Hematopoietic Function

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LEARNING OBJECTIVES

• Discuss normal hematopoietic function.
• Describe and compare diseases of the white blood cells.
• Describe and compare diseases of the red blood cells.
• Describe and compare diseases of the platelets.

KEY TERMS

- anemia
- disseminated intravascular coagulation (DIC)
- erythrocyte
- hematocrit
- hematopoiesis
- hemoglobin
- hemoglobin S
- hemolysis
- hemophilia A
- idiopathic thrombocytopenic purpura (ITP)
- infectious mononucleosis
- leukemia
- leucocyte
- leucocytopenia
- leukocytosis
- multipip myeloma
- neutropenia
- neutrophil
- pancytopenia
- plasma
- plasmin
- pus
- thrombocyte
- thrombocytopenia
- thromboplastin
- thrombotic thrombocytopenic purpura (TTP)
- von Willebrand's disease

Blood is the life fluid of the human body, and it is essential for health and homeostasis. The approximately 5 liters of blood continuously circulating in the human body provides nutrients and oxygen to tissues while aiding in the excretion of waste products. Blood consists of plasma, blood cells, and platelets. Disease occurs when there are too few, too many, or dysfunctional blood components. These conditions can result from congenital or genetic causes, but they can also be acquired from medical treatment. Healthcare providers, especially nurses, play a pivotal role in identifying those persons at risk and assisting in the management of these diseases.

Normal Hematopoietic Function

Blood is both a viscous fluid and a tissue. Hematopoiesis is the process of blood formation, and it occurs primarily in the bone marrow. Stem cells (primitive cells) differentiate the precursors for the different blood cells. Blood accomplishes its functions through its various components—the plasma (liquid protein), leukocytes (white blood cells), erythrocytes (red blood cells), and thrombocytes (platelets) (TABLE 3-1). Plasma is a transport medium that carries the blood cells as well as antibodies, nutrients, electrolytes, hormones,
lipids, and waste products. Leukocytes are key players in the inflammatory response and infectious process (see the Body Defenses chapter).

Erythrocytes are disk-shaped cells that carry oxygen to tissues and transport carbon dioxide for removal. Erythrocytes contain proteins and hemoglobin, which binds to oxygen, giving blood its red color. The brighter the shade of red, the more the blood is saturated with oxygen. Hematocrit refers to how much of the blood volume comprises erythrocytes.

Thrombocytes, along with clotting factors, control coagulation. Carried passively in the blood, thrombocytes are coated with a sticky material that causes them to adhere to irregular surfaces. Clotting is a quick chain reaction stimulated by the release of thromboplastin from damaged cells lining blood vessels (FIGURE 3-1). In conjunction with the initiation of the clotting cascade (FIGURE 3-3), platelets containing contractile proteins pull the edges of the wound together. Blood clots do not persist indefinitely; if they did so, they would clog up the entire circulatory system. Plasmin is an enzyme that dissolves clots once healing has occurred.

**Diseases of the White Blood Cells**

Leukocytes are a diverse group of cells that trigger the inflammatory process and combat infections. Normal white blood cell (WBC) levels range from 5,000 to 10,000 cells/mL$^3$ blood. Leukocytosis describes states characterized by increased WBC levels, and leukocytopenia refers to decreased WBC levels. Leukocytosis

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**TABLE 3-1 Summary of Blood Cells**

<table>
<thead>
<tr>
<th>Name</th>
<th>Light Micrograph</th>
<th>Description</th>
<th>Concentration (Number of Cells/mm$^3$)</th>
<th>Life Span</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red blood cells (RBCs)</td>
<td><img src="image" alt="RBCs" /></td>
<td>Biconcave disk; no nucleus</td>
<td>4 to 6 million</td>
<td>120 days</td>
<td>Transport oxygen and carbon dioxide</td>
</tr>
<tr>
<td>White blood cells (WBCs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutrophil</td>
<td><img src="image" alt="Neutrophil" /></td>
<td>Approximately twice the size of RBCs; multilobed nucleus; clear-staining cytoplasm</td>
<td>3,000 to 7,000</td>
<td>6 hours to a few days</td>
<td>Phagocytize bacteria</td>
</tr>
<tr>
<td>Eosinophil</td>
<td><img src="image" alt="Eosinophil" /></td>
<td>Approximately same size as neutrophil; large pink-staining granules; bilobed nucleus</td>
<td>100 to 400</td>
<td>8 to 12 days</td>
<td>Phagocytizes antigen–antibody complex; attacks parasites</td>
</tr>
<tr>
<td>Basophil</td>
<td><img src="image" alt="Basophil" /></td>
<td>Slightly smaller than neutrophil; contains large, purple cytoplasm granules; bilobed nucleus</td>
<td>20 to 50</td>
<td>A few hours to a few days</td>
<td>Releases histamine during inflammation</td>
</tr>
<tr>
<td>Monocyte</td>
<td><img src="image" alt="Monocyte" /></td>
<td>Larger than neutrophil; cytoplasm is grayish blue; no cytoplasmic granules; U- or kidney-shaped nucleus</td>
<td>100 to 700</td>
<td>Lasts many months</td>
<td>Phagocytizes bacteria, dead cells, and cellular debris</td>
</tr>
<tr>
<td>Lymphocyte</td>
<td><img src="image" alt="Lymphocyte" /></td>
<td>Slightly smaller than neutrophil; large, relatively round nucleus that fills the cell</td>
<td>1,500 to 3,000</td>
<td>Can persist for many years</td>
<td>Involved in immune protection, either attacking cells directly or producing antibodies</td>
</tr>
<tr>
<td>Platelets</td>
<td><img src="image" alt="Platelets" /></td>
<td>Fragments of megakaryocytes; appear as small dark-staining granules</td>
<td>250,000</td>
<td>5 to 10 days</td>
<td>Play several key roles in blood clotting</td>
</tr>
</tbody>
</table>

can indicate an active infectious process, whereas leukocytopenia can indicate an immune deficiency state (e.g., bone marrow suppression). The blood, by way of the circulatory system, transports leukocytes to the site of an infection. When the leukocytes arrive at the scene, they leak through the capillary wall to the site of trauma or invasion (Figure 3-4). Most leukocyte disorders originate from deficiencies of one or more of the varying leukocytes.

