**Subject Name: MEDICAL PATHOLOGY**
**Subject code: SBM1206**

## UNIT – II FLUID AND HEMODYNAMIC DEARANGEMENT

### EDEMA

**Definition: Edema** (also **oedema**, **dropsy**, and **hydropsy**) is an abnormal accumulation of fluid in the interstitium, located beneath the skin and in the cavities of the body which cause severe pain. Clinically, edema is the medical term for swelling; the amount of interstitial fluid is determined by the balance of fluid homeostasis, and the increased secretion of fluid into the interstitium, or the impaired removal of the fluid can cause edema.

**Generalized Edema:**

A rise in hydrostatic pressure occurs in cardiac failure. A fall in osmotic pressure occurs in nephrotic syndrome and liver failure.[3]

Causes of edema which are generalized to the whole body can cause edema in multiple organs and peripherally.

**Organ-specific**

An edema will occur in specific organs as part of inflammations, tendonitis or pancreatitis, for instance. Certain organs develop edema through tissue specific mechanisms.

Examples of edema in specific organs:

Cerebral edema is extracellular fluid accumulation in the brain. It can occur in toxic or abnormal metabolic states and conditions such as systemic lupus or reduced oxygen at high altitudes. It causes drowsiness or loss of consciousness.

Pulmonary edema occurs when the pressure in blood vessels in the lung is raised because of obstruction to the removal of blood via the pulmonary veins. This is usually due to failure of the left ventricle of the heart.

Edema may also be found in the cornea of the eye with glaucoma, severe conjunctivitis or keratitis or after surgery. Sufferers may perceive coloured haloes around bright lights.

Edema surrounding the eyes is called *periorbital edema*. The periorbital tissues are most noticeably swollen immediately after waking, perhaps as a result of the gravitational redistribution of fluid in the horizontal position.

Common appearances of cutaneous edema are observed with mosquito bites, spider bites, bee stings and skin contact with certain plants such as Poison Ivy or Western Poison Oak.

lymphedema abnormal removal of interstitial fluid is caused by failure of the lymphatic system. This may be due to obstruction from, for example, pressure from a cancer or enlarged lymph nodes, destruction of lymph vessels by radiotherapy, or infiltration of the lymphatics by infection (such as elephantiasis).

Hydrops fetalis is a condition of the fetus characterized by an accumulation of fluid, or edema, in at least two fetal compartments.

**Causes of Edema**

Edema is a normal response of the body to inflammation or injury. For example, a twisted ankle, a bee sting, or a skin infection will all result in edema in the involved area. In some cases, such as in an infection, this may be beneficial. Increased fluid from the blood vessels allows more infection-fighting white blood cells to enter the affected area.

Edema can also result from medical conditions or problems in the balance of substances normally present in blood. Some of the causes of edema include:

**Low albumin (hypoalbuminemia):** Albumin and other proteins in the blood act like sponges to keep fluid in the blood vessels. Low albumin may contribute to edema, but isn't usually the sole cause.

**Allergic reactions:** Edema is a usual component of most allergic reactions. In response to the allergic exposure, the body allows nearby blood vessels to leak fluid into the affected area.

**Obstruction of flow:** If the drainage of fluid from a body part is blocked, fluid can back up. A blood clot in the deep veins of the leg can result in leg edema. A tumor blocking lymph or blood flow will cause edema in the affected area.

**Critical illness:** Burns, life-threatening infections, or other critical illnesses can cause a whole-body reaction that allows fluid to leak into tissues almost everywhere. Widespread edema throughout the body can result.

**Treatment of Edema**

Treatment of edema often means treating the underlying cause of edema. For example, allergic reactions causing edema may be treated with antihistamines and corticosteroids.
Edema resulting from a blockage in fluid drainage can sometimes be treated by eliminating the obstruction:
A blood clot in the leg is treated with blood thinners, and the clot slowly breaks down; leg edema then resolves as fluid drainage improves.
A tumor obstructing a blood vessel or lymph flow can sometimes be reduced in size or removed with surgery, chemotherapy, or radiation.

**SHOCK**

Definition: Shock is a life-threatening condition that occurs when the body is not getting enough blood flow. Lack of blood flow means that the cells and organs do not get enough oxygen and nutrients to function properly.

**Causes**

Shock can be caused by any condition that reduces blood flow, including:

Heart problems (such as heart attack or heart failure)

Low blood volume (as with heavy bleeding or dehydration)

Changes in blood vessels (as with infection or severe allergic reactions)

Certain medications that significantly reduce heart function or blood pressure

Shock is often associated with heavy external or internal bleeding from a serious injury. Spinal injuries can also cause shock.

Toxic shock syndrome is an example of a type of shock from an infection.

**Symptoms**

A person in shock has extremely low blood pressure. Depending on the specific cause and type of shock, symptoms will include one or more of the following:

- Anxiety or agitation/restlessness
- Bluish lips and fingernails
- Chest pain
- Confusion
- Dizziness, lightheadedness, or faintness
- Pale, cool, clammy skin
- Low or no urine output

Profuse sweating, moist skin

Rapid but weak pulse

Shallow breathing

Unconsciousness

**Pathophysiology**

There are four stages of shock. As it is a complex and continuous condition there is no sudden transition from one stage to the next.[12] At a cellular level shock is the process of oxygen demand becoming greater than oxygen supply.

**Initial**

During this stage, the state of hypoperfusion causes hypoxia. Due to the lack of oxygen, the cells perform lactic acid fermentation.

