulation.

The actual etiology for primary myelofibrosis is still unknown. As with polycythemia vera and essential thrombocythemia, mutations of the *JAK2* or *CALR* gene are frequently seen; prognosis is worse in those without genetic mutations. Myelofibrosis may also be secondary in nature, evolving from polycythemia vera, or less frequently, from essential thrombocythemia. In these instances, the disease progression is then called *secondary myelofibrosis* (Harrison et al., 2017).

Primary myelofibrosis is a disease of the older adult, with a median age of diagnosis at approximately 65 to 70 years of age, and is more common in males (Leukemia & Lymphoma Society, 2019e). Another risk factor is exposure to chemicals (e.g., benzene). Average survival ranges from 2 to 14 years. Common causes of death are due to cardiovascular disease, liver failure, leukemic transformation, and consequences of marrow failure (e.g., infection or bleeding).

Approximately 90% of patients present at the time of diagnosis with splenomegaly, causing abdominal discomfort and early satiety. Many patients also experience constitutional symptoms such as fatigue, night sweats, and fever, as well as pruritus, bone pain, weight loss, cachexia, thrombosis, and bleeding (see Fig. 30-6) (Tefferi, 2018). Arterial or venous thrombosis can occur but is less frequent than that found in polycythemia vera or essential thrombocythemia. Anemia occurs due to impaired erythropoiesis.

Medical Management

The goals of therapy are based upon reducing the burden of disease (by decreasing symptoms and splenomegaly) and improving blood counts (NCCN, 2019f). Treatment is based upon a patient's risk stratification; risks are increased in patients older than 65 years of age, with WBC counts above 25,000/mm³, with hemoglobin levels less than 10 g/dL, with blast cells present in the peripheral blood, and with presence of constitutional symptoms (e.g., pruritus, night sweats, weight loss; see Table 30-2) (NCCN, 2019f).

For patients who are at low risk and asymptomatic, observation and monitoring every 3 to 6 months is recommended. Patients at intermediate risk may be started on the *JAK2* inhibitor ruxolitinib if symptomatic (see previous discussion in Polycythemia Vera), or may be considered for allogeneic HSCT. HSCT is a useful treatment modality in younger, otherwise healthy patients; it is the only current therapy that can reverse the fibrosis within the marrow (NCCN, 2019f).

Splenectomy may be performed to control potential or actual complications of an enlarged spleen. However, a reactive thrombocytosis and leukocytosis can develop because the platelets and leukocytes are no longer sequestered by the spleen and enter the circulation. Careful considerations of the advantages and disadvantages of a splenectomy should be discussed with the patient as the procedure is not without risk.

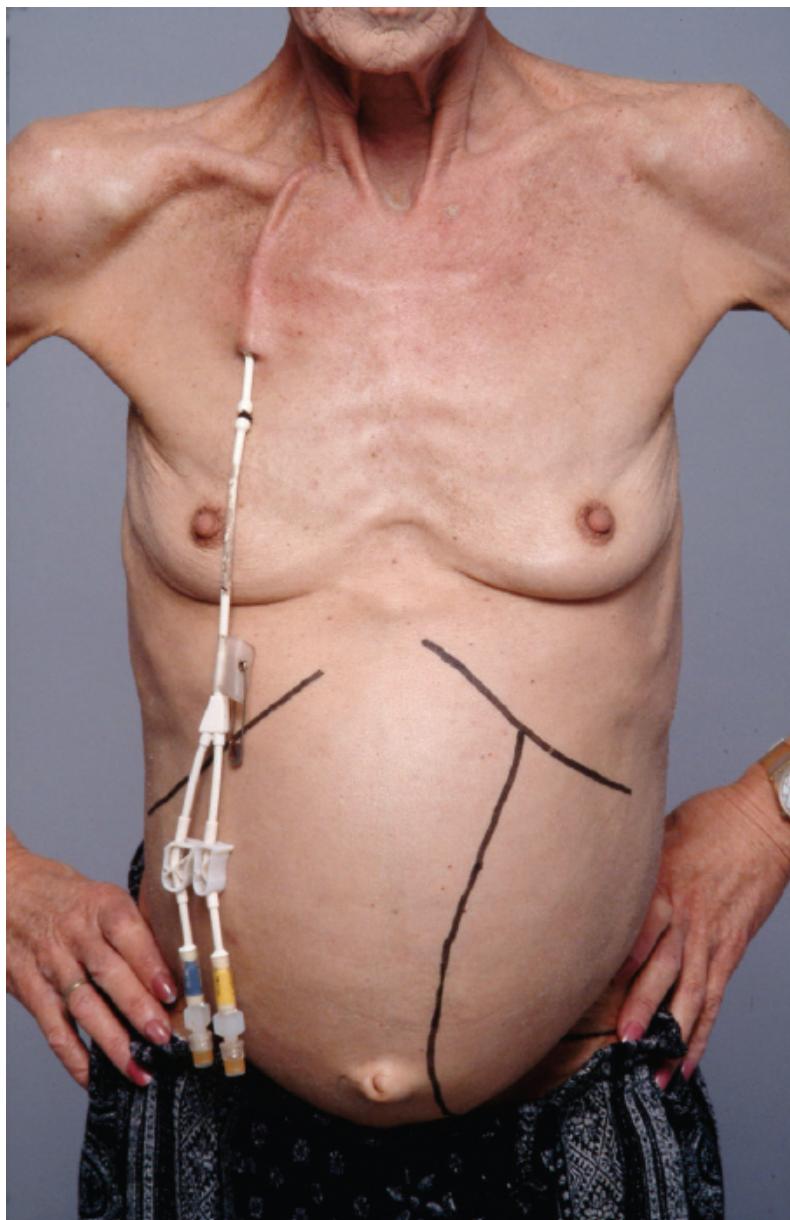


Figure 30-6 • Cachexia, severe wasting, and massively enlarged liver and spleen (hepatosplenomegaly) are seen in advanced myeloproliferative disorders, particularly myelofibrosis. (Note also the lack of adequate dressing over the patient's vascular access device.) Reprinted with permission from Tkachuk, D. C., & Hirschman, J. V. (2007). *Wintrobe's atlas of clinical hematology* (Fig. 4.1, p. 111). Philadelphia, PA: Lippincott Williams & Wilkins.

Anemia is most commonly managed with PRBC transfusions. Erythropoietin-stimulating agents (e.g., recombinant erythropoietin) may improve anemia to the extent that transfusion requirements are reduced. Other pharmacologic agents are used to diminish splenomegaly and improve blood counts. Hydroxyurea is often used to control high leukocyte and platelet counts and to

reduce the size of the spleen. Angiogenic inhibitors such as thalidomide or pomalidomide may be useful in improving anemia and reducing an enlarged spleen.

Nursing Management

Splenomegaly can be profound in patients with myelofibrosis, with enlargement of the spleen that may extend to the pelvic rim. This condition is extremely uncomfortable and can severely limit nutritional intake. Analgesic agents are usually ineffective. Splenomegaly, coupled with the hypermetabolic state that ensues with having an active neoplasm, results in significant weight loss, muscle wasting, and weakness. Patients benefit from small, frequent meals of foods that are high in calories and protein. Fatigue has been reported in up to 94% of patients with primary myelofibrosis (Geyer & Mesa, 2014). The nurse should educate patients about appropriate energy conservation methods. [Table 30-3](#) identifies useful strategies at managing fatigue.

TABLE 30-3 Fatigue in Patients with Myeloproliferative Neoplasms

Self-reported strategies used to ameliorate fatigue by patients with myeloproliferative neoplasms. Data obtained from online surveys ($N = 1788$) gathered via myeloproliferative neoplasm Web sites.

Strategy	% Patients Reported Use
Setting priorities	75%
Postponing nonessential activities	74%
Exercise	73%
Naps	70%
Walking	66%
Socializing	65%
Nutrition	64%
Reading	62%
Scheduling activity during peak energy periods	62%
Pacing activities	58%
Structured daily routine	54%
Delegation	52%

Adapted from Scherber, R. M., Kosiorek, H. E., Senyak, Z., et al. (2016). Comprehensively understanding fatigue in patients with myeloproliferative neoplasms. *Cancer*, 122(3), 477–485.

The patient needs to be educated about signs and symptoms of infection, bleeding, and thrombosis, as well as appropriate interventions if these occur. Ensuring that the patient takes steps to decrease cardiovascular risk factors

associated with developing thrombosis (e.g., obesity, smoking, and poorly controlled hypertension, diabetes, or hyperlipidemia) is also important.

LYMPHOMA

The lymphomas are neoplasms of cells of lymphoid origin. These tumors usually start in lymph nodes but can involve lymphoid tissue in the spleen, GI tract (e.g., the wall of the stomach), liver, or bone marrow (see [Chapter 31](#), [Fig. 31-1](#)). They are often classified according to the degree of cell differentiation and the origin of the predominant malignant cell. Lymphomas are broadly classified into two categories: Hodgkin lymphoma and NHL.

Hodgkin Lymphoma

Hodgkin lymphoma is a relatively rare malignancy that has a high cure rate. It is somewhat more common in males than in females and has two peaks of incidence: one from ages 15 to 34 and the other after 60 years of age (Leukemia & Lymphoma Society, 2018c). The cause of Hodgkin lymphoma is unknown. However, several risk factors have been identified, which include age, a history of viral infections (particularly the Epstein–Barr virus, human immune deficiency virus [HIV], or human herpesvirus 8 [HHV8]), having a family history, and being exposed to cytotoxic agents. Additionally, Hodgkin lymphoma is seen more commonly in patients receiving long-term immunosuppressive therapy (e.g., organ transplant recipients) and in veterans who were exposed to the herbicide Agent Orange (see Veterans Considerations section in CLL) (Leukemia & Lymphoma Society, 2018c). The 5-year survival rate for Hodgkin lymphoma is about 92% to 94% for localized/regional disease (stage I or II) and 78% for those with distant disease (stage IV) (ACS, 2019a).