**Neutropenia**

Usually the first to arrive on the scene of an infection, neutrophils are attracted by various chemicals released by infected tissue (Figure 3-5). These cells escape from the capillary wall and migrate to the site of infection. Once they get to the site, neutrophils phagocytize microorganisms, preventing the infection from spreading. As the neutrophils are fully utilized, the infected cells die and become part of the yellowish wound drainage, or pus.

Neutropenia refers to a decrease in circulating neutrophils to fewer than 1,500 cells/mL (the normal range is 2,000–7,500 cells/mL). When fewer of these first responders are available, the body is poorly equipped to fight infections. The degree to which the body can fight infections, especially bacterial infections, is related to the severity of the neutropenia. In other words, the lower the neutrophil count, the less the body’s ability to fight infections. Causes of neutropenia may include the following conditions:

- Increased usage (e.g., infection and inflammation)
- Drug suppression (e.g., immunosuppressants and chemotherapies)
- Radiation therapy
- Congenital conditions (e.g., periodic or cyclic)
- Bone marrow cancers (e.g., leukemias and lymphomas)
Figure 3-3 Clotting cascades.


- Spleen destruction (e.g., Felty’s syndrome)
- Vitamin deficiency (e.g., B12 and folate deficiency)

Clinical manifestations of neutropenia initially include signs and symptoms of bacterial and fungal infections (e.g., malaise, chills, and fever). The respiratory tract is the most common site of infection. Mouth ulcerations are also often associated with neutropenia, as are ulcerations of the skin, vagina, and gastrointestinal tract.

Diagnostic procedures center primarily on serum neutrophil levels. Additionally, a bone marrow biopsy may be conducted to determine the cause of the neutropenia. Antibiotic therapy is used to treat infections as they develop. Identification and treatment of the cause of the neutropenia is crucial for positive outcomes. Hematopoietic growth factors such as granulocyte colony-stimulating factor may be used to stimulate maturation and differentiation of neutrophils.

Infectious mononucleosis

Infectious mononucleosis, also known as “mono” and the “kissing disease,” is a disease caused by the Epstein-Barr virus (EBV). EBV is a commonly encountered virus of the herpes family. Infectious mononucleosis is most frequently seen in adolescents and young adults. According to the Centers for Disease Control and Prevention (CDC, 2007), as many as 95% of adults ages 35–40 in the United States test positive for EBV antibodies. Most people have been exposed to the virus as children, and because of this exposure, they have developed immunity to the virus. Consequently, most people who are exposed to EBV do not develop infectious mononucleosis.

EBV infects B cells by killing the cells or being incorporated into their genome. The B cells infected with EBV produce heterophile antibodies that can be identified to diagnose the disease. Once the disease is eliminated, a few B cells remain altered, giving the individual an asymptomatic infection for life and the potential to occasionally spread EBV to others. Infectious mononucleosis is usually spread by person-to-person contact. Saliva is the primary method of transmission, but transmission can also occur through coughing or sneezing, which causes small droplets of infected saliva and/or mucus to become suspended in the air to be inhaled by others. EBV can also survive several hours outside the body, so transmission can occur through sharing utensils and glasses. The incubation period for infectious mononucleosis is between 4 and 6 weeks. During an infection, a person is able to transmit the virus to others for at least a few weeks.

According to the CDC (2007), depending on the method used to detect the virus, anywhere from 20% to 80% of people who have recovered from infectious mononucleosis will continue to secrete EBV in their saliva for years due to periodic reactivations of the viral infection. Because healthy people without symptoms also secrete the virus during reactivation episodes throughout their lifetime, isolation of people infected with EBV is not necessary. It is currently believed that these healthy people who secrete EBV particles are the primary reservoir for transmission of EBV among humans.

Onset of the clinical manifestations of infectious mononucleosis is usually insidious. The initial manifestations of malaise, anorexia, and
1. Foreign invaders signal nearby neutrophils to squeeze through endothelial cells that line the blood vessel and enter the infected tissue.

2. Through a cell-eating process known as phagocytosis, the neutrophil ingests the bacteria and releases toxic products that kill the bacteria.

**FIGURE 3-4** Leukocyte movement.


**FIGURE 3-5** The role of neutrophils.
chills can last 1–3 days. Following this period, the manifestations intensify and include severe sore throat, fever, and lymphopathy. The acute phase usually lasts 2–3 weeks. Some patients may not fully recover for 2–3 months, but most people recover without incident. Possible complications of infectious mononucleosis include hepatitis, ruptured spleen, and meningitis.

Diagnosis of infectious mononucleosis can be confirmed through the heterophile antibody test (Monospot test) 2–3 weeks post exposure. At that time, increased lymphocytes, increased monocytes, and atypical T lymphocytes (enlarged) in the blood will be present and can be identified by the test. Other laboratory tests can be performed to exclude other disorders that present similarly to infectious mononucleosis (e.g., strep throat). Leukocyte counts may also be increased when a person has infectious mononucleosis.

Treatment of infectious mononucleosis is primarily symptomatic and supportive. Strategies may include bed rest, hydration, analgesics, corticosteroids, and antipyretics. Vigorous contact sports should be avoided in the acute illness and recovery phases to prevent rupture of the spleen.

### Lymphomas

According to the CDC (2009b), lymphoma is the sixth most common cancer in adults and the third most common cancer in children. There are two main types of lymphomas—Hodgkin's and non-Hodgkin's lymphoma. Non-Hodgkin's lymphoma is far more common than Hodgkin's disease. Risk factors for both types of lymphoma include infection with the human immunodeficiency virus (HIV) or EBV. Additional risk factors for non-Hodgkin's include (1) the presence of an inherited immune or autoimmune condition and (2) infection with Helicobacter pylori or human T-cell leukemia/lymphoma virus type 1 (HTLV-1).