**Compensatory**

This stage is characterized by the body employing physiological mechanisms, including neural, hormonal and bio-chemical mechanisms in an attempt to reverse the condition. As a result of the acidosis, the person will begin to hyperventilate in order to rid the body of carbon dioxide ($CO_2$). $CO_2$ indirectly acts to acidify the blood and by removing it the body is attempting to raise the pH of the blood. The baroreceptors in the arteries detect the resulting hypotension, and cause the release of epinephrine and norepinephrine. Norepinephrine causes predominately vasoconstriction with a mild increase in heart rate, whereas epinephrine predominately causes an increase in heart rate with a small effect on the vascular tone; the combined effect results in an increase in blood pressure. The lack of blood to the renal system causes the characteristic low urine production.

**Progressive**

Should the cause of the crisis not be successfully treated, the shock will proceed to the progressive stage and the compensatory mechanisms begin to fail. The hydrostatic pressure will increase and, combined with histamine release, this will lead to leakage of fluid and protein into the surrounding tissues. As this fluid is lost, the blood concentration and viscosity increase, causing sludging of the micro-circulation.

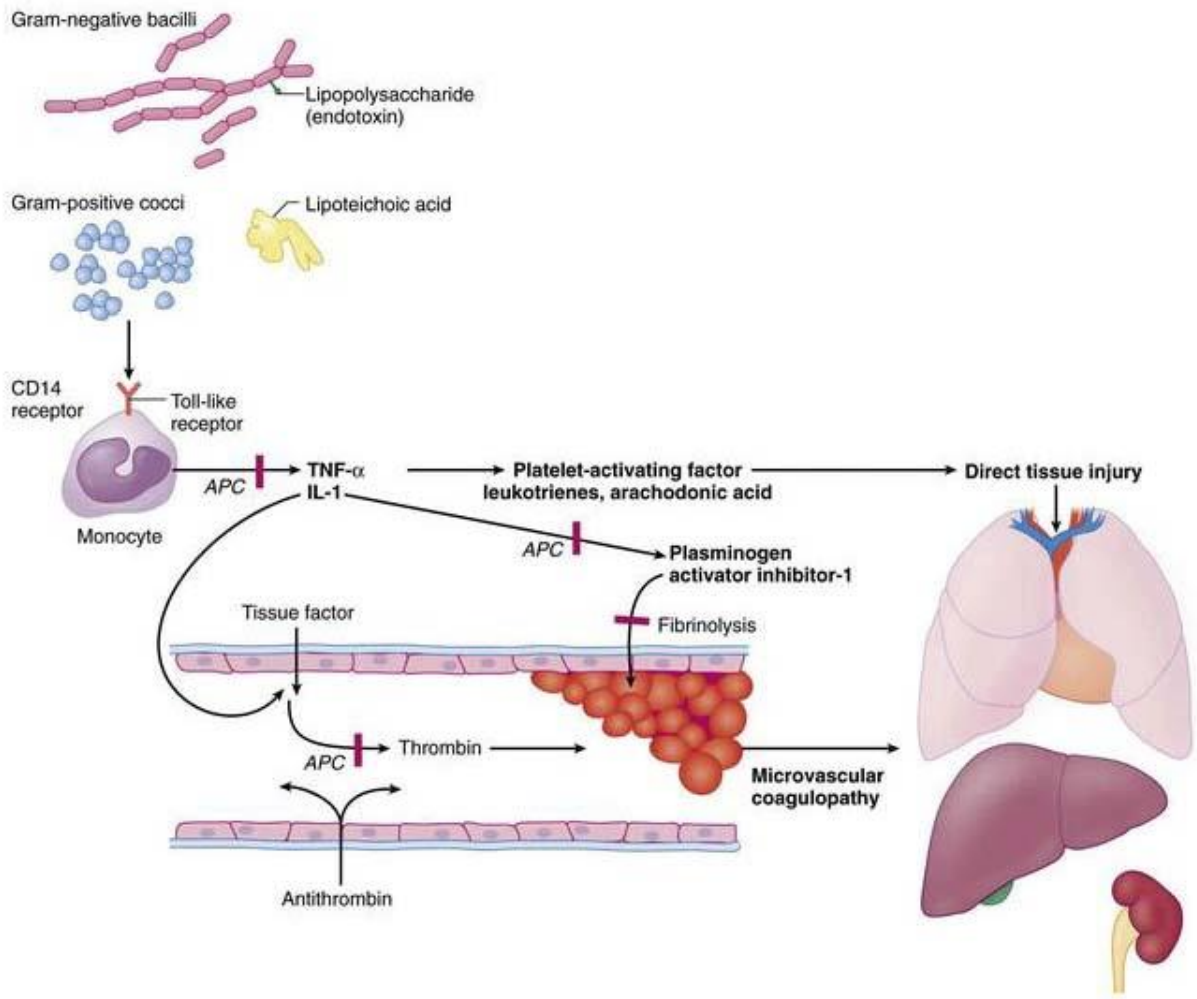
**Refractory**

At this stage, the vital organs have failed and the shock can no longer be reversed. Brain damage and cell death are occurring, and death will occur immediately. One of the primary reasons that

shock is irreversible at this point is that much cellular ATP has been degraded into adenosine in the absence of oxygen as an electron receptor in the mitochondrial matrix. Adenosine easily perfuse out of cellular membranes into extracellular fluid, furthering capillary vasodilation, and then is transformed into uric acid.

**Diagnosis**

The first changes seen in shock is an increased cardiac output followed by a decrease in mixed venous oxygen saturation (SmvO2) as measured in the pulmonary artery via pulmonary artery catheter. Central venous oxygen saturation (ScvO2) as measured via a central line correlates well with SmvO2 and are easier to acquire. If shock progresses anaerobic metabolism will begin to occur with an increased blood lactic acid as the result. A chest X-ray or emergency department ultrasound may be useful to determine volume state.



