**ANEMIA**

A condition in which hemoglobin concentration is lower than normal, reflects the presence of fewer erythrocytes within the circulation.As a result the amount of oxygen delivered to tissues is also diminished.It is not a specific disease per se but a sign of an underlying disorder and it is by far the most common hematologic condition.It is a common occurrence among all age groups but particularly prevalent among the elderly.

**General classification**

If the red blood cells are smaller than normal, this is called **microcytic anemia**. The major causes of this type are iron deficiency (low level iron) anemia and thalassemia (inherited disorders of hemoglobin). If the red blood cells size are normal in size (but low in number), this is called **normocytic anemia**, such as anemia that accompanies chronic disease or anemia related to kidney disease. If red blood cells are larger than normal, then it is called **macrocytic anemia**. Major causes of this type are pernicious anemia and anemia related to [alcoholism](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58899).

**Classification of Anaemia**

1. **Hypoproliferative;** Results from defective red blood cell production.
2. **Iron deficiency anemia;-**characterized by decreased reticulocytes, iron, ferritin, iron saturation, MCV,and increased TIBC.
3. **Vit. B12 deficiency anaemia**( megaloblastic) ;- decreased B12 level and increased MCV
4. **Folate deficiency** ( megaloblastic) ;- decreased folate level and increased MCV

d. Decreased erythropoietin production e.g. from renal dysfunction;- decreased erythropoietin level, normal MCV and MCH, increased creatinine level.

e. Cancer/ inflammation;- normal MCV,MCH normal or decreased erythropoietin level, increased % of iron saturation ferritin level; decreased iron TIBC.

2. **Bleeding resulting in RBC loss**;- from the GIT, menorrhagia, epistaxis, trauma. Characterized by increased reticulocyte level, normal Hgb and Hct if measured soon after bleeding starts, but levels decrease thereafter, normal MCV initially but later decreases, decreased ferritin and iron levels later.

3. **Hemolytic anemia**. Results from RBC destruction

1. Altered erythropoiesis (sickle cell anemia, thalassemia, otherhemoglobinopathies);-decreased MCV, fragmented RBCs, increased reticulocyte level.
2. Hypersplenism ( hemolysis) ;- increased MCV
3. Drug induced anemia;- increased spherocyte level
4. Autoimmune anemia;- increased spherocyte level
5. Mechanical heart valve related anemia;- fragmented RBCs

On the basis of the following it is possible to determine whether the cause of anemia is destruction or inadequate production of RBCs;-

* The marrow’s ability to respond to inadequate erythrocyte as evidenced by increased reticulocyte count in the circulating blood.
* The degree to which young erythrocyte proliferate in the bone marrow and the manner in which they mature as observed in marrow biopsy.
* Presence or absence of end products of red cell destruction within the circulation e.g. increased bilirubin, decreased haptoglobin.

**Clinical manifestations**

Aside from the severity of anemia itself, several factors influence the development of anemia associated symptoms;-

* Rapidity with which the anemia has developed.
* The duration of the anemia (its chronicity)
* The metabolic requirements of the patient.
* Other concurrent disorders or disabilities e.g. cardiopulmonary disease.
* Special complications or concomitant features of the condition that produced the anemia.

In general the more rapidly an anemia develops the more severe its symptoms.An otherwise healthy person can often tolerate as much as 50% gradual reduction in Hb without pronounced symptoms or significant incapacity whereas the rapid loss of as little as 30% may precipitate profound vascular collapse in the same person.Gradual development of anemia with Hb 9-11 g/dl show few or no symptoms other than slight tachycardia on exertion.

Customarily very active persons or those with significant demands on their lives more likely have symptoms more pronounced than sedentary individuals.Hypothyroidism pts may be completely asymptomatic at Hb 10g/dl.Pts with coexistent cardiac, vascular or pulmonary disease may develop more pronounced symptoms of anemia at a higher Hb level than those without.Anemia is also complicated by other abnormalities inherently associated with these particular disease and not from anemia e.g. painful crisis of sickle cell anemia.