**Hodgkin's Lymphoma**

Hodgkin's lymphoma can start in any lymph node of the lymphatic system, but most often arises in the lymph nodes of the upper body (e.g., the neck, chest, and upper arms). The affected lymph nodes swell and compress surrounding tissue. Systemically, the cancer cells spread from one lymph node to the next through the lymphatic vessels. In rare cases, the disease spreads into the blood vessels and other structures, a process that continues until late in the disease. The cancer cells of Hodgkin's lymphoma are unique; they are called Reed-Sternberg cells (or Hodgkin cells) (Figure 3-6). These cells are an abnormal type of B lymphocyte that is much larger than normal lymphocytes. The T lymphocytes also appear defected, and the total lymphocyte number decreases.

The two main types of Hodgkin’s lymphoma are classical Hodgkin’s disease (which has several subtypes) and nodular lymphocyte predominance Hodgkin’s disease. These types differ in the way the cancer cells appear under a microscope. Identification of which type the patient is experiencing is important because each grows and spreads in a different way, and they are often treated differently. Classical Hodgkin’s disease will be discussed further here because it accounts for 95% of Hodgkin’s disease cases.

Though the incidence of this disease is on the decline, the CDC (2009b) reports that Hodgkin’s disease occurs primarily in adults 20–40 years of age, with equal prevalence across genders. A second peak occurrence is seen in men older than 50 years of age. Due to improvements in the treatment of Hodgkin’s lymphoma, mortality has decreased by nearly 50% over the past 25 years. Over the same period, incidence has remained relatively steady. Prognosis is further improved when the disease is localized and is treated early, with many cases considered cured. Although the prognosis is excellent for patients with Hodgkin’s disease, those who are treated with radiation may be at increased risk of stroke and transient ischemic attack (DeBruin et al., 2009).

Hodgkin’s disease has the following clinical manifestations:

- Swollen, painless lymph nodes
- Weight loss
- Persistent fever
- Night sweats
- Generalized pruritus
- Coughing, trouble breathing, or chest pain
- Malaise
- Recurrent infections
- Splenomegaly

Diagnostic procedures primarily center on biopsy of the affected lymph node. Biopsy samples reveal the presence of Reed-Sternberg cells. Other diagnostic procedures consist of a physical examination, complete blood count, and chest X-rays.

A staging system is used to grade the severity and progression of the disease (FIGURE 3-7):

- **Stage I:** The lymphoma cells are in one lymph node group (such as in the neck or the underarm), or if the lymphoma cells are not in the lymph nodes, they are in only one part of a tissue or an organ (such as the lung).
- **Stage II:** The lymphoma cells are in at least two lymph node groups on the same side of (either above or below) the diaphragm, or the lymphoma cells are in one part of a tissue or an organ and the lymph nodes near that organ (on the same side of the diaphragm). Lymphoma cells may be in other lymph node groups on the same side of the diaphragm.
- **Stage III:** The lymphoma cells are in lymph nodes above and below the diaphragm. Lymphoma cells may be found in one part of a tissue or an organ (such as the liver, lung, or bone) near these lymph node groups. The cells may also be found in the spleen.
- **Stage IV:** Lymphoma cells are found in several parts of one or more organs or tissues, or the lymphoma cells are in an organ (such as the liver, lung, or bone) and in distant lymph nodes.
- **Recurrent:** The disease returns after treatment.

Staging involves computed tomography scan, magnetic resonance imaging, positron emission tomography scan, and bone marrow biopsy. Other staging procedures may include biopsies of other lymph nodes, the liver, or other tissue. After diagnosis, the usual cancer treatment is implemented (combination of chemotherapy, radiation, and surgery).

**Non-Hodgkin’s Lymphoma**

Non-Hodgkin’s lymphoma can start at any age and in any lymph node. Non-Hodgkin’s lymphoma is more common in Caucasians as compared to other ethnic groups. Many different types of this disease are possible. These types can be divided into aggressive (fast-growing) and indolent (slow-growing) types, and they can arise from either B cells (80% of cases) or T cells. Non-Hodgkin’s lymphoma is similar to Hodgkin’s lymphoma in its clinical manifestations, staging, and treatment; the differences lie in the spread and diagnosis of the disease. Non-Hodgkin’s lymphoma involves multiple nodes scattered throughout the body and metastasizes in an unorganized manner. Metastasis is often
present at diagnosis. With non-Hodgkin’s lymphoma, no Reed-Sternberg cells are present. Additionally, non-Hodgkin’s lymphoma is more difficult to treat, and the prognosis is poor but improving.

### Leukemias

**Leukemia** is a cancer of the leukocytes. With this disease, the bone marrow makes abnormal leukocytes, or leukemia cells. Unlike normal blood cells, leukemia cells do not die when they should, so they sometimes begin crowding normal leukocytes, erythrocytes, and thrombocytes. This crowding makes it difficult for normal blood cells to function properly. The exact cause of leukemia is unknown.

According to the CDC (2009a), leukemia is the most common blood cancer. Although it affects 10 times as many adults as children, leukemia is the most common cancer among children. Incidence rates have remained relatively consistent over the past 20 years, but the mortality rates have decreased. Men are more likely to develop leukemia than are women. Other risk factors include exposure to chemical, viral, and radiation mutagens; smoking; use of chemotherapy; certain disease conditions (e.g., Down syndrome); and immunodeficiency disorders.

Leukemias are grouped as either acute or chronic. The four most common types of leukemia are identified here:

- **Acute lymphoblastic leukemia (ALL):** Affects primarily children (accounts for approximately 75% of all childhood leukemias); responds well to therapy, and carries a good prognosis.
- **Acute myeloid leukemia (AML):** Affects primarily adults; responds fairly well to treatment, and carries a prognosis somewhat worse than that of acute lymphoblastic leukemia.
- **Chronic lymphoid leukemia (CLL):** Affects primarily adults; responds poorly to therapy, yet most patients live many years after diagnosis.
- **Chronic myeloid leukemia (CML):** Affects primarily adults; responds poorly to chemotherapy, but the prognosis is improved with allogeneic bone marrow transplant.