Pathophysiology

Unlike other lymphomas, Hodgkin lymphoma is unicentric in origin, meaning that it initiates in a single node. The disease spreads by contiguous extension along the lymphatic system. The malignant cell of Hodgkin lymphoma is the Reed–Sternberg cell, a gigantic tumor cell that is morphologically unique and thought to be of immature lymphoid origin. These cells arise from the B lymphocyte. They may have more than one nucleus and often have an owl-like appearance (see [Fig. 30-7](#)). The presence of Reed–Sternberg cells is the pathologic hallmark and essential diagnostic criterion.

The World Health Organization (WHO) has classified Hodgkin lymphoma into five subtypes based on pathologic analyses that reflect the natural history of the disease and suggest the prognosis (NCCN, 2019g). Four of these subtypes of Hodgkin lymphoma are recognized as being consistent with classical disease (Leukemia & Lymphoma Society, 2018c; Spinner, Varma, & Advani, 2018):

- *Nodular sclerosis*: This is the most common form of Hodgkin lymphoma, accounting for about 70% of all cases. It is seen most often in the young; among these patients, the lymph node contains elements of fibrous (sclerotic) tissue; approximately 40% of patients have B symptoms (see **Chart 30-1**). This type of Hodgkin lymphoma is highly curable.

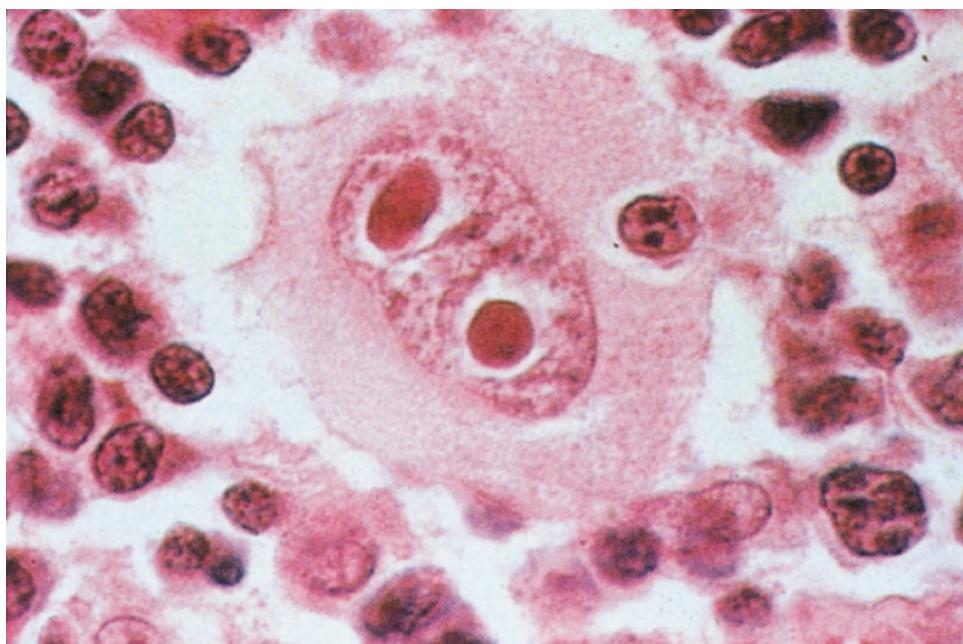


Figure 30-7 • Reed–Sternberg cell. Reed–Sternberg cells are large, abnormal lymphocytes that may contain more than one nucleus. These cells are found in Hodgkin lymphoma. Adapted with permission from Rubin, R., Strayer, D. S., & Rubin, E. (2011). *Rubin's pathology* (6th ed.). Philadelphia, PA: Lippincott Williams & Wilkins.

- *Mixed cellularity*: This is the second most common form of Hodgkin lymphoma, accounting for 20% to 25% of all cases. This subtype is more common in older adults and in males; it is frequently seen in patients with HIV infection, and B symptoms are frequently reported.
- *Lymphocyte-depleted*: This form of Hodgkin lymphoma is rare; it is characterized by involved lymph node(s) with few normal

lymphocytes but numerous Reed–Sternberg cells. B symptoms are commonly reported.

- *Lymphocyte-rich*: This type of Hodgkin lymphoma is also an uncommon form of the disease; the lymph node(s) has numerous normal lymphocytes and Reed–Sternberg cells and B symptoms are rare.
- *Nodular lymphocytes predominant Hodgkin lymphoma* (NLPHL): This is the lone type of Hodgkin lymphoma that is not considered of the classical type. In NLPHL there are few Reed–Sternberg cells; rather, there is a predominance of lymphocyte cells called “popcorn” cells. Furthermore, there is minimal involvement of the lymph nodes as compared to the subtypes that fall under the four classical Hodgkin types. NLPHL is seen more often in males than females and the age at diagnosis is more often between 30 and 50 years. Patients tend to present with peripheral adenopathy and with early-stage disease. NLPHL is slow growing and highly curable, but some patients can relapse while others can transform to an aggressive NHL (see later discussion).

Clinical Manifestations

Hodgkin lymphoma usually begins as an enlargement of one or more lymph nodes on one side of the neck. The individual nodes are painless and firm but not hard. The most common sites for lymphadenopathy are the cervical nodes. However, other nodes that can be affected include the supraclavicular and mediastinal nodes; involvement of the iliac or inguinal nodes or spleen is much less common (Leukemia & Lymphoma Society, 2018c). A mediastinal mass may be seen on chest x-ray; occasionally, the mass is large enough to compress the trachea and cause dyspnea. B symptoms, if present, are indicative of more advanced disease (see **Chart 30-1**). These symptoms are found in about 40% of patients with Hodgkin lymphoma and are used in determining stage and prognosis (NCCN, 2019g).

All organs are vulnerable to invasion by tumor cells. Clinical manifestations result from compression of organs by the tumor, such as cough and pulmonary effusion (from pulmonary infiltrates), jaundice (from hepatic involvement or bile duct obstruction), abdominal pain (from splenomegaly or retroperitoneal adenopathy), or bone pain (from skeletal involvement). A mild anemia is the most common hematologic finding. The leukocyte count may be elevated or decreased. The platelet count is typically normal, unless the tumor has invaded the bone marrow, suppressing hematopoiesis. Laboratory tests that may be assessed to detect disease activity include the serum copper level, which may be elevated, and the **erythrocyte sedimentation rate** (ESR). The ESR

measures the rate of settling of RBCs; elevation is indicative of inflammation; it is also called the *sed rate*.



Figure 30-8 • Herpes zoster is a common complication in patients with lymphoproliferative disease, such as Hodgkin lymphoma here. Zoster infections are also common in patients on chronic steroid use for hematologic conditions and some chemotherapy regimens.

Reprinted with permission from Tkachuk, D. C., & Hirschman, J. V. (2007). *Wintrobe's atlas of clinical hematology* (Fig. 5.152, p. 207). Philadelphia, PA: Lippincott Williams & Wilkins.

Other symptoms seen in patients with Hodgkin lymphoma are pruritus, which is common and can be extremely distressing, fatigue, decreased appetite, abdominal pain, splenomegaly, and although rare, occasional pain in affected lymph node after drinking alcohol (Leukemia & Lymphoma Society, 2018c). Patients may also have impaired cellular immunity, as evidenced by an absent or decreased reaction to skin sensitivity tests (i.e., Candida, mumps) and increased susceptibility to infections, particularly herpes zoster (see Fig. 30-8).

Assessment and Diagnostic Findings

Because many manifestations are similar to those occurring with infection, diagnostic studies are performed to rule out an infectious origin of the disease. The diagnosis is made by means of an excisional lymph node biopsy and the presence of Reed–Sternberg cells. Once the diagnosis is confirmed and the histologic type is established, it is necessary to assess the stage of the disease.

During the health history, the patient is assessed for any B symptoms (see [Chart 30-1](#)). Physical examination requires a careful, systematic evaluation of all palpable lymph node chains (see [Chapter 28, Fig. 28-4](#)), as well as the size of the spleen and liver. A chest x-ray and a computed tomography (CT) scan of the chest, abdomen, and pelvis are crucial to identify the extent of lymphadenopathy within these regions. A positron emission tomography (PET) scan is the most sensitive imaging test and is recommended for initial staging to help determine the extent of disease as well as later for evaluation of response to treatment (NCCN, 2019g). Laboratory tests include CBC with differential; serum electrolytes, blood urea nitrogen (BUN) and creatinine; ESR; liver and renal function studies; immunohistochemistry and cytogenetic evaluation; HIV testing; and hepatitis B and C testing. A multiple-gated acquisition (MUGA) scan and/or ECG should be performed prior to the start of therapy if the patient is to receive an anthracycline-based treatment regimen, as these chemotherapeutic agents are associated with adverse cardiovascular effects. Bone marrow biopsies are not routinely performed unless cytopenias are present and the PET scan is negative (NCCN, 2019g).

Medical Management

The goal in the treatment of Hodgkin lymphoma is cure, as the overall cure rate is about 90% (ACS, 2019a). Treatment is determined primarily by stage of disease, not histologic type, utilizing the Ann Arbor staging system (see [Fig. 30-9](#)).