**Assessment and diagnostic findings**

* Hb, Hct, reticulocyte count and RBC indices particularly MCV, RDW,
* Iron studies; serum iron level, Total Iron Binding Capacity,% saturation and ferritin
* Serum B12 and folate
* Haptoglobin and erythropoietin levels
* Other CBC values for determining if the anemia is isolatd or pat of another hematologic problem e.g. leukemia, MDS
* Bone marrow aspiration
* Other Dx studies to rule out underlying conditions e.g. malignancy, GI bleeding etc.

**Complications**

* General heart failure, parasthesias and confusion
* In heart disease angina or symptoms of heart failure
* Others are specific to type of anemia.

**Management**

Aimed at correcting or controlling the cause of anemia

**Iron deficiency anemia**

Due to inadequate intake of dietary iron for Hb synthesis. Usually the body stores ¼ to 1/3 of its iron and not until these stores are depleted that the anemia begins to develop.It is the most common anemia in all age groups and in the world.

**Causes**

1. Inadequate intake in children adolescents and pregnant women
2. In men and postmenopausal women bleeding from ulcers, gastritis, inflammatory bowel disease and/or tumors
3. Menorrhagia in premenopausal women
4. Chronic alcoholism due to GI loses
5. Iron malabsorption as seen after gastrectomy or in celiac disease.

**Clinical manifestations**

* History of multiple pregnancies, GI bleeding or pica.
* They primarily have symptoms of anemia. In severe or prolonged deficiency pts may have;
* Smooth sore tongue
* Brittle and ridged nails
* Angular cheilosis (ulceration of the corner of the mouth.
* These signs subside with iron replacement.

**Assessment and diagnostic findings**

* Definitive method is bone marrow aspiration. Stained aspirate detect iron low or absent.
* Low serum ferritin levels
* Decreased MCV, and Hct
* TIBC (transferrin) transport protein supplying marrow with iron is elevated.

**Medical management**

* Unless it is in pregnancy the cause should be investigated e.g. stool for occult blood & in pts over 50yrs old periodic colonoscopy, endoscopy, X-rays to check for ulcerations, gastritis, polyps or cancers.
* Oral iron preparations; ferrous sulfate, ferrous gluconate and ferrous fumarate are given and in a few weeks Hb level may increase and anemia corrected in a few months. Iron store replenishing takes longer so supplements should be taken for 6-12 months.
* Increase vitamin C intake to facilitate absorption of iron.
* When oral iron is poorly absorbed, tolerated or large amounts needed, IV or IM iron dextran may be given
* To avoid the risk of anaphylaxis, before administering a full parenteral dose, a small test dose is given and monitored with emergency medications e.g. epinephrine at hand. If no signs of allergic reactions within 30 minutes the remaining dose may be administered.
* Several doses are required to replenish the pts iron stores.

**Nursing management**

* Preventive education on high iron food sources with vitamin C.
* Nutritional counseling for strict vegetarians and
* Encourage compliance to supplements prescribed & to be taken on empty stomach, avoid coated tablets and S/E especially constipation.
* Advice thept on polysaccharide iron complex/ liquid forms of iron with less GI distress though more expensive whereas the liquid prep stains teeth so good oral hygiene is necessary.
* Stool may be colored dark green but will not affect results of occult blood in stool analysis.
* IV supplementation in pts with depleted iron stores
* IM supplementation avoided due to excessive iron volume, staining the skin but Z-track technique is used to administer iron dextran deep into the gluteus.
* Avoid rubbing the injection site vigorously after the injection.

2. **Megaloblastic anemia**

Caused by folate & B12 deficiencies which are essential for DNA synthesis.The RBCs produced are abnormally large. Megaloblastic& other derivative cells of the myeloid stem cells are abnormal. Bone marrow analysis reveals hyperplasia and precursor erythroid and myeloid cells are large and bizarre in appearance.Many of these abnormal cells are destroyed within the marrow hence mature cells that leave the marrow are fewer thus pancytopenia (decrease in all myeloid-derived cells) may develop. In advanced disease, Hb may be as low as 4-5g/dL, leukocyte count 2000-3000/ mm3& platelet count <50000/mm3.