Leukemia has the following clinical manifestations:

- Leukopenia (frequent infections)
- Anemia (pallor, fatigue, dyspnea, and decreased activity tolerance)
- Thrombocytopenia (petechiae, bleeding gums, hematuria, and prolonged bleeding time)
- Lymphadenopathy
- Joint swelling
- Bone pain
- Weight loss
- Anorexia
- Hepatomegaly
- Splenomegaly
- Central nervous system dysfunction

Diagnostic procedures include a history, physical examination, peripheral blood smears, complete blood count, and bone marrow biopsy. Chemotherapy is the mainstay of treatment for leukemia, and several courses may be necessary to eradicate the cancer. Chemotherapy is more effective for the acute types of leukemia than for the chronic types. Bone marrow transplants may be attempted if chemotherapy is unsuccessful. Other treatments may include targeted therapy, radiation, biological therapy, surgery, and donor lymphocyte infusion.

### Multiple Myeloma

**Multiple myeloma** is a cancer of the plasma cells that most often affects older adults. This disease is characterized by excessive numbers of abnormal plasma cells in the bone marrow crowding the blood-forming cells and causing Bence Jones proteins to be excreted in the urine. Multiple bone tumors develop and bone destruction occurs, leading to hypercalcemia and pathologic fractures. Hypercalcemia leads to renal impairment and neuromuscular issues. Tumor cells can spread through the lymph nodes and infiltrate organs.

According to the CDC (2013), multiple myeloma is the second most common blood cancer. Over the past 20 years, its incidence and mortality rates have remained relatively stable. This disease is more common in men than in women. Additionally, African Americans have about twice the incidence and mortality rates of Caucasians.

The onset of multiple myeloma is usually insidious, and malignancy is often well advanced upon diagnosis. Clinical manifestations of multiple myeloma include the following:

- Anemia (pallor, fatigue, dyspnea, and decreased activity tolerance)
- Thrombocytopenia (petechiae, bleeding gums, hematuria, and prolonged bleeding time)
• Leukopenia (frequent infections)
• Decreased bone density
• Bone pain
• Hypercalcemia (neuromuscular dysfunction)
• Renal impairment

The diagnosis of multiple myeloma is often made incidentally during routine blood tests for other conditions. For example, the existence of anemia and a high serum protein may suggest further testing is needed. Diagnostic procedures include serum and urine protein, calcium, renal function tests, complete blood count, biopsy, X-rays, computed tomography, and magnetic resonance imaging.

Multiple myeloma is not considered curable, but chemotherapy improves remission rate. Additional treatments may include corticosteroids, angiogenesis inhibitors, targeted therapies, stem cell transplants, biological therapy, radiation therapy, and supportive care. The median survival time is 3 years. Analgesics are used to treat bone pain. Blood dyscrasias, hypercalcemia, and renal impairment are treated as needed.

Diseases of the Red Blood Cells

Erythrocytes are the most prevalent blood cell in the human body—millions can be found in a single drop of blood (normal range is 4.2–5.9 million uL). These cells function primarily to transport oxygen to the tissue and the waste products for excretion. Most diseases of the red blood cells (RBCs) are related to the quantity or quality of the erythrocytes.

Anemia

Anemia is a common acquired or inherited disorder of the erythrocytes that impairs the oxygen-carrying capacity of the blood. This condition can result from (1) a decrease in the number of circulating erythrocytes (e.g., blood loss or decreased production), (2) a reduction in hemoglobin content, or (3) the presence of abnormal hemoglobin. Some anemias are treated easily, whereas others can cause lifelong problems. The clinical manifestations of anemia reflect the decreased oxygen-carrying capacity, regardless of the disease’s cause:

• Weakness
• Fatigue

Pallor
• Syncope
• Dyspnea
• Tachycardia

Anemia is diagnosed when hematocrit is less than 41% in males and less than 37% in females. Respectively, hemoglobin concentration falls to less than 13.5 g/dL in males and less than 12 g/dL in females. Treatment depends on the specific type of anemia experienced.

Iron-Deficiency Anemia

According to the World Health Organization (2013), iron-deficiency anemia is the most widespread anemia in the world. This type of anemia is most commonly seen in women of childbearing age, children younger than 2 years of age, and the elderly. Iron-deficiency anemia occurs when the supply of iron necessary to produce hemoglobin is inadequate to meet the demand of hemoglobin production. It may be caused by decreased iron consumption, decreased iron absorption, or increased bleeding (such as occurs during menstruation and as a result of some cancers). Iron is ingested through both animal and plant sources. Although the average American absorbs more than 10 mg of iron each day, which is within the recommended daily allowance, only about 10% of the ingested iron is actually absorbed. When an iron deficiency exists, erythrocytes will become pale (hypochromic) and small (microcytic) (FIGURE 3-8).

In addition to the previously mentioned anemia signs and symptoms, the following clinical manifestations may be associated with iron-deficiency anemia:

FIGURE 3-8 Iron-deficiency anemia.
• Cyanosis (blue coloration) to sclera of the eyes
• Brittle nails
• Decreased appetite (especially in children)
• Headache
• Irritability
• Stomatitis
• Unusual food cravings (pica)
• Delayed healing

Diagnostic procedures for iron-deficiency anemia include a complete blood count, serum ferritin, serum iron, and transferring saturation. Additional tests may be performed to determine the cause (e.g., fecal occult blood test).

Treatment includes the identification and resolution of the underlying cause of the iron-deficiency anemia. Other strategies to increase iron levels include increasing consumption of iron-rich foods (e.g., liver, red meat, fish, beans, raisins, and green leafy vegetables) or administering iron supplements. Additionally, foods or supplements high in vitamin C should be increased because vitamin C increases the absorption of iron.

Pernicious Anemia

Pernicious anemia is also known as vitamin B12 deficiency and megaloblastic anemia. This type of anemia is characterized by large (macrocytic), immature erythrocytes (FIGURE 3-9). Pernicious anemia results most often from cyanocobalamin (vitamin B12) deficiency. This deficiency usually occurs gradually and from a lack of intrinsic factor. Intrinsic factor is a protein produced by the stomach that is necessary for vitamin B12 to be absorbed in the stomach. The lack of intrinsic factor results from autoantibodies, and the subsequent immune reaction leads to atrophy of the gastric mucosa and glands.