**HEMORRHAGE**

The term "hemorrhagic" comes from the Greek "haima," blood + rhegnumai," to break forth; a free and forceful escape of blood.

The escape of blood from a ruptured vessel; it can be either external or internal. Blood from an artery is bright red in color and comes in spurts; that from a vein is dark red and comes in a steady flow.

An escape of blood from the intravascular space. A loss of a large amount of blood in a short period, either externally or internally. Hemorrhage may be arterial, venous, or capillary.

**Causes**

High blood pressure is the most common cause of intracerebral hemorrhage. In younger people, another common cause is abnormally formed blood vessels in the brain. Other causes include: head injury or trauma.

The most obvious cause of hemorrhage is trauma or injury to a blood vessel. Hemorrhage can also be caused by weak spots in the artery wall that are often present at birth. Over time, the blood vessel walls at the site of an aneurysm tend to become thinner and bulge out like water balloons as blood passes through them, making them more likely to leak and rupture.

Hypertension, or high blood pressure, is often a contributing factor in brain hemorrhage, which can cause a stroke. Uncontrolled diabetes can also weaken blood vessels, especially in the eyes; this is called retinopathy . Use of medications that affect blood clotting, including aspirin, can make hemorrhage more likely to occur.

Bleeding disorders can also spark hemorrhages. Among them is hemophilia , an inherited disorder that prevents the blood from clotting.

**Symptoms**

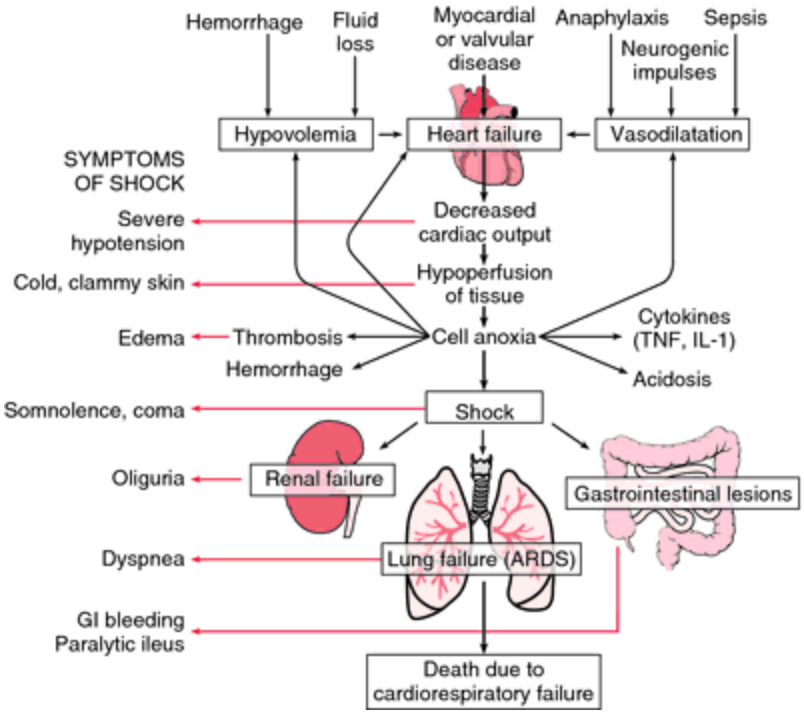
Orthostatic dizziness, weakness, fatigue, shortness of breath, and palpitations are common symptoms of hemorrhage. Signs of hemorrhage include tachycardia, hypotension, pallor, and cold moist skin.

**Treatment**

Pressure should be applied directly to any obviously bleeding body part, and the part should be elevated. Cautery may be used to stop bleeding from visible vessels. Ligation of blood vessels, surgical removal of hemorrhaging organs, or the instillation of sclerosants is often effective in managing internal hemorrhage. Procoagulants (such as vitamin K, fresh frozen plasma, cryoprecipitate, desmopressin) may be administered to patients with primary or drug-induced bleeding disorders. Transfusions of red blood cells may be given if bleeding compromises heart or lung function or threatens to do so because of its pace or volume.

For trauma patients with massive bleeding, the experienced nurse or emergency care provider may apply pneumatic splints or antishock garments during patient transportation to the hospital. These devices may prevent hemorrhagic shock.

**Pathophysiology**




**Prevention**

A healthy diet, regular exercise, reduce excess sodium intake, maintaining a normal weight, and taking prescribed medication properly can often control high blood pressure. Avoiding drug use can also help prevent brain hemorrhage. Cocaine, amphetamines, and alcohol are increasingly associated with brain hemorrhages, particularly in young people.

**THROMBUS**

**Definition:** a clot of blood formed within a blood vessel and remaining attached to its place of origin.

There are two components to a thrombus: aggregated platelets that form a platelet plug, and a mesh of cross-linked fibrin protein. The substance making up a thrombus is sometimes called **cruor**. A thrombus is a healthy response to injury intended to prevent bleeding, but can be harmful in thrombosis, when clots obstruct blood flow through healthy blood vessels.

**Cause**

1. Endothelial injury (injury to the endothelial cells that line enclosed spaces of the body, such as the inside of blood vessels) (e.g. trauma, )
2. Abnormal blood flow
3. Hypercoagulability

Disseminated intravascular coagulation (DIC) involves widespread microthrombi formation throughout the majority of the blood vessels. This is due to excessive consumption of coagulation factors and subsequent activation of fibrinolysis using all of the body's available platelets and clotting factors. The end result is hemorrhaging and ischaemic necrosis of tissue/organs. DIC may also be seen in pregnant females. Treatment involves the use of fresh frozen plasma to restore the level of clotting factors in the blood, platelets and heparin to prevent further thrombi formation.

