

HEMATOLOGICAL DISORDER

Definition: Hematologic diseases are disorders which primarily affect the blood. Hematology includes the study of these disorders.

There are many conditions of or affecting the human hematologic system — the biological system that includes plasma, platelets, leukocytes, and erythrocytes, the major components of blood and the bone marrow.

People may be affected by many different types of blood conditions and blood cancers. Common blood disorders include anemia, bleeding disorders such as hemophilia, blood clots, and blood cancers such as leukemia, lymphoma, and myeloma.

Anemias

An anemia is a decrease in number of red blood cells (RBCs) or less than the normal quantity of hemoglobin in the blood. However, it can include decreased oxygen-binding ability of each hemoglobin molecule due to deformity or lack in numerical development as in some other types of hemoglobin deficiency.

Anemia is the most common disorder of the blood. There are several kinds of anemia, produced by a variety of underlying causes. Anemia can be classified in a variety of ways, based on the morphology of RBCs, underlying etiologic mechanisms, and discernible clinical spectra, to mention a few. The three main classes of anemia include excessive blood loss, excessive blood cell destruction or deficient red blood cell production.

BLEEDING DISORDER

What is a Bleeding Disorder?

A bleeding disorder is a condition that affects the way your blood normally clots. The clotting process, also known as coagulation, changes blood from a liquid to a solid. When you're injured, your blood normally begins to clot to prevent a massive loss of blood. Sometimes, certain conditions prevent blood from clotting properly, which can result in heavy or prolonged bleeding.

MEDICAL PATHOLOGY

Bleeding disorders can cause abnormal bleeding both outside and inside the body. Some disorders can drastically increase the amount of blood leaving your body. Others cause bleeding to occur under the skin or in vital organs, such as the brain.

Causes of Bleeding Disorder

Bleeding disorders often develop when the blood can't clot properly. For blood to clot, your body needs blood proteins called clotting factors and blood cells called platelets. Normally, platelets clump together to form a plug at the site of a damaged or injured blood vessel. The clotting factors then come together to form a fibrin clot. This keeps the platelets in place and prevents blood from flowing out of the blood vessel.

In people with bleeding disorders, however, the clotting factors or platelets don't work the way they should or are in short supply. When the blood doesn't clot, excessive or prolonged bleeding can occur. It can also lead to spontaneous or sudden bleeding in your muscles, joints, or other parts of your body.

The majority of bleeding disorders are inherited, which means they're passed from a parent to their child. However, some disorders may develop as a result of other medical conditions, such as liver disease.

Bleeding disorders may also be caused by:

- a low red blood cell count
- a vitamin K deficiency
- side effects from certain medications

Medications that can interfere with the clotting of the blood are called anticoagulants.

Types of Bleeding Disorders

Bleeding disorders can be inherited or acquired. Inherited disorders are passed down through genetics. Acquired disorders can develop or spontaneously occur later in life. Some bleeding

MEDICAL PATHOLOGY

disorders can result in severe bleeding following an accident or injury. In other disorders, heavy bleeding can happen suddenly and for no reason.

There are numerous different bleeding disorders, but the following are the most common ones:

- Hemophilia A and B are conditions that occur when there are low levels of clotting factors in your blood. It causes heavy or unusual bleeding into the joints. Though hemophilia is rare, it can have life-threatening complications.
- Factor II, V, VII, X, or XII deficiencies are bleeding disorders related to blood clotting problems or abnormal bleeding problems.
- von Willebrand's disease is the most common inherited bleeding disorder. It develops when the blood lacks von Willebrand factor, which helps the blood to clot.

Symptoms of Bleeding Disorder

The symptoms can vary depending on the specific type of bleeding disorder. However, the main signs include:

- unexplained and easy bruising
- heavy menstrual bleeding
- frequent nosebleeds
- excessive bleeding from small cuts or an injury
- bleeding into joints

Schedule an appointment with your doctor right away if you have one or more of these symptoms. Your doctor can diagnose your condition and help to prevent complications associated with certain blood disorders.