Treatment guidelines for classical Hodgkin lymphoma (NCCN, 2019g) divide patients into groups. Patients with early disease (stage I-II) may receive one of the following combination chemotherapy regimens: ABVD (doxorubicin [trade name Adriamycin], bleomycin, vinblastine, and dacarbazine) or Stanford V (doxorubicin, vinblastine, mechlorethamine, etoposide, vincristine, bleomycin, and prednisone) (see [Chapter 12, Table 12-7](#), for further discussion of specific categories of chemotherapeutic/antineoplastic agents). Radiation therapy may or may not be included as part of the treatment regimen.

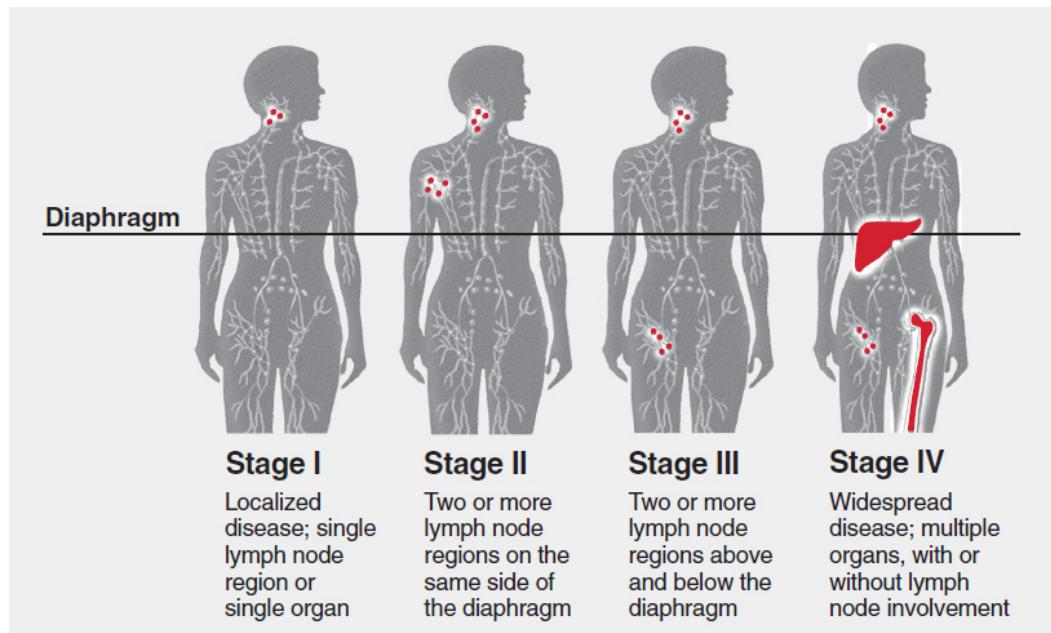


Figure 30-9 • Stages of Hodgkin lymphoma based upon the Ann Arbor staging system. Each category is subdivided and assigned to one of the following categories: Category A indicates no symptoms are present. Category B indicates the presence of B symptoms (see Chart 30-1). Category E indicates involvement of organs or tissues beyond the lymphatic system. Category S indicates involvement of the spleen. Image used with permission of The Leukemia & Lymphoma Society (Hodgkin Lymphoma, 2020).

The standard treatment for patients with advanced disease (stages III to IV) and those with B symptoms is also ABVD chemotherapy, although these patients typically receive additional cycles of chemotherapy treatment. Other combinations of chemotherapy may be used; however, these options have more toxic effects.

When a patient has a suspected relapse of disease, a biopsy and a PET scan are performed to confirm the diagnosis and stage of disease. Treatment options for patients with refractory or relapsed disease include immunotherapeutic agents, such as a monoclonal antibody (MoAb) (e.g., everolimus, brentuximab), or a checkpoint inhibitor (e.g., nivolumab, pembrolizumab) (see discussion of MoAbs and checkpoint inhibitors in Chapter 12) (Leukemia & Lymphoma Society, 2018c; NCCN, 2019g).

Treatment for patients with NLPHL in the early stage of disease may include radiation therapy only. In a few instances (patients who are stage IA), observation rather than any therapy may be an option (Spinner et al., 2018). Patients with stage IB to IIB disease may receive ABVD, CHOP (cyclophosphamide, doxorubicin [also less commonly called hydroxydaunorubicin], vincristine [trade name of **Oncovin**], and **prednisone**),

or CVP (*cyclophosphamide*, *vincristine*, and *prednisone*) regimens in combination with rituximab. Those with advanced stage disease are treated with these same regimens but with radiation therapy added.

Patients typically feel better following therapy. Late effects of treatment, which may occur months to years following treatment, include development of a secondary malignancy, or cardiovascular disease, hypothyroidism, and infertility (Leukemia & Lymphoma Society, 2018c; NCCN, 2019g). Secondary malignancies (most common are lung and breast) often develop more than 10 years following completion of therapy. This is especially true in females who received radiation therapy to the chest or axillary areas (NCCN, 2019g).

Cardiovascular disease (e.g., coronary artery disease, arrhythmias, and cardiomyopathy) is also seen 10 years posttreatment and tends to occur in patients who received mediastinal radiation or an anthracycline-based chemotherapeutic agent (e.g., daunorubicin, doxorubicin). Hypothyroidism may occur in about 50% of long-term survivors of Hodgkin lymphoma, particularly in those who received neck or upper mediastinal radiation (NCCN, 2019g). The use of some chemotherapy combinations can lead to infertility in both males and females. For instance, females of childbearing years may experience premature menopause following treatment with alkylating agents (e.g., cyclophosphamide, dacarbazine, mechlorethamine). Other organ dysfunction is also well documented, including that of the endocrine system. Persistent fatigue is common in survivors and can be exacerbated by depression and other treatment-related comorbidities (ACS, 2019a; Leukemia & Lymphoma Society, 2018c; NCCN, 2019g). Potential long-term complications associated with chemotherapy are listed in [Chapter 12, Chart 12-4](#).

Nursing Management

The potential development of a second malignancy should be addressed with the patient when initial treatment decisions are made. However, patients need to be informed that Hodgkin lymphoma is often curable. The nurse should encourage patients to reduce factors that increase the risk of developing second cancers, such as use of tobacco and alcohol and exposure to environmental carcinogens and excessive sunlight. Screening for late effects of treatment, such as chemotherapy (see [Chapter 12, Chart 12-4](#)), is necessary. In addition, the nurse should provide education about relevant self-care strategies and disease management. See also the Nursing Management Section for Non-Hodgkin Lymphoma.

Non-Hodgkin Lymphomas

The NHLs are a heterogeneous group of cancers that originate from the neoplastic growth of lymphoid tissue. Similar to CLL, the neoplastic cells are thought to arise from a single clone of lymphocytes; however, in NHL, the cells may vary morphologically. In contrast to Hodgkin lymphoma, the lymphoid tissues involved are largely infiltrated with malignant cells. The spread of these malignant lymphoid cells occurs unpredictably; true localized disease is uncommon. Lymph nodes from multiple sites may be infiltrated, as may sites outside the lymphoid system (i.e., extranodal tissue; see [Fig. 30-10](#)).



Figure 30-10 • Any extranodal location can be a site for diffuse B-cell lymphoma, such as the thyroid, as shown here. Reprinted with permission from Tkachuk, D. C., & Hirschman, J. V. (2007). *Wintrobe's atlas of clinical hematology* (Fig. 5.87, p. 183). Philadelphia, PA: Lippincott Williams & Wilkins.

TABLE 30-4 Select Types of Lymphomas

Indolent	Aggressive
Cutaneous T cell	Anaplastic large cell
Follicular	AIDS associated
Gastric MALT	Burkitt
Lymphoplasmacytic: Waldenstrom macroglobulinemia	Diffuse large B cell
Marginal zone B cell	Mantle cell
Small-cell lymphocytic	Peripheral T cell

AIDS, acquired immune deficiency syndrome; MALT, mucosa-associated lymphoid tissue.

Adapted from Leukemia & Lymphoma Society. (2016). NHL subtypes. Retrieved on 5/14/2020 at: www.lls.org/lymphoma/non-hodgkin-lymphoma/diagnosis/nhl-subtypes

Approximately 85% of NHLs involve malignant B-cell lymphocytes, with the remaining 15% involving T-cell lymphocytes or natural killer cells (NCCN, 2019h). NHL is the seventh most common type of cancer diagnosed in the United States, accounting for about 4% to 5% of all new cancer cases each year. It occurs more commonly in males (NCCN, 2019h). The incidence increases with each decade of life; the median age at diagnosis is 66 years (Leukemia & Lymphoma Society, 2018d). The natural course of the disease is variable and dependent upon the type of lymphoma. NHLs can be categorized as **indolent** (i.e., a slow-growing cancer that often remains localized or causes few symptoms) or aggressive (i.e., a fast-growing cancer that spreads rapidly and causes significant morbidity) (see Table 30-4). For example, the 5-year survival rate for diffuse large B-cell lymphoma is 72%; for follicular lymphoma it is about 90% (96% localized disease and 85% for distant disease) (ACS, 2019b).

Although no common etiologic factor has been identified, the incidence of NHL is increased in patients who have immune deficiencies or autoimmune disorders; had prior treatment for cancer; been an organ transplant recipient; had a history of viral infections (e.g., Epstein–Barr virus, HIV, HHV8); and been exposed to herbicides, pesticides, solvents, dyes, and defoliating agents, such as Agent Orange (see Veterans Considerations section in CLL) (ACS, 2019b).

Clinical Manifestations

Symptoms of NHL are highly variable, reflecting the diverse nature of the disease. Similar to Hodgkin lymphoma, NHL may start as a painless swelling in one or more lymph nodes in the neck, axillary region, or groin. If the lymphoma is indolent in nature, symptoms may be absent or very minor.