Cells released into the circulation are abnormally shaped with hyper segmented neutrophils, abnormally large platelets & abnormally shaped erythrocytes whose shapes may vary widely (poikilocytosis).

**PATHOPHISIOLOGY**

Megaloblastic changes occur in:

■ Folic acid deficiency or abnormal folate metabolism

■ Vitamin B12 deficiency or abnormal vitamin B12 metabolism

1. **FOLIC ACID DEFICIENCY**

Folic acid is found in green vegetables and liver. It’s stored in the body as folates.With dietary deficiencies, stores are depleted in four months.The following may increase requirements

* Alcohol intake
* Chronic hemolytic anemias.
* Pregnant women
* Mal-absoptive diseases

**PATHOPHISIOLOGY**

**II. VITAMIN B12 DEFICIENCY**

Deficiency can occur in several ways:

* Inadequate dietary intake esp. in vegetarians.
* Mal-apbsorptioneg. In chrohn’s disease or after gastrectomy or ileal resection.
* Absence of intrinsic factor(pernicious anemia)
* Infestation with D.latum(competitive utilization of VitB12 by parasite)

The body normally has large stores of Vit B12 and It may take several years before deficiency results in anemia.

**Clinical manifestations**

After depletion of body stores, patients start showing signs and symptoms of anaemia.The onset is insidious, with progressively increasing symptoms of anaemia. Symptoms of Vit. B12 and folic acid deficiency are similar, and the two may coexist.However the neurological symptoms of vitamin B 12 do not occur with folic acid deficiency.Because the onset and progress is so gradual the body may compensate very well until the anemia is severe. So the typical manifestations of anemia (weakness, restlessness, fatigue)may not be apparent.

The hematologic effects are accompanied by effect of other organ systems particularly the GIT and the nervous system.The patients with pernicious anemia may develop a smooth, sore red (glossitis) tongue and mild diarrhea, Mild jaundice due to breakdown of RBCs, They are extremely pale and particularly the mucous membranes, They may become confused and more often have paresthesias in the extremities.

The classical neurological features are those of a polyneuropathy progressively involving the peripheral nerves and the posterior and eventually the lateral columns of the spinal cord.The neurological changes, if left untreated for a long time, can be irreversible.

**Assessment and diagnosis**

The most sensitive test to measure true folate deficiency is by measuring red cell folate (the amount of folate within the red cell itself). The classical method of determining the cause of Vit B 12 deficiency is the Schilling test – a small oral dose of radioactive Vit B12 is given followed by a larger dose of non-radioactive Vit B12.If absorption the GIT is adequate more than 8% will be excreted in urine within 24hrs. If none is in urine then the problem is in the GIT (Malabsorption)

**Medical management**

Folate deficiency is treated by increasing the amount of folate in diet and administering 1mg of folic acid daily. It is only administered IM to those with malabsoption.

Vit.B12 deficiency is treated by replacement by monthly injections of Vit. B12 if deficiency is due to mal-absorption or lack of intrinsic factor.

**Nursing management**

Asses for risk of megalobalsticanaemia by:

Inspecting the skin and mucus membrane(Vitilgo, jaundice and premature graying of hair)

Tongue (Smooth, red and sore), Careful neurological assessment including test for position(gait and stability) and vibration sense.

Nutritional assessment.(Advice patient to take small amount of bland soft foods frequently.)

**3. Hemolytic anemias**

Normal red cell destruction lifespan is 120 days & cell are extravascularly removed by macrophages in the marrow, liver & spleen.Intravascular hemolysis plays little or no part in normal RBC destruction.

Hemolytic anemias are those resulting from increased red cell destruction.

Due to erythropoietichypeplasia, anatomic extension of the bone marrow cell production may increase several fold (normal adult marrow 6-8 times normal rate) before the patient becomes anemic.