**Classification**

Thrombi are classified in three major groups depending on the relative amount of platelets and red blood cells (RBCs).The three major groups are:

1. White thrombi (characterized by predominance of platelets)
2. Red thrombi (characterized by predominance of Red Blood Cells)
3. Mixed (with features of both white and red thrombi - an intermediate).

There are two distinct forms of thrombosis, venous thrombosis and arterial thrombosis, each of which can be presented by several subtypes.

**Venous thrombosis**

Venous thrombosis is the formation of a thrombus (blood clot) within a vein. There are several diseases which can be classified under this category:

**Arterial thrombosis**

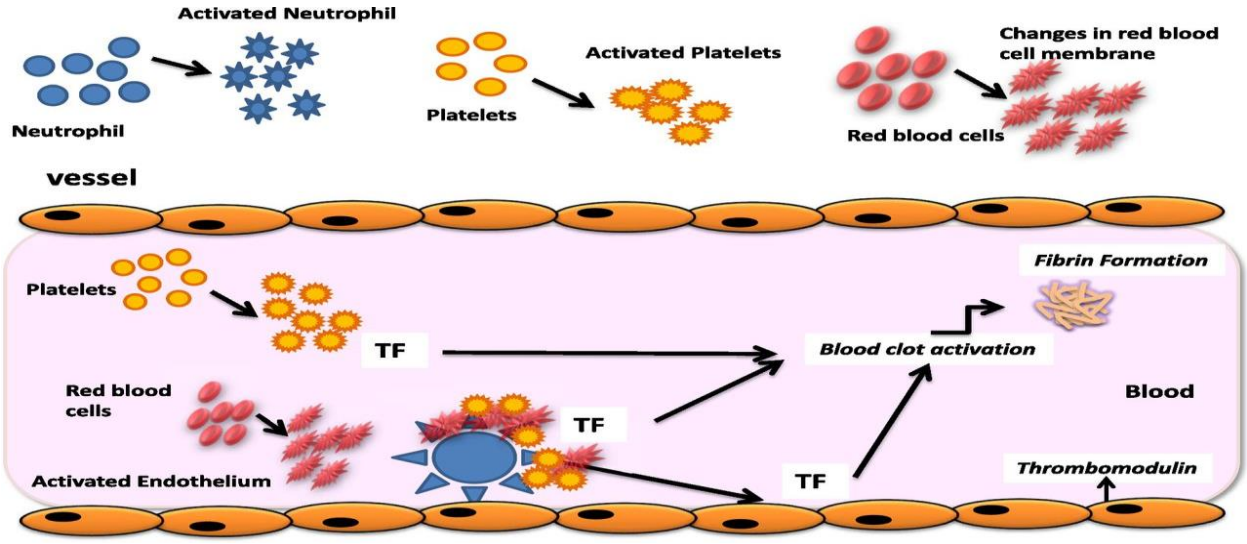
Arterial thrombosis is the formation of a thrombus within an artery. In most cases, arterial thrombosis follows rupture of atheroma, and is therefore referred to as *atherothrombosis*.

Arterial thrombosis can embolize and is a major cause of arterial embolism, potentially causing infarction of almost any organ in the body.

**Pathophysiology**

A thrombus occurs when the hemostatic process, which normally occurs in response to injury, becomes activated in an uninjured or slightly injured vessel. A thrombus in a large blood vessel will decrease blood flow through that vessel (termed a mural thrombus). In a small blood vessel, blood flow may be completely cut off (termed an occlusive thrombus), resulting in death of tissue supplied by that vessel. If a thrombus dislodges and becomes free-floating, it is considered an embolus.

Some of the conditions which elevate risk of blood clots developing include atrial fibrillation (a form of cardiac arrhythmia), heart valve replacement, a recent heart attack (also known as a myocardial infarction), extended periods of inactivity (see deep venous thrombosis), and genetic or disease-related deficiencies in the blood's clotting abilities.


Activated Neutrophil
Neutrophil
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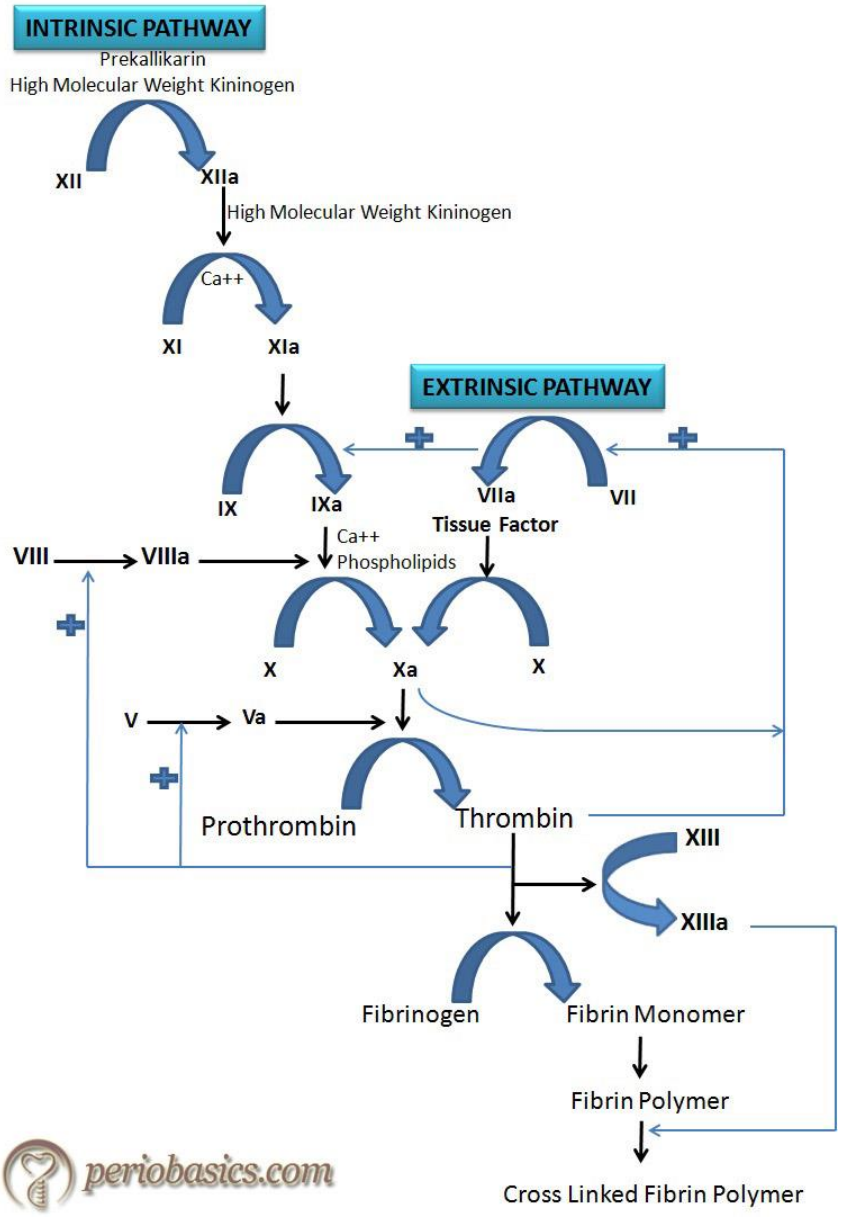