Indolent disease accounts for about 40% of all NHL cases (Leukemia & Lymphoma Society, 2018d). However, the majority of patients are not diagnosed until the disease has progressed to a later stage, when they have become symptomatic. About one third of patients with NHL have B symptoms (see **Chart 30-1**) at the time of diagnosis (Leukemia & Lymphoma Society, 2018d).

Other symptoms depend upon enlarged lymph node site and size, which can compress organs, compromising function. For example, a mass in the mediastinum can cause cough, shortness of breath, and chest pain that may lead to cardiovascular or respiratory distress. An abdominal mass may compromise the bowel or ureters, leading to acute kidney injury or bowel obstruction. Splenomegaly can cause abdominal pain, nausea, early satiety, and weight loss.

Assessment and Diagnostic Findings

Similar to Hodgkin lymphoma, an incisional or excisional lymph node biopsy is required for immunophenotyping and cytogenetic analysis testing (NCCN, 2019h). The specific histopathologic type of the disease is used to differentiate the subtype of NHL; it also has important prognostic implications and is used to determine appropriate treatment (Leukemia & Lymphoma Society, 2018d). Flow cytometry is commonly performed to determine the specific antigen on the malignant cell. Another test that may be performed is fluorescence in situ hybridization (FISH), which analyzes the DNA and RNA of the biopsy or blood sample for chromosomal abnormalities.

Laboratory studies mirror those done for a patient with Hodgkin lymphoma (see that previous discussion). In addition, there may be testing for viruses (e.g., Epstein–Barr, HHV8, hepatitis B); polymerase chain reaction (PCR); CT scans of the chest, abdomen, and pelvis; PET scan; MUGA or ECG (if patient is to receive anthracycline-based regimen); and bone marrow biopsy and aspirate (if marrow involvement is suspected).

Although the stage of disease is important, often it is not an accurate predictor of prognosis. Two prognostic classification systems are used: the International Prognostic Index (IPI) and, for follicular lymphomas, the Follicular Lymphoma International Prognostic Index (FLIPI). Age, performance status, lactate dehydrogenase levels, stage of disease, and extranodal involvement are scored to determine risk of failure or death from disease (ACS, 2020b).

Medical Management

The goal of treatment for NHL is to obtain remission of disease by killing as many of the malignant cells as possible; in contrast, the goal is cure for

Hodgkin lymphoma. Treatment for NHL is based upon the specific subtype of lymphoma and the stage of disease. Other factors that impact treatment decisions include the patient's age, functional status, laboratory values (especially renal, hepatic, and cardiac), comorbid conditions, and presence of extranodal involvement (i.e., presence of cancer cells outside of the lymph nodes) (Leukemia & Lymphoma Society, 2016). If the disease is indolent and localized, the treatment of choice may be radiation therapy alone. "Watchful waiting" may also be a choice for patients with an indolent form of NHL, such as stage I follicular lymphoma, who have no or few symptoms at time of diagnosis.

For aggressive subtypes of NHL, combination chemotherapy is typically indicated. One of the most common combinations is CHOP. A MoAb (e.g., rituximab, obinutuzumab) may be given along with the chemotherapy (NCCN, 2019h). Radiation therapy may or may not be added to the treatment regimen. In some cases, a MoAb may be conjugated with a radioactive isotope and used for treatment (e.g., ibritumomab tiuxetan). CNS involvement is common with some aggressive forms of NHL; in this situation, cranial radiation or intrathecal chemotherapy is used in addition to systemic chemotherapy.

When NHL has relapsed or is refractory to standard treatments, other single agent or combination chemotherapy regimens may be used. For instance, the ICE regimen (i.e., ifosfamide, carboplatin, and etoposide) may be implemented; or agents such as bendamustine, brentuximab vedotin, romidepsin, or axicabtagene may be tried (NCCN, 2019h). Autologous HSCT (AuHSCT) is another treatment option for relapsed or refractory NHL, particularly in patients younger than 60 years (see [Chapter 12](#) for further discussion of AuHSCT).

A rare but potentially life-threatening complication of chemotherapy is tumor lysis syndrome. Tumor lysis syndrome occurs when the intracellular content of the malignant cell breaks down and is released into the peripheral blood and typically occurs 12 to 72 hours after initiation of therapy (NCCN, 2019h). Patients with NHL at highest risk for the development of tumor lysis syndrome are those with large bulky disease and/or deemed to have high-risk or aggressive NHL (e.g., Burkitt's or diffuse large B-cell lymphoma [DLBCL]). See [Chapter 12, Table 12-13](#), for a discussion of manifestations of and treatment for tumor lysis syndrome.

Reactivation of hepatitis B virus may be seen in patients with NHL who become immunosuppressed following chemotherapy. For example, hepatitis B reactivation can occur in patients treated with rituximab-containing regimens, even if the patient had tested negative for hepatitis B prior to start of treatment (Leukemia & Lymphoma Society, 2018d). Preemptive treatment is recommended, including antiviral therapy (i.e., lamivudine or entecavir) and close surveillance in patients at high risk.

Another rare but potentially life-threatening complication is progressive multifocal leukoencephalopathy, which may occur in patients with NHL who are severely immunocompromised and treated with chemotherapeutic agents (Leukemia & Lymphoma Society, 2018d; NCCN, 2019h). Symptoms include confusion, motor weakness or poor motor coordination, and visual and possibly speech changes. Currently, there is no effective treatment for this complication. The fatality rate is 90% and tends to occur within 2 months after the diagnosis is confirmed (NCCN, 2019h).

Nursing Management

Lymphoma is a highly complex constellation of diseases. When caring for patients with lymphoma, it is extremely important for the nurse to know the specific disease type, stage of disease, treatment history, and current treatment plan. Most of the care for patients with Hodgkin lymphoma or NHL takes place in the outpatient setting, unless complications occur (e.g., infection, respiratory compromise due to mediastinal mass). The most commonly used treatment methods are chemotherapy (often combined with a MoAb) and radiation therapy. Chemotherapy causes systemic side effects (e.g., myelosuppression, nausea, hair loss, risk of infection), whereas radiation therapy causes specific side effects that are limited to the area being irradiated. For example, patients receiving abdominal radiation therapy may experience nausea and diarrhea but not hair loss. Regardless of the type of treatment, all patients may experience fatigue (see [Chapter 12, Chart 12-6, Fatigue](#)).

The risk of infection is significant for these patients, not only from treatment-related myelosuppression but also from the defective immune response that results from the disease itself. Patients need to be educated to minimize the risks of infection, to recognize signs of possible infection, and to contact their primary provider if such signs develop (see [Chapter 12, Chart 12-6, Infection](#)).

Many lymphomas can be cured with current treatments. However, as survival rates increase, the incidence of second malignancies, particularly AML or MDS, also increases. Therefore, survivors should be screened regularly for the development of second malignancies. Survivors of both Hodgkin lymphoma and NHL may be faced with managing persistent fatigue, depression, anxiety, and cardiac and pulmonary toxicity (ACS, 2019b). Therefore, survivors should be encouraged to have regular follow-up appointments and be screened for the signs and symptoms of possible secondary malignancies. Additionally, patients should be evaluated for cardiovascular and fertility concerns with each patient visit.

The ACS (2019b) developed health behavior recommendations for cancer survivors, which include avoiding or stopping smoking, maintaining a normal body weight, practicing good nutrition habits (i.e., consuming fruits and

vegetables), and engaging in a minimum of 150 minutes of exercise per week. While many survivors do not adhere to these recommendations, those patients who do report higher health-related quality of life (ACS, 2019b).

MULTIPLE MYELOMA

Multiple myeloma is a malignant disease of the most mature form of B lymphocyte—the plasma cell. Plasma cells secrete immunoglobulins, which are proteins necessary for antibody production to fight infection. This disease accounts for approximately 1.8% of all cancers and about 17% of the hematologic malignancies in the United States (NCCN, 2019i). The etiology of multiple myeloma is not known, but risk factors are identified (see **Chart 30-3**). The incidence of multiple myeloma increases with age; the median age at diagnosis is approximately 70 years (NCCN, 2019i; Rajkumar, 2018). This disease, if left untreated, can lead to bone destruction and bone marrow failure. Due to the increased number of newer agents to fight multiple myeloma, survival of this disease has significantly improved in the last 5 years.

Pathophysiology

In multiple myeloma, the malignant plasma cells produce a specific immunoglobulin that is nonfunctional. Functional types of immunoglobulins are still produced by nonmalignant plasma cells, but in lower-than-normal quantities. The specific immunoglobulin secreted by the malignant plasma cells is referred to as the monoclonal protein, or M protein. Malignant plasma cells also secrete certain substances to stimulate angiogenesis to enhance the growth of these clusters of plasma cells. Occasionally, the malignant plasma cells infiltrate other tissue, in which case they are referred to as plasmacytomas. Plasmacytomas can occur in the sinuses, spinal cord, and soft tissues.

Chart 30-3 RISK FACTORS

Multiple Myeloma

- Age: rarely occurs in those less than 35 years of age; risks increase with increasing age
- African Americans have twice the risk of Whites
- Exposure to radiation, petroleum products, benzenes, and Agent Orange
- Family history, particularly among first-degree relatives (e.g., siblings, parents)
- Men have slightly higher risks than women
- Overweight or obesity
- Plasma cell disease history:
 - Monoclonal gammopathy of undetermined significance (MGUS)
 - Plasmacytoma^a

^aNote: in rare instances, may precede multiple myeloma.