**Clinical features**

* Patient may show pallor of the mucous membrane
* Mild flactuating jaundice
* Spenomegally
* No bile in urine but this may turn dark on standing due to excess urobilinogen.
* Pigment gallstones may complicate the condition & some pts particularly those with sickle cell disease develop ulcers around the ankle.
* Aplastic crisis may occur usually precipitaed by infection with parvovirus which switches off erythropoiesis and there is sudden increase in anemia and drop in reticulocyte count.
* Folate deficiency is likely to occur in chronic hemolytic anemias due to increased utilization of the vitamin by the rapidly proliferating bonemarrow.

**Classification**

1. Hereditary

Membrane;- hereditary spherocytsis, hereditary elliptocytosis

Metabolism;- G6PD (glucose-6-phosphate-dehydrogenase) deficiency, pyruvate kinase deficiency.

Hemoglobin;-HbS, HbC

2. Acquired

1. Immune
2. Autoimmune;- warm antibody type, cold antibody type.
3. Alloimmune ;- hemolytic transfusion reactions, hemolytic disease of the newborn, allografts esp. marrow transplants
4. Drug associated

B. Red cell fragmentation syndromes

1. Arterial grafts, cardiac valves

* Microangiopathic;-
* Thrombotic thrombocytopenia purpura
* Hemolytic uraemic syndrome
* Meningococcal sepsis
* Pre- eclampsia
* DIC

C. March hemoglobinurias;-btwn small bones of the feet.

D. Infections;- malaria, clostridia

E. Chemical and physical agents;- drugs, industrial and domestic substances, burns.

F. Secondary; liver & renal diseases

G. Paroxysmal nocturnal hemoglobinuria

**Investigations**

Lab studies show features of;

1. Increased RBC breakdown
2. Increased RBC production
3. Damaged RBC; morphology, osmotic fragility, shortened red cell survival.

**Causes of intravascular hemolysis**

* Mismatched blood transfusion
* G6PD deficiency with oxidant stress
* Red cell fragmentation syndromes
* Some autoimmune hemolytic anemias
* Some drug and infection induced hemolytic anemias
* Paroxysmal nocturnal hemoglobinurias
* March hemoglobinurias
* Unstable hemoglobin.

**Treatment**

Address the underlying cause and treatment is also specific to cause.

Hereditary spherocytosis;-splenectomy is the treatment of choice; avoided in childhood.

G6PD deficiency offending drug stopped, high urine output is maintained and in neonates jaundice due to effect on liver function is managed by phototherapy & exchange transfusion.

Warm antibody type; remove underlying cause, corticosteroids, spenectomy, IgG only respond better. Immunosuppression, folate supplementation.

Cold antibody type; keep pt warm, treat the underlying cause. Chronic varieties alkylating agents may be helpful. Steroids &splenectomy are not helpful but splenectomy only in massive splenomegaly.

**BLEEDING DISORDERS**

A bleeding disorder is an acquired or inherited tendency to bleed excessively.

**Von willebrand’s disease**

A bleeding disorder that affects blood's ability to clot. If blood doesn't clot, one can have heavy, hard-to-stop bleeding after an injury. The bleeding can damage internal organs. Rarely, the bleeding may even cause death. It is the most common inherited bleeding disorder, affecting about 1% to 2% of people.A substance in the blood known as von Willebrand factor helps platelets stick to damaged blood vessels.Von Willebrand factor carries one of these clotting factors, called **factor VIII**, in the blood.

**Types**

**Type 1**-less von Willebrand factor in the blood than normal. Very mild symptoms. Worsened by NSAIDS

**Type 2-** the person's body makes von Willebrand factor that is abnormal, leading to bleeding problems.

**Type 3-**patients have severe bleeding problems. The person has no measurable von Willebrand factor and very low factor VIII levels.

**Clinical features**

* bruising easily
* unusually heavy periods or other abnormal menstrual bleeding in girls
* bleeding from the gums, nose, and lining of the intestines
* prolonged oozing of blood from cuts or bleeding too much or for too long after a tooth is pulled or tonsils are removed

**Management**

* Avoid unnecessary trauma, including contact sports like football and hockey, but other sports and activities are usually OK.
* Apply pressure when bleeding occurs
* Menorrhagia; extra pads or birth control pills maybe prescribed.
* The most common treatment used for type 1 von Willebrand disease is the drug desmopressin, which causes a temporary increase in the von Willebrand factor level in the blood.
* HumateP, that contains both factor VIII and von Willebrand factor is given IV for type 3 and some type 2.