Diagnosis

To diagnose a bleeding disorder, your doctor will ask you about your symptoms and medical history. They will also perform a physical examination. During your appointment, make sure to mention:

- any medical conditions you currently have
- any medications or supplements you may be taking
- any recent falls or trauma
- how often you experience the bleeding
- how long the bleeding lasts
- what you were doing before the bleeding began

MEDICAL PATHOLOGY

After gathering this information, your doctor will run blood tests to make a proper diagnosis. These tests may include:

- a complete blood count (CBC), which measures the amount of red and white blood cells in your body
- a platelet aggregation test, which checks how well your platelets clump together
- a bleeding time, which determines how quickly your blood clots to prevent bleeding

Treatment

Treatment options vary depending on the type of bleeding disorder and its severity. Though treatments can't cure bleeding disorders, they can help relieve the symptoms associated with certain disorders.

Iron Supplementation

Your doctor may prescribe iron supplements to replenish the amount of iron in your body if you have significant blood loss. A low iron level can result in iron deficiency anemia. This condition can make you feel weak, tired, and dizzy. You may need a blood transfusion if symptoms don't improve with iron supplementation.

Blood Transfusion

A blood transfusion replaces any lost blood with blood taken from a donor. The donor blood has to match your blood type to prevent complications. This procedure can only be done in the hospital.

LEUKEMIA

Leukemia, also spelled **leukaemia**, is a group of cancers that usually begin in the bone marrow and result in high numbers of abnormal white blood cells.^[2] These white blood cells are not fully developed and are called *blasts* or *leukemia cells*.

The word *leukemia*, which means 'white blood', is derived from the disease's namesake high white blood cell counts that most leukemia patients have before treatment. The high number of white blood cells are apparent when a blood sample is viewed under a microscope. Frequently, these extra white blood cells are immature or dysfunctional. The excessive number of cells can also interfere with the level of other cells, causing a harmful imbalance in the blood count.

Some leukemia patients do not have high white blood cell counts visible during a regular blood count. This less-common condition is called *aleukemia*. The bone marrow still contains

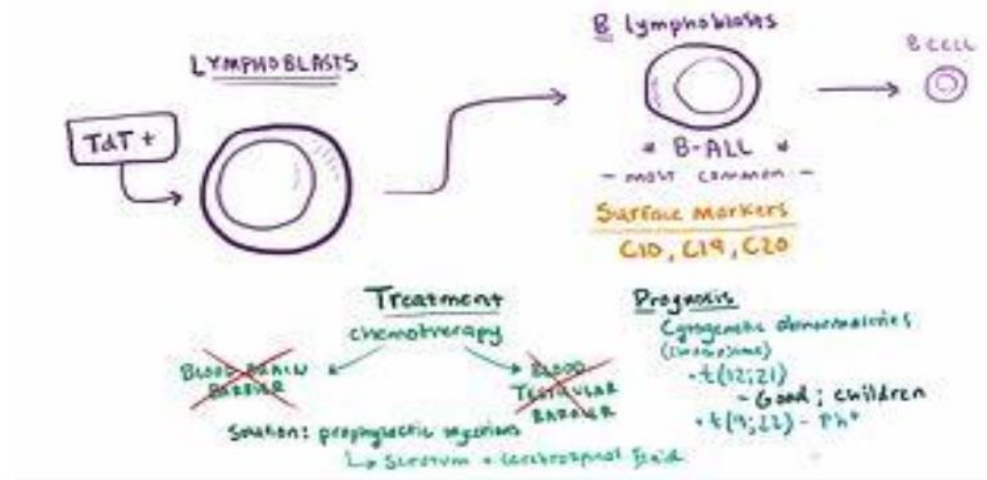
MEDICAL PATHOLOGY

cancerous white blood cells which disrupt the normal production of blood cells, but they remain in the marrow instead of entering the bloodstream, where they would be visible in a blood test. For an aleukemic patient, the white blood cell counts in the bloodstream can be normal or low. Aleukemia can occur in any of the four major types of leukemia, and is particularly common in hairy cell leukemia.