Adapted from American Cancer Society (ACS). (2018). Risk factors for multiple myeloma. Retrieved on 5/15/2020 at: www.cancer.org/cancer/multiple-myeloma/causes-risks-prevention/risk-factors.html; National Comprehensive Cancer Network (NCCN). (2019i). Clinical practice guidelines in oncology: Multiple myeloma. Version 2.2019. Retrieved on 7/10/2019 at: www.nccn.org/professional/physician_gls/pdf/myeloma.pdf; Rajkumar, S. (2018). Multiple myeloma: 2018 update on diagnosis, risk-stratification, and management. *American Journal of Hematology*, 93, 1091–1110.

Multiple myeloma may evolve from a premalignant stage, known as monoclonal gammopathy of undetermined significance (MGUS) (NCCN, 2019i). Although patients with MGUS have the M protein in their blood, they generally do not have any signs and symptoms that are seen in multiple myeloma. Patients with MGUS are monitored for signs and symptoms indicative of disease progression to multiple myeloma. The rate of progression from MGUS to multiple myeloma is 0.5% to 1% per year (Rajkumar, 2018).

Clinical Manifestations

Clinical manifestations of multiple myeloma result not only from the malignant cells themselves, but also from the abnormal protein they produce. The classic clinical manifestations of multiple myeloma are referred to as the CRAB features, because they refer to the following:

- hyper**Calcemia**
- **Renal** dysfunction
- **Anemia**
- **Bone** destruction

Bone-related manifestations may be seen in up to 85% of patients with multiple myeloma (NCCN, 2019i). Bone pain (usually in the back or ribs) is considered to be a classic presenting symptom. Bone pain associated with multiple myeloma increases with movement and decreases with rest; patients may report that they have less pain on awakening but more during the day. In multiple myeloma, a substance secreted by the malignant plasma cells, osteoclast activating factor, and other substances, such as interleukin-6 (IL-6) stimulate osteoclasts, which break down bone matrix. In some cases, the bone breakdown or lysis can be severe enough to cause vertebral collapse and fractures, including spinal fractures, which can impinge on the spinal cord and result in spinal cord compression (see Fig. 30-11). When vertebral collapse occurs, the patient's height is reduced and kyphosis (an excessive curvature of the spine) is common.

If the bone lysis is extensive, bone lesions result and excessive ionized calcium is lost from the bone and enters the serum; hypercalcemia may therefore develop and may be manifested by excessive thirst, dehydration, constipation, altered mental status, confusion, and perhaps coma.



Quality and Safety Nursing Alert

Any older adult whose chief complaint is back pain and who has an elevated total protein level should be evaluated for possible multiple myeloma.

Renal dysfunction occurs in 33% of patients at the time of diagnosis, while 50% will experience renal dysfunction at some point during the course of the disease (Chim, Kumar, Orlowski, et al., 2018; NCCN, 2019i). The etiology of renal dysfunction is multicausal and related to: myeloma kidney as the result of Bence–Jones proteins (i.e., myeloma infiltration of the kidneys) causing obstruction in the renal tubules; hypercalcemia as the result of bone matrix lysis; amyloid deposits which may lead to renal insufficiency and/or hydronephrosis; and hyperviscosity leading to renal tubule obstruction. Other

causes of renal dysfunction in patients with multiple myeloma are infections, use of NSAIDs, and nephrotoxic agents (e.g., chemotherapy) to treat multiple myeloma (Faiman, Doss, Colson, et al., 2017).

As more malignant plasma cells are produced, the marrow has less space for erythrocyte production, and anemia may develop. If renal dysfunction is also present, anemia may also be caused by a diminished production of erythropoietin by the kidney. In the late stage of the disease, a reduced number of leukocytes and platelets may also be seen because the bone marrow is infiltrated by malignant plasma cells.

Assessment and Diagnostic Findings

All patients suspected of having multiple myeloma should have a CBC with differential, BUN, serum creatinine, creatinine clearance, serum electrolytes (especially calcium and albumin), LDH, and beta-2 microglobulin analyzed. Elevated BUN and creatinine may be indicative of renal dysfunction. The total protein level is frequently elevated because of the production of M protein. LDH and beta-2 microglobulin measure degree of tumor burden. In addition to these, a peripheral smear of the blood may reveal an abnormal stacking of RBCs (known as Rouleaux formation) due to elevated serum proteins (NCCN, 2019i). Serum protein electrophoresis or free light chain assay should be performed to detect the presence of M protein (see Fig. 30-12). This protein is elevated in patients with multiple myeloma and serves as a useful marker to monitor the extent of the disease and to gauge the patient's eventual response to therapy. Additionally, cytogenetic studies are performed to see if any of several chromosomal abnormalities typically found in patients with multiple myeloma are present. Radiographic evaluation (CT scan, MRI, and PET scan) should be performed to determine the presence of lytic bone lesions. Bone marrow aspiration and biopsy are conducted to evaluate bone marrow plasma cell abnormalities.

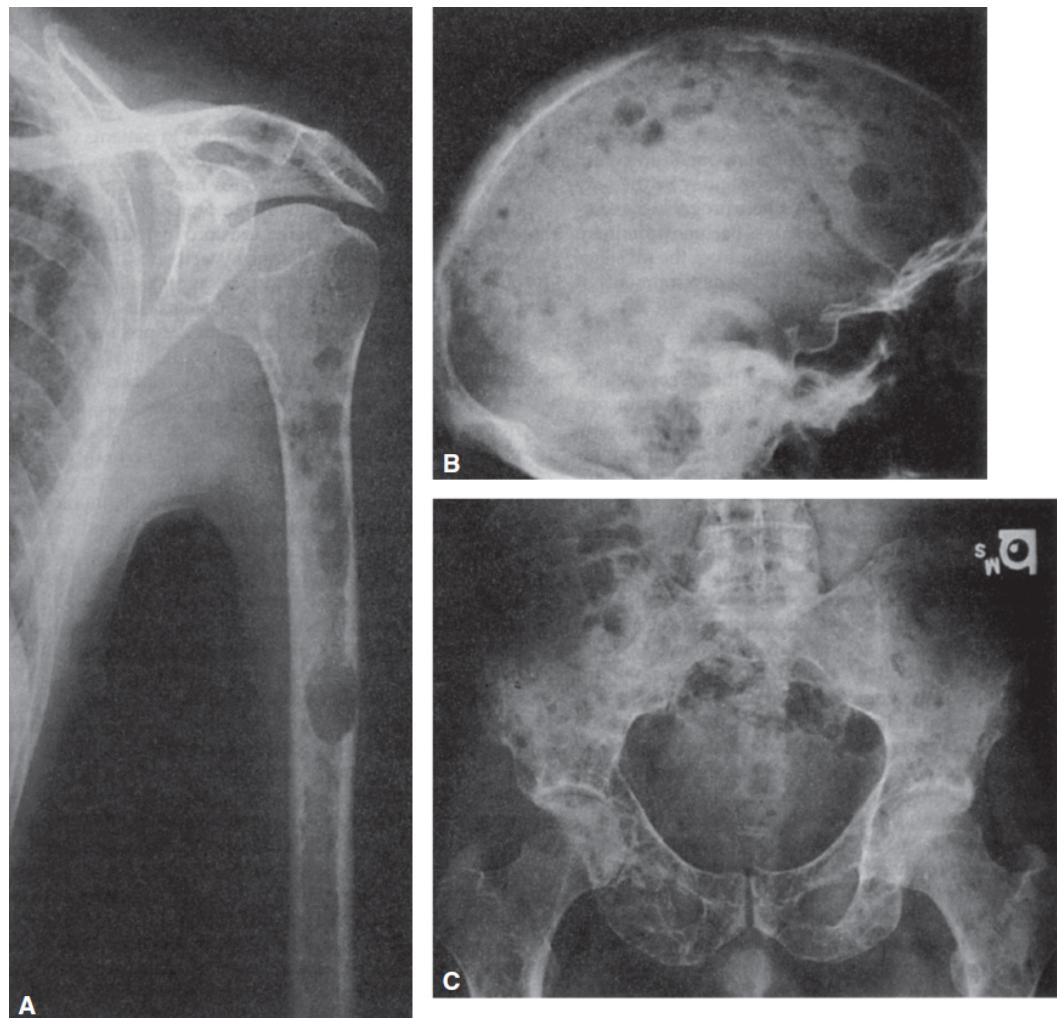


Figure 30-11 • Lytic lesions seen in the humerus and skull in patients with multiple myeloma. These lesions typically occur in the long bones, vertebrae, and skull. Long bones are susceptible to fracture when the lesion occurs near the surface of the bone; vertebrae are susceptible to collapse, resulting in loss of height and potential for spinal cord compression. Reprinted with permission from *Wintrobe's clinical hematology* (10th ed., p. 2640). Philadelphia, PA: Lippincott Williams & Wilkins.