**2. Thrombotic thrombocytopenic purpura (TTP)**

This is a rare blood disorder. In TTP, blood clots form in small blood vessels throughout the body.The clots can limit or block the flow of oxygen-rich blood to the body's organs, such as the brain, kidneys, and heart. As a result, serious health problems can develop.The increased clotting that occurs in TTP also uses up platelets. With fewer platelets available in the blood, bleeding problems can occur.

TTP =**T**hrombotic-blood clots that form, **T**hrombocytopenic-the blood has a lower than normal number of platelets,**P**urpura-purple bruises caused by bleeding under the skin.

Bleeding under the skin also can cause tiny red or purple dots on the skin. These pinpoint-sized dots are called petechiae as shown in the diagram

**Types**

* **Inherited**- faluty gene that controls the enzyme that breaks down von willbrands factor.
* **Acquired-** the body makes antibodies that block the activity of the enzyme.

**Factors that play a role in development of TTP**

* Some diseases and conditions e.g. pregnancy, cancer, HIV, lupus, and infections
* Some medical procedures e.g. surgery and blood and marrow stem cell transplant
* Some medicines e.g. chemotherapy, ticlopidine, clopidogrel, cyclosporine A, and hormone therapy and estrogens
* Quinine, which is a substance often found in tonic water and nutritional health products

Other Names for Thrombotic Thrombocytopenic Purpura

**Inherited Thrombotic Thrombocytopenic Purpura**

* Familial thrombotic thrombocytopenic purpura
* Upshaw-Schulman syndrome (USS)

**Acquired Thrombotic Thrombocytopenic Purpura**

* Moschcowitz disease
* Microangiopathic hemolytic anemia

**Signs and symptoms**

* Purplish bruises on the skin or mucous membranes (such as in the mouth). These bruises, called purpura, are caused by bleeding under the skin.
* Pinpoint-sized red or purple dots on the skin. These dots, called petechiae, often are found in groups and may look like a rash. Bleeding under the skin causes petechiae.
* Paleness or jaundice (a yellowish color of the skin or whites of the eyes).
* Fatigue (feeling very tired and weak).
* Fever.
* A fast heart rate or shortness of breath.
* Headache, speech changes, confusion, coma, stroke, or seizure.
* A low amount of urine, or protein or blood in the urine.

**Management.**

TTP is treated with plasma therapy to include:

* Fresh frozen plasma for newborns and children who have inherited TTP
* Plasma exchange for people who have acquired TTP
* For acquired TTP, medicines can slow or stop antibodies to the enzyme that breaks down vonwilbrands factor from forming e.g. glucocorticoids, vincristine, rituximab, and cyclosporine A.
* Sometimes surgery to remove the spleen (an organ in the abdomen) is needed. This is because cells in the spleen make the antibodies that block ADAMTS13 enzyme activity.

**3. Hemophilia**

Hemophilia is a rare inherited disorder in which the blood does not clot normally. Occurs in 2 forms, hemophilia A factor VIII deficiency and B Factor IX deficiency. In both forms, a gene is defective. The defective gene interferes with the ability of the body to produce the clotting factors that allow for normal clotting. The result is a tendency for abnormal, excessive bleeding.

**Causes**

Both hemophilia A and B are linked to the X chromosome, which means they primarily affect men. A man who has hemophilia has a 100% chance that his daughters will be carriers, since they must inherit the defective x chromosome from the father. His sons will not be affected if the mother is not a carrier.

The transmission of this gene to offspring accounts for 70% of the cases of hemophilia. The remaining 30% occur from spontaneous changes in genes responsible for causing hemophilia.