General classification

Clinically and pathologically, leukemia is subdivided into a variety of large groups. The first division is between its *acute* and *chronic* forms:

- Acute leukemia is characterized by a rapid increase in the number of immature blood cells. The crowding that results from such cells makes the bone marrow unable to produce healthy blood cells. Immediate treatment is required in acute leukemia because of the rapid progression and accumulation of the malignant cells, which then spill over into the bloodstream and spread to other organs of the body. Acute forms of leukemia are the most common forms of leukemia in children.



Explanation of acute leukemia

- Chronic leukemia is characterized by the excessive buildup of relatively mature, but still abnormal, white blood cells. Typically taking months or years to progress, the cells are produced at a much higher rate than normal, resulting in many abnormal white blood cells. Whereas acute leukemia must be treated immediately, chronic forms are sometimes monitored for some time before treatment to ensure maximum effectiveness of therapy. Chronic leukemia mostly occurs in older people, but can occur in any age group.

MEDICAL PATHOLOGY

Specific types

- Acute lymphoblastic leukemia (ALL) is the most common type of leukemia in young children. It also affects adults, especially those 65 and older. Standard treatments involve chemotherapy and radiotherapy. The survival rates vary by age: 85% in children and 50% in adults.
- Chronic lymphocytic leukemia (CLL) most often affects adults over the age of 55. It sometimes occurs in younger adults, but it almost never affects children. Two-thirds of affected people are men. The five-year survival rate is 75%. It is incurable, but there are many effective treatments.
- Acute myelogenous leukemia (AML) occurs more commonly in adults than in children, and more commonly in men than women. It is treated with chemotherapy. The five-year survival rate is 40%, except for APL (Acute Promyelocytic Leukemia), which has a survival rate greater than 90%. Subtypes of AML include acute promyelocytic leukemia, acute myeloblastic leukemia, and acute megakaryoblastic leukemia.
- Chronic myelogenous leukemia (CML) occurs mainly in adults; a very small number of children also develop this disease. It is treated with imatinib (Gleevec in United States, Glivec in Europe) or other drugs. The five-year survival rate is 90%.^{[15][16]} One subtype is chronic myelomonocytic leukemia.
- Hairy cell leukemia (HCL) is sometimes considered a subset of chronic lymphocytic leukemia, but does not fit neatly into this category. About 80% of affected people are adult men. No cases in children have been reported. HCL is incurable but easily treatable. Survival is 96% to 100% at ten years.
- T-cell prolymphocytic leukemia (T-PLL) is a very rare and aggressive leukemia affecting adults; somewhat more men than women are diagnosed with this disease. Despite its overall rarity, it is the most common type of mature T cell leukemia; nearly all other leukemias involve B cells. It is difficult to treat, and the median survival is measured in months.
- Large granular lymphocytic leukemia may involve either T-cells or NK cells; like hairy cell leukemia, which involves solely B cells, it is a rare and indolent (not aggressive) leukemia.^[20]

MEDICAL PATHOLOGY

- Adult T-cell leukemia is caused by human T-lymphotropic virus (HTLV), a virus similar to HIV. Like HIV, HTLV infects CD4+ T-cells and replicates within them; however, unlike HIV, it does not destroy them. Instead, HTLV "immortalizes" the infected T-cells, giving them the ability to proliferate abnormally. Human T-cell lymphotropic virus types I and II (HTLV-I/II) are endemic in certain areas of the world.

Causes

The cause for most cases of leukemia is unknown. The different leukemias likely have different causes.

Leukemia, like other cancers, results from mutations in the DNA. Certain mutations can trigger leukemia by activating oncogenes or deactivating tumor suppressor genes, and thereby disrupting the regulation of cell death, differentiation or division. These mutations may occur spontaneously or as a result of exposure to radiation or carcinogenic substances.

Among adults, the known causes are natural and artificial ionizing radiation, a few viruses such as human T-lymphotropic virus, and some chemicals, notably benzene and alkylating chemotherapy agents for previous malignancies. Use of tobacco is associated with a small increase in the risk of developing acute myeloid leukemia in adults. Cohort and case-control studies have linked exposure to some petrochemicals and hair dyes to the development of some forms of leukemia.