Vitamin B12 is necessary for DNA synthesis, and a deficiency of this nutrient leads to decreased cell division and cell maturation. Too little vitamin B12 gradually causes neurologic problems because of a breakdown in myelin. The neurologic effects may be seen before anemia is diagnosed. In addition to the usual signs and symptoms of anemia, pernicious anemia is associated with the following clinical manifestations:

• Bleeding gums
• Diarrhea
• Impaired sense of smell
• Loss of deep tendon reflexes
• Anorexia
• Personality or memory changes
• Positive Babinski’s sign (a pathological reflex in which the first toe extends and flexes toward the top of the foot and the other toes fan out when the sole of the foot is firmly stroked)
• Stomatitis
• Paresthesia of the hands and feet
• Unsteady gait, especially in the dark

Diagnostic tests for pernicious anemia include serum vitamin B12 levels, Schilling’s test (measures vitamin B12 absorption), complete blood count, gastric analysis, and bone marrow biopsy. Treatment of pernicious anemia includes vitamin B12 injections if no intrinsic factor is being produced; oral vitamin B12 can be administered for those individuals who are producing intrinsic factor.
Mrs. Williams is a 45-year-old Caucasian woman who sought medical attention for fatigue that developed during the previous month. She reported no chest pain, but she did feel mildly short of breath with exertion such as after walking up a flight of stairs. She denied any rectal bleeding, but she had heavy menstrual periods for about a year. Her past medical history included being treated for anemia following her third pregnancy 10 years prior. She was not taking any prescribed medications. Her family history revealed that her parents were born in Italy and died when she was in grade school. She did not know their medical history.

A physical examination revealed that Mrs. Williams’s general appearance was pale but with no acute distress. Her vital signs were blood pressure 125/90, heart rate 88 regular, and respirations 12/min. No significant changes in the blood pressure and heart rate were noted between the supine and upright positions. Other findings included pale conjunctiva and moist mucous membranes without lesions. No adenopathy or hepatosplenomegaly was noted. Breath sounds were clear to auscultation, and the heart had a regular rate and rhythm with a murmur. The abdomen was soft, nontender, and nondistended. A rectal examination revealed no masses, and hemnegative brown stool was present. Additionally, Mrs. Williams reported that she was taking aspirin 81 mg daily, she is a vegetarian who eats a lot of cereal, and she did not have an urge to eat ice.

Mrs. Williams’s laboratory tests revealed the following results:

<table>
<thead>
<tr>
<th>CBC</th>
<th>Result</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>8.2 × 10³/mL</td>
<td>4.8–10.8 × 10³/mL</td>
</tr>
<tr>
<td>Hgb</td>
<td>8.0 g/dL</td>
<td>12–15.6 g/dl</td>
</tr>
<tr>
<td>Hct</td>
<td>24%</td>
<td>35–46%</td>
</tr>
<tr>
<td>RBC</td>
<td>4.0 × 10⁶/mL</td>
<td>3.8–5 × 10⁶/mL</td>
</tr>
<tr>
<td>MCV</td>
<td>60 μL/red cell</td>
<td>80–96.1 μL/red cell</td>
</tr>
<tr>
<td>MCH</td>
<td>20 pg/red cell</td>
<td>27.5–33.2 pg/red cell</td>
</tr>
<tr>
<td>MCHC</td>
<td>33 g/L</td>
<td>33.4–35.5 g/L</td>
</tr>
<tr>
<td>RDW</td>
<td>16.5</td>
<td>11.5–14.5</td>
</tr>
<tr>
<td>Platelets</td>
<td>500,000/mL</td>
<td>150–400,000/mL</td>
</tr>
<tr>
<td>Reticulocyte count</td>
<td>3%</td>
<td>0.5–1.7%</td>
</tr>
<tr>
<td>Absolute reticulocyte count</td>
<td>40,000/mL</td>
<td>25,000–75,000/mL</td>
</tr>
<tr>
<td>LDH</td>
<td>210 U/L</td>
<td>0–304 U/L</td>
</tr>
</tbody>
</table>

CBC = complete blood count; WBC = white blood cells; Hgb = hemoglobin; Hct = hematocrit; RBC = red blood cells; MCV = mean corpuscular volume; MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; RDW = red cell distribution width; LDH = lactate dehydrogenase.

Mrs. Williams’s laboratory tests revealed the following results:

Mrs. Williams was diagnosed with iron-deficiency anemia and was placed on iron supplements. Her hemoglobin (Hgb) was expected to be normal after about 8 weeks of iron therapy, which was anticipated to raise the Hgb about 1 g/dL per week. However, her Hgb was 9.5 g/dL after 8 weeks.

Following those results, Mrs. Williams was asked whether she had been taking the iron supplements as ordered and whether she had been tolerating the medication. Additionally, she was asked whether she was having dark, tarry stools, which would indicate gastrointestinal bleeding. Mrs. Williams reported that she had taken the iron supplement for only 2 weeks because it made her nauseated and constipated. Mrs. Williams was instructed to take the iron supplement with a light carbohydrate such as crackers or toast to minimize the nausea and to take measures to prevent constipation (e.g., increasing fiber and water intake). After implementing these measures and taking the iron supplement as ordered for 8 weeks, Mrs. Williams’s Hgb returned to normal.

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Aplastic Anemia

Aplastic anemia is a rare but serious type of anemia that is a result of the bone marrow failing to make enough blood cells. This lack of erythrocytes, leukocytes, and platelets is referred to as pancytopenia. A lack of these blood cells leads to a series of complications (e.g., infections, bleeding, hypoxia, fatty replacement of marrow, and death). Aplastic anemia may be temporary or permanent. Causes of aplastic anemia include the following:

- Idiopathic causes
- Autoimmune causes (e.g., systemic lupus erythematosus and rheumatoid arthritis)
- Medications and treatments (e.g., chemotherapy and radiation)
- Viruses
- Toxins (e.g., pesticides, arsenic, and benzene)
- Genetic abnormalities (e.g., myelodysplastic syndrome)
- Infectious diseases (e.g., EBV, cytomegalovirus, parvovirus, and HIV)
- Pregnancy (often resolves after delivery)
- Cancer

Clinical manifestations include signs and symptoms of general anemia (e.g., weakness, pallor, and dyspnea), leukocytopenia (e.g., recurrent infections), and thrombocytopenia (e.g., bleeding). As blood cell levels decline, clinical manifestations worsen.