**EMBOLISM**

**Definition**: An embolism is an obstruction in a blood vessel due to a blood clot or other foreign matter that gets stuck while traveling through the bloodstream. The plural of embolism is emboli.

**Description**

Emboli have moved from the place where they were formed through the bloodstream to another part of the body, where they obstruct an artery and block the flow of blood. The emboli are usually formed from blood clots but are occasionally comprised of air, fat, or tumor tissue. Embolic events can be multiple and small, or single and massive. They can be life-threatening

and require immediate emergency medical care. There are three general categories of emboli: arterial, gas, and pulmonary. Pulmonary emboli are the most common. According to the American Heart Association, an estimated 600,000 Americans develop pulmonary emboli annually and 60,000 die from it.

**Types of embolism**

***Arterial embolism***

In arterial emboli, blood flow is blocked at the junction of major arteries, most often at knee, or thigh. Arterial emboli are generally a complication of heart disease. An arterial embolism in the brain causes stroke, which can be fatal. An estimated 5-14% of all strokes are caused by cerebral emboli. Arterial emboli to the extremities can lead to tissue death and amputation of the affected limb if not treated effectively within hours.

***Gas embolism***

Gas emboli result from the compression of respiratory gases into the blood and other tissues due to rapid changes in environmental pressure, for example, while flying or scuba diving. As external pressure decreases, gases (like nitrogen) that are dissolved in the blood and other tissues become small bubbles that can block blood flow and cause organ damage.

***Pulmonary embolism***

In a pulmonary embolism blood flow is blocked at a pulmonary artery. When emboli block the main pulmonary artery, and in case where there are no initial symptoms, a pulmonary embolism can quickly become fatal. A pulmonary embolism is difficult to diagnose. Less than 10% of patients who die from a pulmonary embolism were diagnosed with the condition. More than 90% of cases of pulmonary emboli are complications of deep vein thrombosis, blood clots in the deep vein of the leg or pelvis.

**Causes**

Arterial emboli are usually a complication of heart disease where blood clots form in the heart's chambers.

Gas emboli are caused by rapid changes in environmental pressure that could happen when flying or scuba diving.

A pulmonary embolism is caused by blood clots that travel through the blood stream to the lungs and block a pulmonary artery.

Risk factors for arterial and pulmonary emboli include: prolonged bed rest, surgery, childbirth, heart attack, stroke, congestive heart failure, cancer, obesity, a broken hip or leg, oral contraceptives, sickle cell anemia, chest trauma, certain congenital heart defects, and old age.

Risk factors for gas emboli include: scuba diving, amateur plane flight, exercise, injury, obesity, dehydration, excessive alcohol, colds, and medications such as narcotics and antihistamines.

**Symptoms**

Symptoms of an arterial embolism include:

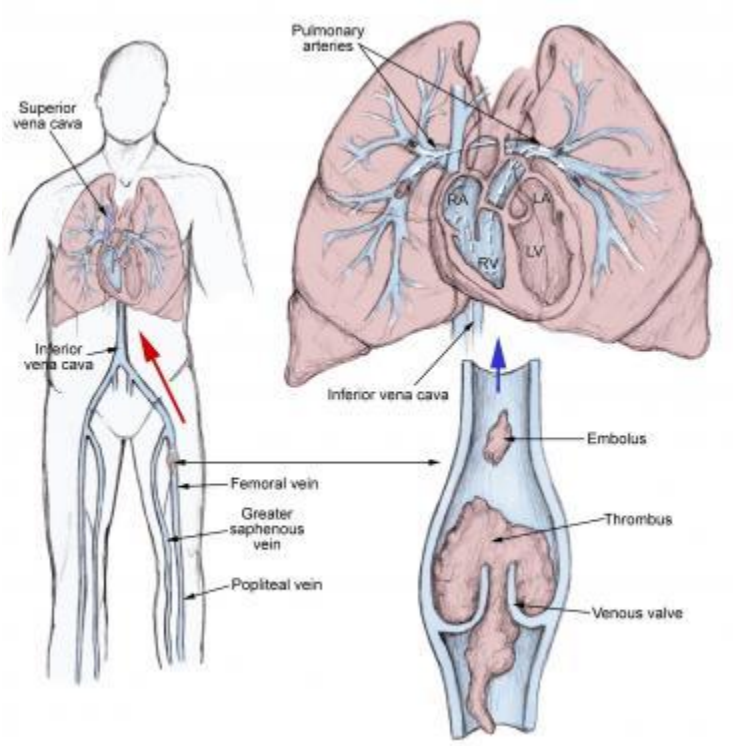
- severe pain in the area of the embolism
- pale, bluish cool skin
- numbness
- tingling
- muscular weakness or paralysis