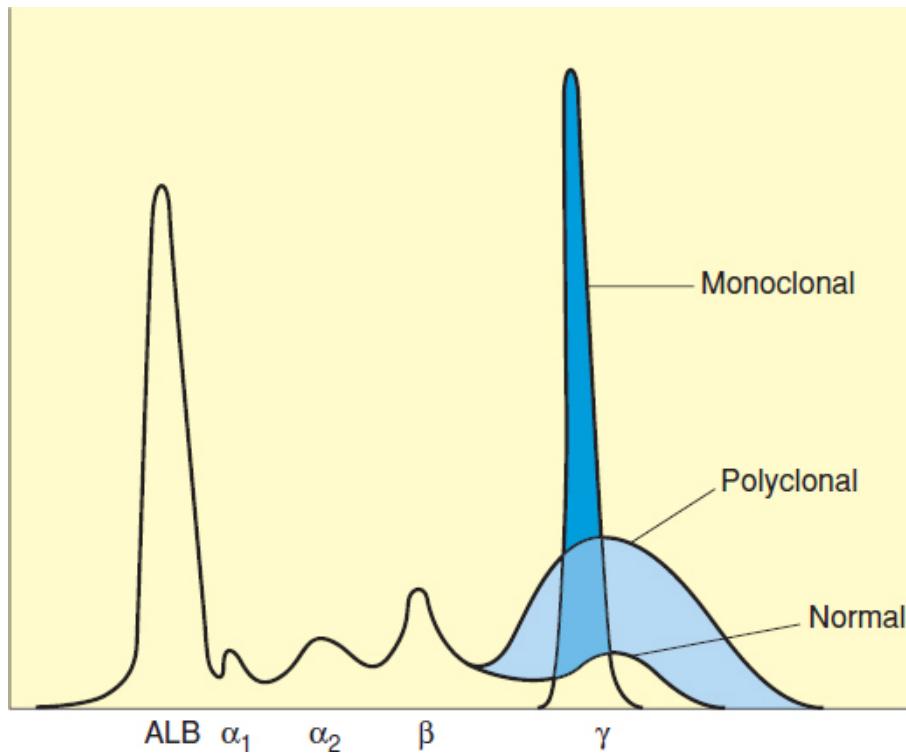


Figure 30-12 • Abnormal serum protein electrophoresis patterns contrasted with a normal pattern. Polyclonal peaks are characterized by a broad-based increase in immunoglobulin (Ig) by myriad reactive plasma cells and indicate a benign reactive process. In contrast, a narrow spike indicates homogeneity of the Ig secreted by a single clone of plasma cells. M spikes are seen in monoclonal gammopathies of undetermined significance or in plasma malignancies (myeloma, Waldenstrom macroglobulinemia). Reprinted with permission from Turgeon, M. (2012). *Clinical hematology theory & procedures* (5th ed., Fig. 20.7, p. 347). Philadelphia, PA: Lippincott Williams & Wilkins.

Diagnosis and staging of multiple myeloma was traditionally based on the CRAB criteria, and included:

- hypercalcemia ($>11.5 \text{ mg/dL}$)
- renal insufficiency (creatinine $>2 \text{ mg/dL}$ or creatinine clearance of less than 40 mL/min)
- anemia (hemoglobin less than 10 g/dL or 2 g/dL less than normal)
- the presence of bony lesions.

The International Myeloma Working Group (IMWG) recently revised the metrics used to define the disease to include specific biomarkers (clonal plasma cells on bone marrow biopsy of 60% or greater, involved/uninvolved serum free light chain ratio of 100 or greater, and/or more than one focal lesion on MRI that is at least 5 mm or greater in size) in addition to any one or more

of the CRAB criteria (NCCN, 2019i; Rajkumar, 2018). This revision is believed to facilitate earlier diagnosis and implementation of treatment (NCCN, 2019i).

Medical Management

There is no cure for multiple myeloma; the aims of treatment are to reduce symptoms and to prolong disease progression. Therapy has changed substantively for multiple myeloma, and has resulted in impressive increases in duration of survival. Importantly, patients not only live longer, the new treatment modalities provide the opportunity for enhanced quality of life. Management of multiple myeloma depends upon whether the patient has smoldering (asymptomatic) or active (symptomatic) disease. Smoldering multiple myeloma is similar to MGUS as patients do not report any symptoms; however, there are higher levels of M protein than seen in MGUS and malignant plasma cells are present.

For most patients with smoldering multiple myeloma, observation with close surveillance for the possibility of transforming to symptomatic disease every 3 to 6 months is the standard of care (NCCN, 2019i; Rajkumar, 2018). Patients who present with symptomatic disease are evaluated for eligibility for an autologous HSCT (AuHSCT), based on age, presence of comorbidities, and risk stratification (Rajkumar, 2018).

Primary treatment for patients who are eligible for AuHSCT includes several cycles of a combination of different pharmacologic agents before stem cells are procured. These drugs all target the disease via different mechanisms than do conventional chemotherapeutic agents. Combinations of two or three drugs are commonly used with the goal of reducing the tumor burden as much as possible. These frequently include either one of the following two regimens (Rajkumar, 2018):

- Proteasome inhibitor–based bortezomib regimen, which commonly includes an immunomodulatory drug (e.g., lenalidomide, pomalidomide, or thalidomide) and the corticosteroid dexamethasone.
- MoAb-based daratumumab regimen, which commonly includes either an immunomodulatory drug (e.g., lenalidomide, pomalidomide, or thalidomide) or a proteasome inhibitor (e.g., bortezomib, carfilzomib, or ixazomib) and the corticosteroid dexamethasone.

Other agents that may be part of these regimens include doxorubicin, cyclophosphamide, cisplatin, or etoposide (see [Table 30-5](#)).

AuHSCT is considered to be the standard of care for patients with multiple myeloma following primary therapy (NCCN, 2019i), as it has demonstrated improved response rates, improved quality of life, and increased overall

survival. AuHSCT may also be indicated in patients with relapsed and refractory multiple myeloma. Single AuHSCT and tandem AuHSCT (with two AuHSCT within a 6-month period) are possible options. Another option could be an allogeneic HSCT; however, this is considered an inferior option to AuHSCT as it is associated with increased morbidity and mortality (Rajkumar, 2018).

Lenalidomide is recommended as maintenance therapy for patients following an AuHSCT and after the initial 8 to 12 cycles of primary therapy for patients who have not received an HSCT. Bortezomib may be used as an alternative maintenance treatment in patients who are intermediate to high risk.

Patients who are not candidates for AuHSCT might be prescribed the three-drug, bortezomib-based regimen, as this regimen is associated with a better response rate. For older adults or frail patients, two-drug regimens may be given (e.g., lenalidomide and dexamethasone) (Rajkumar, 2018). The regimen for patients with renal dysfunction includes bortezomib, cyclophosphamide, and dexamethasone (NCCN, 2019i).

In addition to these agents, all patients with multiple myeloma should be prescribed a bisphosphonate, such as pamidronate or zoledronic acid (NCCN, 2019i). Bisphosphonates have been shown to strengthen bone by diminishing survival of osteoclasts, thus controlling bone pain and potentially preventing bone fractures. These agents are also effective in managing and preventing hypercalcemia by preventing excessive bone resorption. Some evidence suggests that bisphosphonates may activate an antimyeloma immune response, inducing myeloma cell death, acting synergistically with antineoplastic drugs, and enhancing immune surveillance (Faiman et al., 2017) (see [Chapter 36](#), [Table 36-1](#), for further discussion of bisphosphonates).

Complications

Infection is a potential complication of multiple myeloma and a frequent cause of morbidity and mortality. In contrast to other hematologic malignancies, the incidence of infection does not appear to be related to the extent of neutropenia in patients with multiple myeloma. Rather, the lack of adequate levels of normal immunoglobulins, as well as other alterations of the immune system, renders the patient at increased risk for developing infection, particularly due to *Streptococcus pneumoniae* or *H. influenzae*. Therapy for the disease also predisposes the patient for acquiring infections, particularly when corticosteroids are used in treating the disease; herpes zoster and *Pneumocystis* are common causative organisms in this context (NCCN, 2019i). Infection prophylaxis with antiviral agents and antibiotics (e.g., trimethoprim-sulfamethoxazole) is important to decrease infection risk.

When plasma cells secrete excessive amounts of immunoglobulin, the serum viscosity can increase. Hyperviscosity may be manifested by bleeding

from the nose or mouth, headache, visual changes such as blurred vision or diplopia, paresthesias, or heart failure. The incidence of hyperviscosity is rare but does have the potential to be lethal. It is considered to be an oncologic emergency and as such, requires immediate intervention with aggressive hydration and plasmapheresis or therapeutic phlebotomy to reduce immunoglobulin and protein levels and to decrease symptoms (see [Chapter 28](#), [Table 28-3](#), for further discussion of plasmapheresis).

Neurologic complications can also occur. Spinal cord compression is the most common (see [Chapter 12](#), [Table 12-13](#), for discussion of manifestations and management of spinal cord compression), and other neurologic symptoms may be present, particularly peripheral neuropathy. Peripheral neuropathy may occur in as many as 75% of patients with multiple myeloma either due to infiltration of malignant plasma cells into the peripheral nerves or due to neurotoxic agents prescribed to treat the disease (e.g., bortezomib and thalidomide) (Faiman et al., 2017). Symptoms of peripheral neuropathy can range from mild discomfort to severe impairment and even paralysis and may lead to dose reduction or discontinuation of therapy.

VTE may occur in patients with myeloma; the incidence is thought to be as high as 10% (NCCN, 2019i). The risk increases substantially when high doses of corticosteroids and immunomodulatory drugs (e.g., thalidomide, lenalidomide, or pomalidomide) are used to treat the disease (see [Chapter 26](#) for further discussion of VTE management).