Diagnostic tests for aplastic anemia include complete blood count and bone marrow biopsy. Prompt treatment of underlying causes and complications as they arise is crucial for positive outcomes. Treatment of underlying causes may include discontinuation of medications or treatments. Treatment of complications may include the following measures:

- Oxygen therapy
- Infection control measures (e.g., hand washing, avoiding groups, and avoiding fresh flowers)
- Infection treatment (e.g., antibiotics)
- Bleeding precautions (e.g., electric razors, soft bristle toothbrushes, and injury prevention)
- Hematopoietic stimulants (e.g., erythropoietin and colony-stimulating factors)
- Immunosuppressant therapy (e.g., cyclosporine and methylprednisolone)
- Anti-infectives (e.g., antibiotics and antiviral medications)
- Blood transfusions
- Bone marrow transplants

Hemolytic Anemia

Hemolytic anemia results from excessive destruction, or hemolysis, of erythrocytes. Causes of hemolytic anemia include idiopathic causes, autoimmune causes, genetics, infections (e.g., malaria), blood transfusion reactions, and blood incompatibility in the neonate. Several types of hemolytic anemia exist, including sickle cell anemia, thalassemia, and erythroblastosis fetalis. Specifics in regard to pathogenesis, clinical manifestations, diagnosis, and treatment vary based on type.

Sickle Cell Anemia

Sickle cell anemia is a genetic type of hemolytic anemia in which the erythrocytes have an abnormal crescent or sickle shape (FIGURE 3-10). It is caused by an abnormal type of hemoglobin called hemoglobin S. Hemoglobin S distorts the shape of erythrocytes, especially when the body’s supply of oxygen is low. These fragile, sickle-shaped cells deliver less oxygen to the body’s tissues. These cells also can clog easily in small blood vessels and break into pieces that disrupt blood flow.

Sickle cell anemia is an inherited disorder that is neither recessive nor dominant (see the Cellular Function chapter). The allele for the sickle cell gene is co-dominant—meaning that if a person inherits the sickle cell gene from one parent and the normal erythrocyte gene from the other parent, both genes will be expressed. Someone who inherits the hemoglobin S gene from one parent and a normal hemoglobin gene (A) from the other parent, meaning a heterozygous pair of alleles, will have sickle cell trait. Persons with sickle cell trait do not have the symptoms of true sickle cell anemia because fewer than half of their erythrocytes are sickled.
Those persons who inherit the hemoglobin S gene from both parents, creating a homozygous allele pair, have sickle cell disease. Sickle cell disease is more severe because almost all of the individual’s erythrocytes are abnormal. Sickle cell disease is much more common in people of African (1 out of every 500 births) and Mediterranean descent. Sickle cell disease is also seen in people from South and Central America, the Caribbean, and the Middle East.

Clinical manifestations usually do not appear in newborns because fetal hemoglobin protects the red blood cells from sickling. The fetal hemoglobin is replaced by adult hemoglobin, however, when a child reaches 4 to 5 months of age. Swelling in the hands and feet, often in conjunction with a fever, is usually the first symptom. The swelling results from the sickled cells occluding the blood vessels and blocking blood flow in and out of the hands and feet. Most patients will experience painful episodes, or crises, that can last for hours to days. Pain is caused by obstruction of small blood vessels as the sickled cells clog up the vessels, leading to ischemia and necrosis. Complications of these blood vessel occlusions depend on their location (Table 3-2).

The number and severity of these crises vary among patients, but episodes can be triggered by dehydration, stress, high altitudes, fever, and extreme temperatures. Because of improved disease understanding and management, most patients with sickle cell anemia now live into their 50s.

The clinical manifestations of sickle cell anemia reflect the hypoxia and tissue ischemia that occurs in the disease, and the complications that can result from them:

- Abdominal pain
- Bone pain
- Dyspnea
- Delayed growth and development
- Fatigue
- Fever
- Jaundice (yellowish skin)
- Pallor
- Tachycardia
- Skin ulcers on the lower legs
- Angina
- Excessive thirst
- Frequent urination
- Painful and prolonged erection (priapism)
- Vision impairment
- Frequent infections
- Acute chest syndrome (a potentially life-threatening condition that causes chest pain, coughing, difficulty breathing, and fever)
- Splenic sequestration (a potentially life-threatening condition that causes sudden weakness, pale lips, tachypnea, extreme thirst, left quadrant abdominal pain, and tachycardia)
- Leg ulcers
- Stroke

Carriers of the defective gene can be detected by hemoglobin electrophoresis, a simple

<table>
<thead>
<tr>
<th>Area of Occlusion</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone</td>
<td>Susceptibility to osteomyelitis due to <em>Staphylococcus</em> infection</td>
</tr>
</tbody>
</table>
| Papillae of renal medulla | Gross hematuria  
Renal tubular concentrating defects |
| Eye               | Retinopathy  
Blindness |
| Sinus             | Stroke |
| Spleen            | Hyposplenism  
Susceptibility to infection |
| Liver             | Jaundice  
Hepatomegaly |
| Miscellaneous     | Cardiomegaly  
Slow-healing leg ulcers |

blood test. Additionally, the sickle cell test can determine whether the hemoglobin is normal or sickled. A complete blood count and bilirubin test are useful in determining diagnosis and progression. There is no single best treatment for all people with sickle cell disease. Stem cell transplants are the option for a cure. Medications (e.g., Hydrea [hydroxyurea]) are available to reduce the frequency of crises. Avoidance of sickling triggers is also helpful. Other strategies include the following measures:

- Oxygen therapy
- Hydration
- Pain management (e.g., opioids, relaxation techniques, distraction)
- Infection control measures
- Vaccinations
- Blood transfusions
- Bone marrow transplants
- Genetic counseling for those persons with sickle cell trait

**Thalassemia**

Thalassemia is another genetic type of anemia, which results in abnormal hemoglobin. This disease follows an autosomal dominant inheritance pattern (see the Cellular Function chapter). The abnormal hemoglobin is a result of a lack of one of two proteins that collectively make up hemoglobin (alpha and beta globin). Thalassemia occurs most frequently in persons of Mediterranean descent. Other ethnic groups affected by thalassemia include those of Asian, Indian, and African descent. Severe cases can lead to death in childhood. Moderate cases and those treated effectively can survive into their 30s.