Common symptoms of a pulmonary embolism include:

- labored breathing, sometimes accompanied by chest pain
- a rapid pulse
- a cough that may produce sputum
- a low-grade fever
- fluid build-up in the lungs

**Pathophysiology of Pulmonary embolism**

Pulmonary emboli usually arise from thrombi that originate in the deep venous system of the lower extremities; however, they rarely also originate in the pelvic, renal, upper extremity veins, or the right heart chambers (see the image below). After traveling to the lung, large thrombi can lodge at the bifurcation of the main pulmonary artery or the lobar branches and cause hemodynamic compromise.




**Pathophysiology of pulmonary embolism**

- Although pulmonary embolism can arise from anywhere in the body, most commonly it arises from the calf veins. The venous thrombi predominately originate in venous valve pockets (inset) and at other sites of presumed venous stasis. To reach the lungs, thromboemboli travel through the right side of the heart. RA, right atrium; RV, right ventricle; LA, left atrium; LV, left ventricle.
- Pulmonary thromboembolism is not a disease in and of itself. Rather, it is a complication of underlying venous thrombosis. Under normal conditions, microthrombi (tiny aggregates of red cells, platelets, and fibrin) are formed and lysed continually within the venous circulatory system.

**Diagnosis**

An embolism can be diagnosed through the patient's history, a physical exam, and diagnostic tests. The use of various tests may change, as physicians and clinical guidelines evaluate the most effective test in terms of accuracy and cost. For arterial emboli, cardiac ultrasound and/or arteriography are ordered. For a pulmonary embolism, a chest x ray, lung scan, pulmonary angiography, electrocardiography, arterial blood gas measurements, and venography or venous ultrasound could be ordered.

**Treatment**

Patients with emboli require immediate hospitalization. They are generally treated with clot-dissolving and/or clot-preventing drugs. Thrombolytic therapy to dissolve blood clots is the definitive treatment for a severe pulmonary embolism. Streptokinase, urokinase, and recombinant tissue plasminogen activator (TPA) are used. Heparin has been the anticoagulant drug of choice for preventing formation of blood clots. A new drug has been approved for treatment of acute pulmonary emboli. Called fondaparinux (Arixtra), it usually is administered with Warfarin, an oral anticoagulant. Warfarin is sometimes used with other drugs to treat acute embolism events and is usually continued after the hospitalization to help prevent future emboli.

**Disseminated intravascular coagulation (DIC)**

**Disseminated intravascular coagulation** (**DIC**), also known as **disseminated intravascular coagulopathy** or less commonly as **consumptive coagulopathy**, is a pathological process characterized by the widespread activation of the clotting cascade that results in the formation of blood clots in the small blood vessels throughout the body. This leads to compromise of tissue blood flow and can ultimately lead to multiple organ damage.

DIC does not occur by itself but only as a complicating factor from another underlying condition, usually in those with a critical illness. The combination of widespread loss of tissue blood flow and simultaneous bleeding leads to an increased risk of death in addition to that posed by the underlying disease. DIC can be overt and severe in some cases, but milder and insidious in others. The diagnosis of DIC depends on the findings of characteristic laboratory tests and clinical background.

**Signs and symptoms**

The onset of DIC can be sudden, as in endotoxic shock or amniotic fluid embolism, or it may be insidious and chronic, as in cancer. DIC can lead to multiorgan failure and widespread bleeding.

**Causes**

DIC can occur in the following conditions

- Solid tumors and blood cancers .
- Massive tissue injury: severe trauma, burns, hyperthermia, rhabdomyolysis, extensive surgery
- Sepsis or severe infection of any kind  of infections by nearly all microorganisms can cause DIC, though bacterial infections are the most common.

- Transfusion reactions (i.e., ABO incompatibility hemolytic reactions)
- Severe allergic or toxic reactions (i.e. snake or viper venom)