**Why prolonged bleeding time in hemophilia?** In hemophilia, one clotting factor is missing, or the level of that factor is low. This makes it difficult for the blood to form a clot, so bleeding continues longer than usual, not faster. Since there are many clotting factors in plasma, each factor is named with a Roman numeral. i.e. Factor VIII and IX

**Signs and symptoms**

* Hematuria
* Muscle pain and swelling especially calf, thigh, forearm due to bleeding
* Pain and swelling in joints as a result of bleeding into the joints mostly knee, elbow, wrist, ankle, shoulder.
* Bleeding in the CNS may cause paralysis if in the spinal column and
* In the brain will cause headache, nausea, vomiting, and seizures.

**Management**

The main **treatment** for **hemophilia** is called replacement therapy. Concentrates of clotting factor VIII (for **hemophilia** A) or clotting factor IX (for **hemophilia** B) are slowly dripped or injected into a vein. These infusions help replace the clotting factor that's missing or low.

**DISSEMINATED INTRAVASCULAR COAGULATION (DIC)**

It’s is a serious disorder in which clotting factors that control blood clotting become abnormally active.It is characterized by a systemic activation of the blood coagulation system, which results in the generation and deposition of fibrin, leading to micro-vascular thrombi in various organs and contributing to the development of multi-organ failure.Consumption and subsequent exhaustion of coagulation proteins and platelets, due to the ongoing activation of the coagulation system, may induce severe bleeding complications, although microclot formation may occur in the absence of severe clotting factor depletion and bleeding

Derangement of the fibrinolytic system further contributes to intravascular clot formation, but in some cases, accelerated fibrinolysis may cause severe bleeding. Hence, a patient with disseminated intravascular coagulation (DIC) can present with a simultaneously occurring thrombotic and bleeding problem, which obviously complicates the proper treatment.

**Risk factors for DIC**

* Severe toxic or immunologic reactions ;Snake bites, recreational drugs, transfusion reactions, transplant rejection
* Organ destruction (e.g. severe pancreatitis)
* Cancer, especially certain types of leukemia
* Infection in the blood by bacteria or fungus
* Severe hepatic failure
* Obstetric calamities e.g. Amniotic fluid embolism, abruptio placentae
* Recent surgery or anesthesia
* Sepsis (a serious infection)
* Severe tissue injury (as in burns and head injury)

Symptoms

* Bleeding, possibly from multiple sites in the body
* Blood clots
* Bruising
* Drop in blood pressure

**Diagnosis**

* CBC
* Fibrin degradation products
* Partial thromboplastin time (PTT)
* Platelet count
* Prothrombin time (PT)
* Serum fibrinogen

**Management**

* The goal is to determine and treat the cause of DIC.
* Blood clotting factors may be replaced with plasma transfusions.
* Platelet transfusions can raise the blood count.
* Heparin, a medication used to prevent clotting, is sometimes used to interrupt clotting events.

LEUKEMIAS

Classification

1. **Acute Lymphoblastic Leukemia**
2. **Acute Myelocytic Leukemia**
3. **Chronic Myelogenous Leukemia**
4. **Chronic Lymphocytic Leukemia**

**1. Acute Lymphoblastic Leukemia**

**Background:**

Acute lymphoblastic leukemia (ALL) is the most common malignancy of childhood, representing nearly one third of all pediatric cancers with a peak incidence in patients aged **2-5 years**. Many environmental factors (e.g. exposure to ionizing radiation and electromagnetic fields and parental use of alcohol and tobacco) have been investigated as potential risk factors. Children with Down syndrome, Bloom syndrome, Fanconi anemia, and ataxia-telangiectasia are at particular risk of ALL. Siblings, especially twins, of children with leukemia are approximately twice more likely to have leukemia than is the general population. Some cases of childhood ALL may be related to hereditary or acquired mutations in the p53 gene.

**Pathophysiology**

The malignant cells of acute lymphoblastic leukemia (ALL) are lymphoid precursor cells (i.e. lymphoblasts) that are arrested in an early stage of development.

This arrest is caused by an abnormal expression of genes, often as a result of chromosomal translocations. The lymphoblasts replace the normal marrow elements, resulting in a marked decrease in the production of normal blood cells. Consequently, [anemia](http://emedicine.medscape.com/article/198475-overview), [thrombocytopenia](http://emedicine.medscape.com/article/201722-overview), and [neutropenia](http://emedicine.medscape.com/article/204821-overview) occur to varying degrees. The lymphoblasts also proliferate in organs other than the marrow, particularly the liver, spleen, and lymph nodes.