Thalassemia has the following clinical manifestations:

- Abortion
- Delayed growth and development
- Fatigue
- Dyspnea
- Heart failure
- Hepatomegaly
- Splenomegaly
- Bone deformities
- Jaundice

Upon examination, erythrocytes will appear microcytic and hypochromic, and they vary in size. Iron levels may be increased. A complete blood count is also useful in diagnosis (low MCV and MCHC). Treatment may not be necessary in mild cases. Severe cases, however, can cause early death due to heart failure, usually between the ages of 20 and 30. If treatment is warranted, it includes blood transfusion, chelation therapy, bone marrow transplants, and splenectomy.

**Polycythemia Vera**

Polycythemia vera is a disorder in which the bone marrow produces too many blood cells. This rare condition is considered a neoplastic disease because of the uncontrolled proliferation of cells. The exact cause of this disease, which occurs most frequently in men, is unknown. As blood cell numbers increase, so does the blood volume and viscosity. Blood vessels become dis tended and blood flow is sluggish. The following complications are possible:

- Tissue ischemia and necrosis
- Thrombosis
- Hypertension
- Heart failure
- Hemorrhage
- Splenomegaly
- Hepatomegaly
- Acute myeloblastic leukemia

Clinical manifestations of polycythemia vera include the following:

- Cyanotic or plethoric (reddish) skin
- High blood pressure
- Tachycardia
- Dyspnea
- Headaches
- Visual abnormalities

Diagnostic procedures for polycythemia vera include complete blood counts, bone marrow biopsy, and uric acid levels. Treatment strategies include chemotherapy (specifically hydroxyurea), radiation, and phlebotomy (removal of blood). Management of clotting and bleeding disorders will be employed as needed.

**Diseases of the Platelets**

Platelets are vital components of the coagulation process. Normal platelet levels range from 150,000 to 350,000 cells/mL³. Thrombocytosis refers to increased platelet levels, and thrombocytopenia describes the condition of decreased platelet levels. Thrombocytosis increases the risk of thrombus formation, while thrombocytopenia increases the risk of bleeding and infection. Capillaries are relatively delicate structures that can leak from even minor injuries. Fortunately, the platelets, along with the coagulation process, quickly halt leaking. Diseases of the platelets include issues in quantity and quality of platelets.
Hemophilia A

Hemophilia A, or classic hemophilia, is an X-linked recessive bleeding disorder (see the Cellular Function chapter). This condition involves a deficiency or abnormality of clotting factor VIII (Figure 3-3). The severity of the disorder varies depending on the amount of factor VIII present in the blood.

Severe forms of hemophilia A become apparent early on. Bleeding is the main symptom of the disease and sometimes, though not always, occurs if an infant is circumcised. Additional bleeding problems may be seen when the infant starts crawling and walking. Internal bleeding may happen anywhere, and bleeding into joints, or hemarthrosis, is common. Other manifestations include petechiae, bruising, gastrointestinal bleeding, and hematuria.

Diagnosis of hemophilia A includes the examination of bleeding studies. Bleeding time and prothrombin time are usually normal, but partial prothromboplastin time, activated partial prothromboplastin time, and coagulation time are prolonged. Serum levels of factor VIII are low.

Treatment strategies include replacing clotting factors through transfusions and Advate (antihemophilic factor, a recombinant DNA product). To prevent a bleeding crisis, patients can be taught to give factor VIII concentrates at the first signs of bleeding. People with severe forms of the disease may need regular preventive treatment. Mild hemophilia may be treated with desmopressin (DDAVP), which helps the body release factor VIII that is stored within the lining of blood vessels. Additionally, bleeding precautions should be employed (e.g., electric razors, soft bristle toothbrush, and injury prevention).

Von Willebrand’s Disease

Von Willebrand’s disease is the most common hereditary bleeding disorder. It results from a deficit of the von Willebrand factor, which ordinarily causes platelets to come together (aggregate) and stick (adhere) to the vessel wall in times of injury. Several forms of Von Willebrand’s disease are distinguished:

- **Type 1** is the most common (70–80%) and mildest form. It follows an autosomal dominant inheritance pattern (see the Cellular Function chapter). The level of von Willebrand factor in the blood is reduced. Because this form is often very mild, most cases go undiagnosed. Type 1 does not usually cause spontaneous bleeding, but significant bleeding can occur with trauma or surgery.
- **Type 2** occurs in 15–20% of cases. It can be either autosomal dominant or recessive, and five subtypes exist. In type 2, the building blocks (multimers) that make up the von Willebrand factor are smaller than usual or break down easily.
- **Type 3** follows an autosomal recessive inheritance pattern. Severe bleeding problems are seen with this type due to the lack of measurable von Willebrand factor or factor VIII.
- **Acquired type** occurs in persons with Wilms’ tumor, congenital heart disease, systemic lupus erythematosus, and hypothyroidism.

Clinical manifestations of von Willebrand’s disease include abnormal bleeding. Diagnosis requires bleeding studies (e.g., bleeding time, prothrombin time, and partial prothromboplastin time) and factor VIII levels. Treatment, if needed, includes infusions of cryoprecipitate or administration of desmopressin (DDVAP); DDVAP increases the release of von Willebrand factor and factor VII. Additionally, measures are used to control bleeding and prevent injury (e.g., pressure dressings).