Viruses have also been linked to some forms of leukemia. For example, human T-lymphotropic virus (HTLV-1) causes adult T-cell leukemia.

Some people have a genetic predisposition towards developing leukemia. This predisposition is demonstrated by family histories and twin studies. The affected people may have a single gene or multiple genes in common. In some cases, families tend to develop the same kinds of leukemia as other members; in other families, affected people may develop different forms of leukemia or related blood cancers.

Whether non-ionizing radiation causes leukemia has been studied for several decades.

A few cases of maternal-fetal transmission (a baby acquires leukemia because its mother had leukemia during the pregnancy) have been reported.

Signs and symptoms

White blood cells, which are involved in fighting pathogens, may be suppressed or dysfunctional. This could cause the patient's immune system to be unable to fight off a simple

MEDICAL PATHOLOGY

infection or to start attacking other body cells. Because leukemia prevents the immune system from working normally, some patients experience frequent infection, ranging from infected tonsils, sores in the mouth, or diarrhea to life-threatening pneumonia or opportunistic infections.

Finally, the red blood cell deficiency leads to anemia, which may cause dyspnea.

Some patients experience other symptoms, such as feeling sick, having fevers, chills, night sweats, feeling fatigued and other flu-like symptoms. Some patients experience nausea or a feeling of fullness due to an enlarged liver and spleen; this can result in unintentional weight loss. Blasts affected by the disease may come together and become swollen in the liver or in the lymph nodes causing pain and leading to nausea.^[22]

If the leukemic cells invade the central nervous system, then neurological symptoms (notably headaches) can occur. Uncommon neurological symptoms like migraines, seizures, or coma can occur as a result of brain stem pressure. All symptoms associated with leukemia can be attributed to other diseases. Consequently, leukemia is always diagnosed through medical tests.

Diagnosis

Diagnosis is usually based on repeated complete blood counts and a bone marrow examination following observations of the symptoms. Sometimes, blood tests may not show that a person has leukemia, especially in the early stages of the disease or during remission. A lymph node biopsy can be performed to diagnose certain types of leukemia in certain situations.

Following diagnosis, blood chemistry tests can be used to determine the degree of liver and kidney damage or the effects of chemotherapy on the patient. When concerns arise about other damage due to leukemia, doctors may use an X-ray, MRI, or ultrasound.

Treatment

Most forms of leukemia are treated with pharmaceutical medication, typically combined into a multi-drug chemotherapy regimen. Some are also treated with radiation therapy. In some cases, a bone marrow transplant is effective.

LYMPHOMA

Definition: Lymphoma is a form of cancer that affects the immune system - specifically, it is a cancer of immune cells called lymphocytes, a type of white blood cell. There are two broad types of lymphoma and many subtypes.

The two types of lymphoma are described as: Hodgkin's or non-Hodgkin's.

Lymphoma can occur at any age but is the most common cancer in young people. It is often very treatable.

Types of lymphoma

There are many different types of lymphoma depending on the type of lymphatic cells affected.

Hodgkin's lymphoma can occur at any age, affects more men than women and the majority will be completely cured.