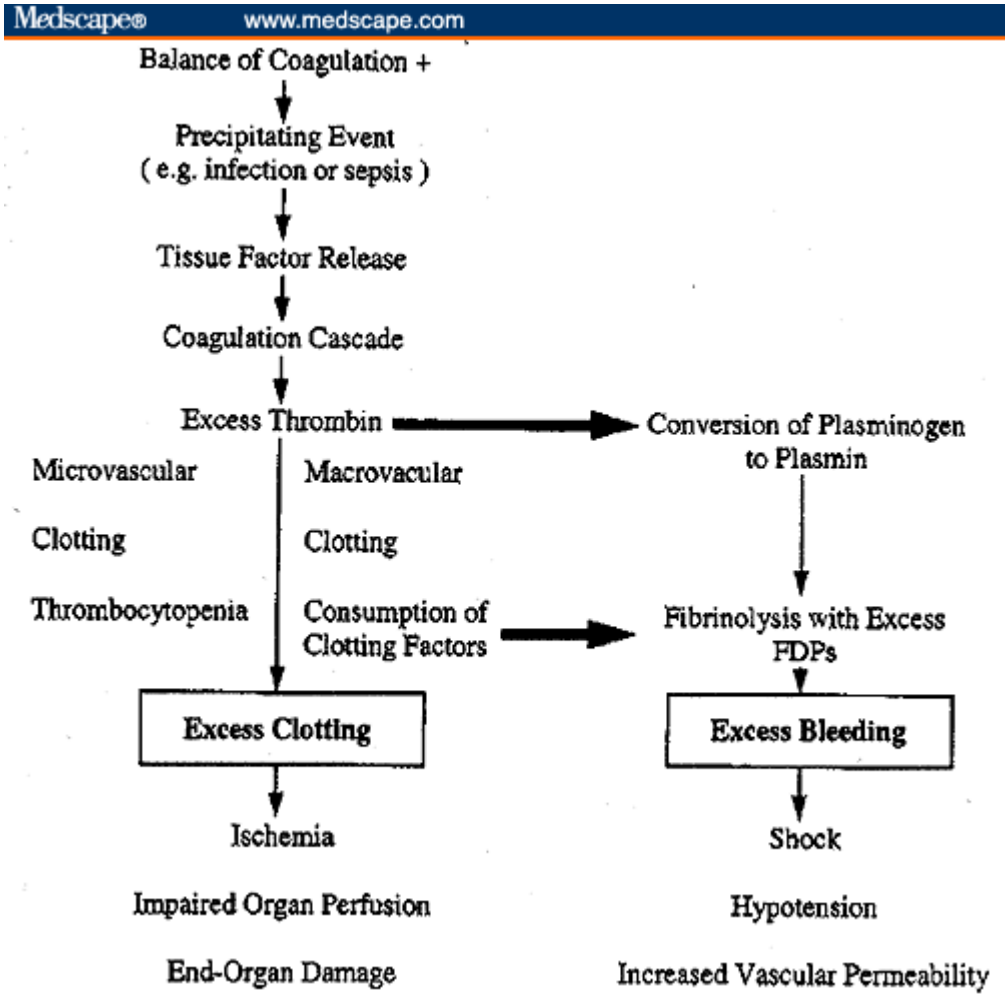
**Pathophysiology of DIC**

The activation of the coagulation cascade yields thrombin that converts fibrinogen to fibrin; the stable fibrin clot being the final product of hemostasis. The fibrinolytic system then functions to break down fibrinogen and fibrin. Activation of the fibrinolytic system generates plasmin (in the presence of thrombin), which is responsible for the lysis of fibrin clots. The breakdown of fibrinogen and fibrin results in polypeptides called fibrin degradation products (FDPs) or fibrin split products (FSPs). In a state of homeostasis, the presence of plasmin is critical, as it is the central proteolytic enzyme of coagulation and is also necessary for the breakdown of clots, or fibrinolysis.

In DIC, the processes of coagulation and fibrinolysis are dysregulated, and the result is widespread clotting with resultant bleeding. Regardless of the triggering event of DIC, once initiated, the pathophysiology of DIC is similar in all conditions. One critical mediator of DIC is the release of a transmembrane glycoprotein called tissue factor (TF). TF is present on the surface of many cell types (including endothelial cells, macrophages, and monocytes) and is not normally in contact with the general circulation, but is exposed to the circulation after vascular damage. For example, TF is released in response to exposure to cytokines (particularly interleukin 1), tumor necrosis factor, and endotoxin.[7] This plays a major role in the development of DIC in septic conditions. TF is also abundant in tissues of the lungs, brain, and placenta. This helps to explain why DIC readily develops in patients with extensive trauma. Upon exposure to blood and platelets, TF binds with activated factor VIIa (normally present in trace amounts in the blood), forming the extrinsic tenase complex. This complex further activates factor IX and X to IXa and Xa, respectively, leading to the common coagulation pathway and the subsequent formation of thrombin and fibrin.

The release of endotoxin is the mechanism by which Gram-negative sepsis provokes DIC. In acute promyelocytic leukemia, treatment causes the destruction of leukemic granulocyte precursors, resulting in the release of large amounts of proteolytic enzymes from their storage granules, causing microvascular damage. Other malignancies may enhance the expression of various oncogenes that result in the release of TF and plasminogen activator inhibitor-1 (PAI-1), which prevents fibrinolysis.

Excess circulating thrombin results from the excess activation of the coagulation cascade. The excess thrombin cleaves fibrinogen, which ultimately leaves behind multiple fibrin clots in the circulation. These excess clots trap platelets to become larger clots, which leads to microvascular and macrovascular thrombosis. This lodging of clots in the microcirculation, in the large vessels, and in the organs is what leads to the ischemia, impaired organ perfusion, and end-organ damage that occurs with DIC.




**Diagnosis**

Fibrinogen level has initially thought to be useful in the diagnosis of DIC but because it is an acute phase reactant, it will be elevated due to the underlying inflammatory condition.

A rapidly declining platelet count

High levels of fibrin degradation products, including D-dimer, are found owing to the intense fibrinolytic activity stimulated by the presence of fibrin in the circulation.

The peripheral blood smear may show fragmented red blood cells due to shear stress from thrombi.

**Treatment**

Treatment of DIC is centered by treating the underlying condition. Transfusions of platelets or fresh frozen plasma can be considered in cases of significant bleeding. The target goal of such transfusion depends on the clinical situation. Cryoprecipitate can be considered in those with a low fibrinogen level.

Treatment of thrombosis with anticoagulants such as heparin is rarely used due to the risk of bleeding.

Recombinant human activated protein C was previously recommended in those with severe sepsis and DIC.

## 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.

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

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

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

**Treatement**

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.