Disseminated Intravascular Coagulation

Disseminated intravascular coagulation (DIC) is a life-threatening disorder that occurs as a complication of other diseases and conditions. Normally, during injury, clotting factors (Figure 3-3) become activated and travel to the injury site to help stop bleeding. However, in persons with DIC, these factors become abnormally active. In fact, they may become active as an inappropriate immune reaction. Consequently, small blood clots form within the blood vessels, and some of these clots can occlude blood supply to tissue and organs. Over time, the clotting factors become used up. When this happens, the person is at risk for serious bleeding from even a minor injury.

LEARNING POINTS

In DIC, hypercoagulation uses up all the available clotting factors. Once available clotting factors are utilized, the patient begins excessively bleeding. In other words, the individual clots, clots, clots, and then bleeds, bleeds, bleeds!
It is not clear why certain disorders lead to DIC, but the typical triggers include the following conditions:

- Blood transfusion reaction
- Cancer (e.g., leukemia, aplastic anemia, and metastatic carcinoma)
- Infection in the blood by bacteria or fungus
- Pregnancy complications (e.g., retained placenta after delivery, abruptio placentae, and eclampsia)
- Recent surgery or anesthesia
- Sepsis (an overwhelming infection)
- Severe liver disease
- Severe tissue injury (e.g., burns and head injury)
- Cardiac arrest
- Poisonous snake bites

Clinical manifestations of DIC include signs and symptoms of tissue and organ ischemia (e.g., angina, confusion, and dyspnea) and abnormal bleeding (e.g., petechiae, epistaxis, and hematuria). Additionally, indicators of complications such as shock and multiple organ failure will appear.

Diagnostic procedures for DIC consist of complete blood counts and bleeding studies (e.g., fibrinogen levels, prothrombin time, partial prothromboplastin time, and fibrinogen degradation products). Management of DIC is complicated but starts with the identification and treatment of the underlying cause. The treatment of the DIC disorder itself is a delicate balance between preventing clots and treating bleeding (FIGURE 3-11).

Idiopathic Thrombocytopenic Purpura

Idiopathic thrombocytopenic purpura (ITP) is a hypocoagulopathy state resulting from the immune system destroying its own platelets. Circulating immunoglobulin G reacts with the platelets, which are then destroyed in the spleen and liver.

ITP can be acute or chronic. Acute ITP is more common in children. This form of the disease typically has a sudden onset and is self-limiting. Chronic ITP is more common in adults aged 20–50 and in women. Prognosis is usually good for both acute and chronic ITP.

Causes of ITP include the following:
- Idiopathic causes
- Autoimmune diseases
- Immunosuppressive therapy
- Idiopathic thrombocytopenic purpura
- Immunodeficiency disorders (e.g., AIDS)
- Viral infections

Clinical manifestations include abnormal bleeding (e.g., petechiae, epistaxis, and hematuria). Diagnostic procedures include complete blood counts, bone marrow biopsy, and humoral studies. Thrombocyte counts will often be less than 20,000/mL.

The following treatment strategies may be employed for acute ITP:
- Glucocorticoid steroids (prevent further platelet immune destruction)
- Immunoglobulins (prevent further platelet destruction)
- Plasmapheresis
- Platelet pheresis

Treatment strategies for chronic ITP include these measures:
- Glucocorticoid steroids
- Immunosuppressant therapy
- Splenectomy
- Blood transfusions
- Immunoglobulins
- Imatinib (Gleevec)
- Interferon-alpha
- Rituximab
- Tyrosine kinase inhibitors

Thrombotic Thrombocytopenic Purpura

Thrombotic thrombocytopenic purpura (TTP) is a coagulation disorder resulting from a deficiency of an enzyme necessary for cleaving von Willebrand’s factor. This enzyme deficiency leads to increased clotting, which in turn decreases available platelets. Fewer platelets can lead to bleeding under the skin and purple-colored spots called purpura; therefore, TTP is characterized by thrombi, thrombocytopenia, and bleeding. TTP may be caused by any of the following conditions:
- Idiopathic causes
- Heredity
- Bone marrow transplants
- Cancer
- Medications (e.g., platelet aggregation inhibitors, immunosuppressants, and hormone replacement)
- Pregnancy
- HIV

TTP is characterized by these clinical manifestations:
- Purpura
- Changes in consciousness
- Confusion
- Fatigue
Diagnostic procedures for TTP include a history, physical examination, complete blood counts, blood smears, and lactate dehydrogenase levels. Plasmapheresis is the centerpiece of TTP treatment. Additionally, a splenectomy and glucocorticoid steroids may be necessary.
CHAPTER SUMMARY

Blood serves many purposes in the body. Without this life fluid functioning properly, the body cannot maintain health and homeostasis; therefore, problems with any of the blood cells can lead to widespread and life-threatening problems. Hematologic problems can result from a variety of origins but usually lead to abnormal cell numbers or function. Timely identification and treatment of these disorders is vital for positive healthcare outcomes.

REFERENCES


Now that we have learned about the various blood dyscrasias, let’s put that knowledge into practice. During shift change, you receive reports on the following patients. Who would you see first following report?

- A 32-year-old with pernicious anemia who needs to receive a vitamin B₁₂ injection
- A 40-year-old with iron-deficiency anemia who needs a Z-track iron injection
- A 67-year-old with acute myelocytic leukemia (AML) who has petechiae on the legs
- An 81-year-old with thrombocytopenia and an increased abdominal girth

Remember to go through the usual thought process—who would die first, acute versus chronic conditions, Maslow’s hierarchy of needs, and patient safety. Starting with the patient with the pernicious anemia, vitamin B₁₂ is the mainstay of treatment, but the therapy is not a matter of life or death. The same is true for the patient with iron-deficiency anemia. Additionally, both of these conditions are chronic. The AML patient with petechiae warrants consideration because that condition is acute and there is some mild bleeding—but hold off on making the decision until you look at all the patients. Finally, consider the thrombocytopenia patient experiencing increased abdominal girth. What would cause the increased abdominal girth? You must consider that the patient may be bleeding into the peritoneal cavity. This active bleeding would be worse than the mild bleeding in the AML patient. You should see the 81-year-old patient to assess for other manifestations of internal hemorrhage (e.g., hypotension and tachycardia) so that measures could be implemented immediately (e.g., notifying the healthcare provider and administering blood products).