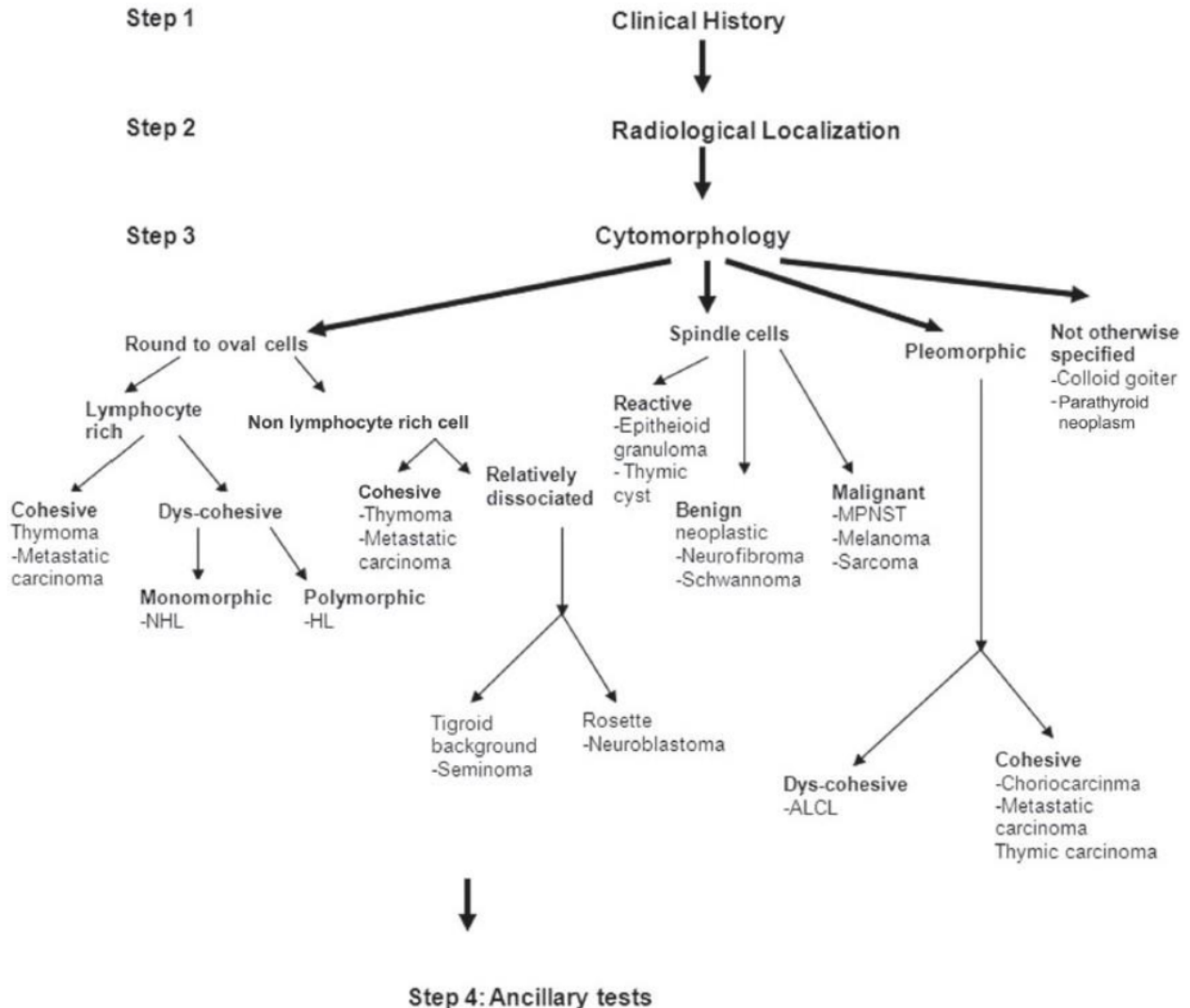
Hodgkin's lymphoma is diagnosed when a special type of cell, the Reed-Sternberg cell, is seen under the microscope.

Non-Hodgkin's lymphoma accounts for all the other types of lymphoma. These can be high grade or low grade and the treatment and prognosis varies.

Non-Hodgkin's lymphoma

- **Age** - most non-Hodgkin lymphomas are in people 60 years of age and over
- **Sex** - there are different rates of different types of non-Hodgkin's lymphoma across the sexes
- **Ethnicity and location** - in the US, African-Americans and Asian-Americans are less prone than white Americans, and the disease is more common in developed nations of the world
- **Chemicals and radiation** - some chemicals used in agriculture have been linked, as has nuclear radiation exposure
- **Immune deficiency** - for example, caused by HIV infection or in organ transplantation
- **Autoimmune disease**, in which the immune system attacks the body's own cells
- **Infection** - certain viral and bacterial infections increase the risk. The Helicobacter Infection has been implicated, as has the Epstein Barr Virus (the virus that causes glandular fever)