TABLE 30-5Select Pharmacologic Agents for Multiple Myeloma^a

Medication	Adverse Effects	Nursing Considerations
CHEMOTHERAPY		
<i>Alkylating Agents</i>		
	Mechanism of Action: Bond with DNA, RNA, and protein molecules leading to impaired DNA replication, RNA transcription, and cell functioning; all resulting in cell death; cell cycle nonspecific	
Cisplatin	Alopecia	Monitor blood counts, blood chemistries and creatinine
Cyclophosphamide	Bone marrow suppression (e.g., anemia, leukopenia, thrombocytopenia) Electrolyte disturbances Hemorrhagic cystitis ^b Hypersensitivity reaction Nausea and vomiting Peripheral neuropathy Renal toxicity ^c Second cancers SIADH Stomatitis	Monitor hydration status; encourage 2–3 L of fluid intake daily May premedicate patient to avoid or minimize risk for hypersensitivity reaction (e.g., dexamethasone, diphenhydramine, famotidine) and/or with antiemetics
<i>Antitumor Antibiotic (Anthracycline-Based)</i>		
	Mechanism of Action: Interfere with DNA synthesis by binding DNA; prevent RNA synthesis; cell cycle nonspecific	
Doxorubicin	Alopecia Bone marrow suppression (e.g., anemia, leukopenia, thrombocytopenia) Cardiotoxicity (e.g., cardiomyopathy, arrhythmias) Diarrhea Nausea and vomiting Red urine Stomatitis	Drug is a vesicant and should be administer via central venous access. Patients should have ECG, MUGA scan to evaluate cardiac function prior to initiation of treatment. Educate patient to understand that urine will be red in color as drug is excreted.
<i>Topoisomerase II Inhibitor</i>		
	Mechanism of Action: Induce breaks in the DNA strand by binding to enzyme topoisomerase, preventing cells from dividing; specific to the S phase of the cell cycle	
Etoposide	Alopecia Anorexia Bone marrow suppression (e.g., anemia, leukopenia, thrombocytopenia) Diarrhea Hypotension Hypersensitivity reaction Nausea and vomiting Stomatitis	Monitor blood counts. Monitor vital signs (especially blood pressure) prior to, during, and following administration. May premedicate patient to avoid or minimize risk for hypersensitivity reaction (e.g., dexamethasone, diphenhydramine, famotidine) and/or with antiemetics
CORTICOSTEROID		

Mechanism of Action: Induce apoptosis in myeloma cells and markedly decrease bone pain

Dexamethasone	Cataract formation Dental caries Fluid retention Immunosuppression Increased appetite, weight gain Insomnia Osteoporosis Peptic ulcers Pseudodiabetes Psychosis Venous thromboembolism	Monitor blood counts Monitor blood glucose levels Monitor intake and output, assess for peripheral edema Assess daily weights Assess stools for occult blood Educate patient on methods to decrease risk for infection (e.g., flu vaccine, antibiotic prophylaxis as indicated) Educate patient to follow-up with dental and eye examinations Risk for venous thromboembolism is increased in patients concomitantly taking immunomodulators
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IMMUNOMODULATORS

Mechanism of Action: Display broad antimyeloma effects by inhibiting angiogenesis and by mitigating the effects of the cytokines interleukin-6 and tumor necrosis factor (both support myeloma cell growth)

Lenalidomide	Arthralgia ^d	Pregnancy test prior to initial therapy; repeat every 4 wk in women of childbearing age
Pomalidomide	Bone marrow suppression (e.g., anemia, leukopenia, thrombocytopenia) ^{d,e}	Male patients should be educated to use strict methods of contraception
Thalidomide	Constipation ^f Fatigue, dizziness, sedation ^f Fetal birth defects Peripheral neuropathy ^f Rash, dry skin Venous thromboembolism	Patients must be educated about the teratogenic effects of therapy Excreted by the kidneys; therefore, monitor renal function, including urine output and serum creatinine and urea nitrogen Patient may be prescribed antithrombotic prophylaxis (e.g., aspirin, DOAC, LMWH, warfarin) (see Chapter 26 for further discussion of these drugs and nursing interventions) Risk for venous thromboembolism is increased in patients concomitantly taking corticosteroids Monitor blood counts in patients taking lenalidomide and pomalidomide Assess for peripheral neuropathy in patients taking thalidomide (see Table 30-6)

MONOCLONAL ANTIBODIES

Mechanism of Action: Antibodies made from clonal immune cells that target specific antigens found on the surface of multiple myeloma cells; various agents target different antigenic receptors and therefore, adverse effects may differ

Daratumumab	Back pain, arthralgia Bone marrow suppression (e.g., anemia, leukopenia, thrombocytopenia) Constipation or diarrhea Fatigue Herpes zoster reactivation Hypersensitivity reaction: most common with first infusions; manifestations include dyspnea, bronchospasm, cough, rhinitis Injection site reaction Insomnia Nausea and vomiting	May premedicate patient to avoid or minimize risk for hypersensitivity reaction (e.g., acetaminophen, diphenhydramine, methylprednisolone) and/or with antiemetics Monitor blood counts. Prophylactic antiviral agents may be considered in patients with history of herpes zoster. Female patients should avoid becoming pregnant or breastfeeding while on drug, as risks to fetus are unknown
Elotuzumab	Anorexia Bone marrow suppression (e.g., anemia, leukopenia, thrombocytopenia) Bradycardia or tachycardia Constipation or diarrhea Fatigue Hypersensitivity reaction: include dyspnea, bronchospasm, cough, rhinitis Peripheral neuropathy	May premedicate patient to avoid or minimize risk for hypersensitivity reaction (e.g., acetaminophen, diphenhydramine, dexamethasone, famotidine) Monitor blood counts Assess for peripheral neuropathy (see Table 30-6)

PROTEASOME INHIBITORS

Mechanism of Action: Proteasomes process and clear the excess mis/unfolded protein that accumulates within malignant plasma cells; inhibiting this process causes an excess accumulation of these proteins that results in apoptosis of malignant cells

Bortezomib	Bone marrow suppression (e.g., anemia, leukopenia, thrombocytopenia)	Monitor blood counts
Carfilzomib		Patients should have ECG, MUGA scan to evaluate cardiac function prior to initiation of treatment, particularly with carfilzomib.
Ixazomib	Cardiovascular events, such as heart failure, ischemia, arrhythmias (<i>more common with carfilzomib</i>) Constipation or diarrhea Fatigue Fetal birth defects Herpes zoster reactivation Metabolized via the cytochrome P450 system	Female patients should avoid becoming pregnant or breastfeeding. Prophylactic antiviral agents may be considered in patients with history of herpes zoster For patients prescribed bortezomib, advocate for SQ rather than IV administration, to diminish

Nausea and vomiting	likelihood of peripheral neuropathy (see Table 30-6 for further discussion)
Peripheral neuropathy (<i>more common with bortezomib</i>)	
Renal dysfunction	Monitor urine output and blood creatinine and urea nitrogen
Reversible posterior leukoencephalopathy syndrome (RPLS), evidenced by seizures, visual disturbances, delirium, and hypertension	If RPLS suspected, discontinue treatment and call primary provider
Transient thrombocytopenia ^b	Monitor platelet counts in patients taking bortezomib; assess for signs of occult bleeding (e.g., black tarry stools, petechiae formation)
	Monitor for drug-to-drug interactions in patients taking ixazomib
	Ixazomib may be taken orally; administer at least 1 h prior to or 2 h post meal

^aRefer to [Chapter 12](#) for additional nursing interventions to mitigate adverse effects of antineoplastic therapy.

^bSpecific to cyclophosphamide.

^cSpecific to cisplatin.

^dSpecific to lenalidomide.

^eSpecific to pomalidomide.

^fSpecific to thalidomide.

^gSpecific to ixazomib.

^hSpecific to bortezomib.

DOAC, direct oral anticoagulant; ECG, electrocardiogram; LMWH, low-molecular-weight heparin; MUGA, multiple-gated acquisition; SIADH, syndrome of inappropriate antidiuretic hormone.

Adapted from National Comprehensive Cancer Network (NCCN). (2019i). Clinical practice guidelines in oncology: Multiple myeloma. Version 2.2019. Retrieved on 7/10/2019 at: www.nccn.org/professional/physician_gls/pdf/myeloma.pdf; Olsen, M., LeFebvre, K., & Brassil, K. (2019). *Chemotherapy and immunotherapy guidelines and recommendations for practice*. Pittsburgh, PA: Oncology Nursing Society; Rajkumar, S. (2018). Multiple myeloma: 2018 update on diagnosis, risk-stratification, and management. *American Journal of Hematology*, 93, 1091–1110.



Gerontologic Considerations

Historically, aggressive multiple myeloma therapy, particularly HSCT, was limited to patients younger than age 65, but this approach has changed. Patients older than age 65 who have excellent organ function (i.e., renal, hepatic, cardiopulmonary) and who have fewer comorbidities may tolerate more intense treatment, including AuHSCT (Faiman et al., 2017; NCCN, 2019i). Determining an older adult patient's ability to tolerate therapy *a priori* is important. In addition to chronologic age, organ function, and comorbidity, the ability to independently perform activities of daily living is another

important factor. A comprehensive assessment of all these factors is useful to better determine the level of “fitness” in a given patient. Patients categorized as frail may develop more severe toxicity associated with therapy and consequently are more likely to discontinue that treatment.

The older adult patient may have different goals of care from that of younger patients. Effective symptom control, preserving cognitive function, and maintaining independence are often viewed as higher priority than survival in the older adult. Discussing these goals of care as well as the patient’s physical and social needs can provide a more personalized approach to treating the older adult with multiple myeloma. Using lower doses of agents and focusing on side effect management are important treatment strategies. Side effects should be managed without additional medications to reduce the burden of polypharmacy. Incorporating the expertise of a palliative care clinician may be extremely beneficial, not only in devising an appropriate treatment plan, but also in managing symptoms and side effects more effectively.

Nursing Management

Pain management is very important in patients with multiple myeloma. NSAIDs can be very useful for mild pain or can be given in combination with opioid analgesics. Because NSAIDs can cause gastritis and renal dysfunction, renal function must be carefully monitored and patients assessed for GI complications; many patients are unable to use NSAIDs due to concurrent or newly developed renal insufficiency. Long-acting opioids are often prescribed to afford adequate pain relief.