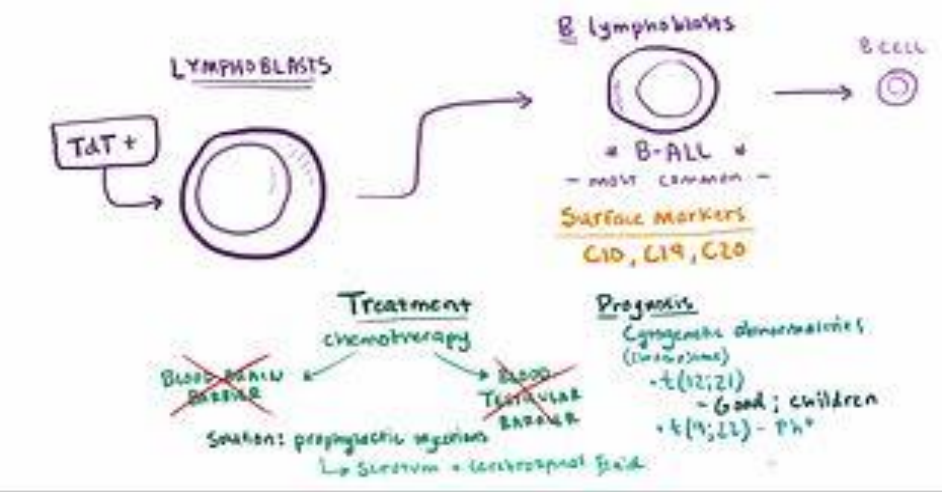
Some leukemia patients do not have high white blood cell counts visible during a regular blood count. This less-common condition is called *aleukemia*. The bone marrow still contains

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.

**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]
- 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 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 that women and the majority will be completely cured.**

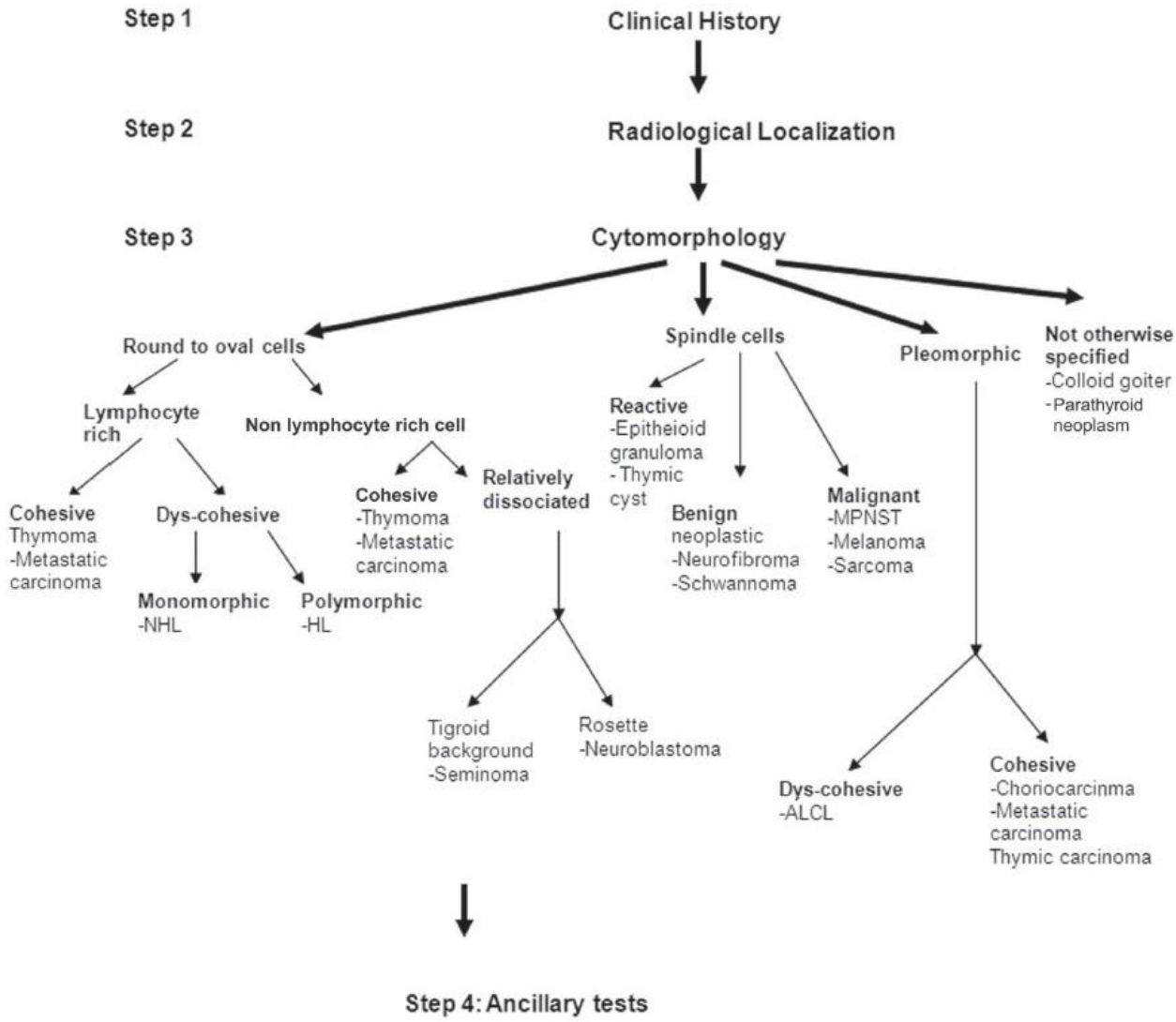
Hodgkin's lymphoma is diagnosed when a special type of cell, the Reed-Sternberg cell, is seen under the microscope.

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)




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
- 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.