MEDICAL PATHOLOGY



Abbreviations: NHL=Non Hodgkin's lymphoma, HL=Hodgkin's lymphoma, Ca=Carcinoma, ALCL=Anaplastic large cell lymphoma, MPNST=Malignant peripheral nerve sheath tumor

Hodgkin's lymphoma

- **Infectious mononucleosis** - infection with Epstein-Barr virus
- **Age** - two specific groups are most affected: typically people in their 20s, and people over the age of 55 years
- **Sex** - slightly more common in men
- **Location** - most common in the US, Canada and northern Europe; least common in Asia
- **Family** - if a sibling has the condition, the risk is slightly higher, and very high if there is an identical twin
- **Affluence** - people from higher socioeconomic status are at greater risk
- **HIV infection**

What causes lymphoma?

- For most cancers, researchers are still trying to understand how they are caused. The same is true for lymphoma - doctors do not know what causes it, although it is more likely to occur in certain people.^{5,7,8}

Symptoms of lymphoma

- The symptoms and signs of lymphoma are very similar to those of simple illnesses such as viral illnesses and the common cold, and this can cause problems with delayed diagnosis.
- The difference is that the symptoms of lymphoma persist long after the usual run of a viral infection.
- The symptoms typically involve painless swelling of the lymph nodes (glands), often in the neck or armpits where these nodes are concentrated. Swelling may also occur in the groin and abdomen, although some people do not experience any detectable swelling in any part of the body.
- The enlarged glands can press on organs, bones and other structures causing pain, but this pain can be similar to that of other less serious causes (such as simple backache), again making lymphoma an easy diagnosis to miss.

The lymph nodes, part of the immunity's lymphatic system, are found all around the body, but their swelling in lymphoma is noticeable.

Other symptoms that can be experienced by people with lymphoma include the following:

- Swelling in the legs or ankles
- Night sweats and fever
- Weight loss and loss of appetite
- Chills
- Unusual itching
- Fatigue
- Pain or altered sensation
- Loss of appetite
- Unusual tiredness/lack of energy
- Persistent coughing
- Breathlessness

Spread of lymphoma

Hodgkin's lymphoma is a cancer of the lymphocytes, a type of white blood cell. This type of cancer affects the lymph nodes and, as lymphatic tissue is connected throughout the body, this gives the cancer cells an easy way of traveling from their original location to spread to other tissues, including those outside of the lymphatic system.

- In Hodgkin's lymphoma, this spread usually occurs in a sequential fashion, affecting one lymph node after another in order
- In non-Hodgkin's lymphoma, tumors may arise in disparate lymph nodes, skipping some nodes.

Tests and diagnosis

A physical examination will follow for all cases of suspected lymphoma - palpating areas of the body where any swollen lymph nodes may be felt. The doctor may also feel around the abdomen to examine the spleen and liver.

The doctor will look for swollen lymph nodes in a number of areas, including the:

- Chin
- Neck
- Tonsils
- Groin
- Axillae (armpit)
- Shoulders
- Elbows.

Treatments and prevention

- A number of treatment options are used against lymphoma, many of which are common to other types of cancer.
- Treatment for Hodgkin's lymphoma also depends on the grade of the cancer
- Unlike non-Hodgkin's lymphoma, however, treatment for early stage Hodgkin's lymphoma usually takes the form of a short course of chemotherapy followed by field radiation to treat the affected lymph nodes
- This offers systemic and localized cancer treatment, but helps minimize damage to healthy tissue

MEDICAL PATHOLOGY

- Treatment for later-stage Hodgkin's lymphoma typically comprises combination chemotherapy to shrink widespread tumors.

In addition to watchful waiting, chemotherapy, and radiation therapy, lymphoma treatment may also take the form of:

- Biologic therapy
- Antibody therapy
- Stem-cell transplantation
- Splenectomy
- Steroid treatment
- Radioimmunotherapy
- Surgery.