Nursing care should focus on assessing for signs and symptoms of hypercalcemia. Common presenting symptoms include polyuria and GI problems (nausea, constipation, anorexia). Patients progressively become more dehydrated, with possible confusion and stupor as well as decreased renal function as the hypercalcemia worsens. Treatment for hypercalcemia includes aggressive hydration, bisphosphonates, and/or corticosteroids. See [Chapter 12, Table 12-13](#), for a discussion of manifestations of and treatment for hypercalcemia.

Patient education should include methods to prevent and minimize the risk of infection, reportable signs and symptoms, medication side effects, and pain management. Any new complaint or worsening of pain requires immediate intervention. Another key nursing responsibility is to assess for and provide emotional/psychological support. Educating patients about effective coping skills to aid in dealing with multiple myeloma and its treatment is a key intervention.

Promoting Home, Community-Based, and Transitional Care



Educating Patients About Self-Care

The patient needs to be educated about activity restrictions (e.g., lifting no more than 10 lb, the use of proper body mechanics) to reduce the risk of pathologic fracture. Braces are occasionally needed to support the spinal column, but may be uncomfortable and hamper adherence. Bisphosphonate therapy has markedly reduced the severity and extent of bone pain. However, patients need to understand the importance of comprehensive oral hygiene and good dental care to diminish the likelihood of developing osteonecrosis of the jaw that may arise from bisphosphonate therapy.

Renal function must be monitored closely. Kidney injury can become severe, and dialysis may be needed. Maintaining high urine output (3 L/day) can be very useful in preventing or limiting this complication, as is treating the underlying disease. The patient also needs to be educated about the signs and symptoms of hypercalcemia. While hypercalcemia usually occurs at the onset of the disease, it can also develop at the time of disease progression or when multiple myeloma becomes refractory to therapy. Maintaining mobility and hydration are important to diminish exacerbations of this complication.

Because antibody production is impaired, infections, particularly bacterial infections, are common and can be life-threatening. The patient needs education regarding appropriate infection prevention measures and should be advised to contact the primary provider immediately if fever or other signs and symptoms of infection develop. The patient should receive pneumococcal and influenza vaccines. Prophylactic antibiotics, such as trimethoprim-sulfamethoxazole, are often used, particularly when patients are treated with corticosteroid-containing regimens to prevent *Pneumocystis jirovecii* pneumonia (NCCN, 2019i). The antiviral agent acyclovir may be prescribed when patients are treated with bortezomib-based regimens to diminish the potential development of viral infection, such as herpes zoster. The patient must be educated about the indications for these prophylactic measures.

Continuing and Transitional Care

Many medications prescribed to treat multiple myeloma, particularly the immunomodulatory drugs (e.g., lenalidomide, thalidomide), are associated with higher risks of VTE formation, particularly when used concurrently with high doses of corticosteroids or erythropoietin. Other VTE risk factors include decreased mobility, obesity, prior thromboembolic events, diabetes, cardiac or renal disease, and the presence of a vascular access device (e.g., PICC). It is important to maintain mobility and to use strategies that enhance venous return (e.g., anti-embolism stockings, avoid crossing the legs). For patients without additional risk factors, VTE can be prevented by taking low-dose aspirin.

Those patients with additional risk factors for developing VTE should receive anticoagulation therapy (see [Chapter 26](#) for further discussion).

Peripheral neuropathy is a frequent issue for patients with multiple myeloma, affecting over 50% at the time of diagnosis (Faiman et al., 2017). It is particularly commonplace in patients who are prescribed thalidomide or bortezomib. Painful neuropathy can be quite disabling and may interfere with the patient's ability to perform normal activities of daily living (Olsen et al., 2019) (see [Table 30-6](#)). The nurse needs to carefully assess for symptoms related to peripheral neuropathy and make assessments of the home for safety. Sensation (touch, temperature, pain, vibration, proprioception), ankle reflexes, distal muscle strength, and blood pressure should be evaluated. Other risk factors for peripheral neuropathy (e.g., diabetes, vitamin deficiencies, viral infection, or excessive alcohol consumption) should be aggressively managed. Patients should be educated to report any symptoms of peripheral neuropathy and to not minimize such symptoms, because prompt cessation of therapy or reducing the dose can prevent the neuropathy from progressing. Resuming treatment with a lower dosage and at a longer interval between dosing may diminish the worsening of peripheral nerve damage. Recovery can occur over time, although it may be incomplete. Gabapentinoids (e.g., gabapentin, pregabalin), tricyclic antidepressants (e.g., amitriptyline, nortriptyline), and selective SSRIs (e.g., duloxetine) can be prescribed to diminish pain; opioids are fairly ineffective in this context.

TABLE 30-6 Peripheral Neuropathy Associated with Multiple Myeloma

Type of Neuropathy	Manifestations	Nursing Interventions/Patient Education
Sensory	Hypoesthesia	Warn patient to avoid extreme temperatures (e.g., bathwater) Inspect feet for trauma, potential infection Use loose-fitting stockings
	Paresthesia (tingling)	Gentle massage Gentle ROM exercises
	Hyperalgesia (pain)	Gentle massage (cocoa butter or menthol-based cream/lotion)
	Toes and fingers Soles of feet/palms	Apply lidocaine 5% patch to affected area every 12 h Consider gabapentin, tricyclic antidepressants (e.g., amitriptyline)
Motor	Muscle cramps	Maximize hydration, ambulation (Quinine is not recommended)
	Tremor	
	↓ Strength in distal muscles	
	Gait disturbance ↓ Fine motor function (e.g., handwriting, buttoning clothes)	Encourage the use of appropriate footwear Consider ambulatory aides (e.g., walker) Remove scatter rugs; perform a home safety evaluation PT referral OT referral (if severe limitations)
Autonomic Nervous System	Orthostatic hypotension	Warn patient to avoid abrupt position change Maximize hydration Consult with primary provider about adjusting antihypertensive medications, diuretics
	Bradycardia	Assess/warn patient for impact (fatigue, impairment in function) Consult with primary provider about adjusting drugs that cause bradycardia (e.g., calcium channel blockers, beta-blockers, alpha-/beta-adrenergic blockers, digoxin). Explore the use of activity to increase heart rate
	Sexual dysfunction	Explore alternative means of sexual activity beyond penile-vaginal intercourse Consult with primary provider about the use of erectile dysfunction medication
	Constipation	Maximize fluid intake, fiber Use stool softeners, laxatives

Note: Peripheral neuropathy can be classified into three main categories. Within each category, specific manifestations are delineated as well as relevant nursing interventions. If the neuropathy is related to multiple myeloma therapy, it is crucial to promptly stop the potentially offending medication. It is also important to reduce the impact from other

predisposing factors. For example, diabetes should be well controlled and alcohol consumption reduced.

↓, decreased; OT, occupational therapy; PT, physical therapy; ROM, range of motion.

Adapted from Autissier, E. (2019). Chemotherapy-induced peripheral neuropathy. *Clinical Journal of Oncology Nursing*, 23(4), 405–410; Olsen, M., LeFebvre, K., & Brassil, K. (2019). *Chemotherapy and immunotherapy guidelines and recommendations for practice*. Pittsburgh, PA: Oncology Nursing Society.

As many drugs used in treating multiple myeloma are given orally, the nurse must ensure that the patient fully understands how to take the medication, manage side effects, and know what steps can be taken to diminish or mitigate adverse effects (see [Table 30-6](#)).

CRITICAL THINKING EXERCISES

1  ipc You work on an inpatient oncology unit and are assigned to care for a 47-year-old woman with AML who is a week and a half post induction therapy. The multidisciplinary team is now rounding on your patient and asks you for a brief report. What complications would you anticipate the patient could experience at this time? What key information do you think you should provide the multidisciplinary team? What aspects of multidisciplinary care do you identify?

2  pq You work in an outpatient infusion center and are assigned to provide a first treatment for a 74-year-old African American man who was recently diagnosed with multiple myeloma. What key assessment and laboratory studies would you focus on and why? Are there any comorbidities that could impact this patient's treatment?

3  ebp You are caring for a 57-year-old patient with diffuse large B-cell lymphoma who is not a candidate for autologous HSCT. The patient had only a partial response to consolidation therapy and is in the hospital to manage an infection. What do you anticipate are the best treatment options available for this patient? What are the possible adverse effects that you need to monitor? What evidence-based nursing interventions would you employ to manage this patient's care?

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*Asterisk indicates nursing research.

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Resources

- AABB (formerly known as the American Association of Blood Banks),
www.aabb.org/Pages/default.aspx
- American Cancer Society, www.cancer.org
- American College of Surgeons Commission on Cancer, www.facs.org/quality-programs/cancer/coc
- American Society for Transplantation and Cellular Therapy (ASTCT),
www.astct.org/home
- Aplastic Anemia & MDS International Foundation, www.aamds.org
- Be The Match (Bone marrow transplantation network), www.bethematch.org
- Blood and Marrow Transplant Information Network, www.bmtinfonet.org
- Department of Veteran Affairs, information on Agent Orange,
www.publichealth.va.gov/exposures/agentorange/benefits/health-care.asp
- International Myeloma Foundation, www.myeloma.org
- Leukemia & Lymphoma Society, www.lls.org
- Lymphoma Research Foundation, lymphoma.org
- Multinational Association of Supportive Care in Cancer, www.mascc.org
- Myelodysplastic Syndromes Foundation (MDS Foundation), www.mds-foundation.org
- National Cancer Institute, www.cancer.gov
- National Comprehensive Cancer Network, www.nccn.org
- National Heart, Lung, and Blood Institute, www.nhlbi.nih.gov
- Oncology Nursing Society (ONS), www.ons.org