**Epidemiology**

**Race:** ALL occurs more frequently in whites than in black.

**Sex:** ALL occurs slightly more frequently in males than in females.

**Clinical features**

Children with ALL generally present with signs and symptoms that reflect bone marrow infiltration and extramedullary disease.

Because the bone marrow is replaced with leukemic blasts, patients present with signs of bone marrow failure, including anemia, thrombocytopenia, and neutropenia.

The "4 Ps," a tetrad comprises the most common presenting symptoms.

**Pallor** (65% of cases),

**Pyrexia** (61% of cases),

**Purpura** (48% of cases), and

**Pain** (23% of cases),

In addition, leukemic spread may be seen as **lymphadenopathy** and **hepatosplenomegaly**.

Other signs and symptoms of leukemia include **weight loss**, **bone pain**, and **dyspnea**.

**Laboratory features**

Normocytic, normochromic anemia and reticulocytopenia are present in approximately 80 to 85% of cases. The presenting leukocyte count ranges from severe leukopenia to extreme leukocytosis. 80% of patients have a leukocyte count less than 50,000/uL; among 50% the leukocyte count is less than 10,000/uL. In spite of normal leukocyte counts, many patients are agranulocytic and are at risk of severe bacterial infection.

Thrombocytopenia is extremely common; 75% of patients have platelet counts less than 100,000/uL, and approximately 25% have a platelet count less than 20,000/uL at diagnosis. For most patients with ALL, examination of the peripheral blood smear usually reveals leukemic lymphoblasts. In ALL, the marrow usually is hypercellular and infiltrated with leukemic lymphoblasts.

Therapy

For most children and adolescents with ALL, treatment protocols are divided into four principal elements:

1. **induction therapy;-** In most clinical trials, remission induction regimens include the use of vincristine and a glucocorticoid with the addition of one or two agents, commonly L-asparaginase or an anthracycline
2. **Intensification or consolidation therapy;-** a period of intensified treatment that usually begins soon after induction therapy. The agents most commonly used in these regimens include cytarabine, anthracyclines, methotrexate, cyclophosphamide, and epipodophyllotoxins
3. Continuation or maintenance therapy, and
4. CNS preventive therapy.

2. **Acute Myelocytic Leukemia**

**Background:**

Acute myelocytic leukemia (AML) is a group of malignant disorders characterized by the replacement of normal bone marrow with abnormal, primitive hematopoietic cells. A defect in hematopoietic cells that differentiate in all myeloid cells; monocytes, granulocytes, erythrocytes and platelets. Acute myeloid leukemia (AML) accounts for about 20% of cases of acute leukemia among children and 80% of cases of acute leukemia among adult.

**Pathophysiology**

Acute leukemia begins in a single somatic hematopoietic progenitor that transforms to a cell incapable of normal differentiation. Many of these cells no longer possess the normal property of apoptosis, or programmed cell death, thus resulting in a cell with a prolonged life span and unrestricted clonal proliferation.

Leukemogenesis is frequently associated with chromosome abnormalities and gene translocations. The result is the accumulation of abnormal cells with qualitative defects. A major cause of morbidity and mortality is the deficiency of normal functioning mature hematopoietic cells rather than the presence of numerous malignant cells. Splenomegaly from leukemic infiltration further contributes to pancytopenia by sequestering and destroying circulating erythrocytes and platelets. As the disease progresses, there are increasing signs and symptoms resulting from anemia, thrombocytopenia, and neutropenia.

**Epidemiology**

**Race:** AML is near equal for all races.

**Sex:** Distribution of affected males and females is nearly equal at all ages. More common in men than in women with aging.

**Age:**The prevalence of acute myelogenous leukemia (AML) increases with age. The median age of onset is approximately 60 years. However, acute myelogenous leukemia (AML) affects all age groups.

**Causes**

1. Antecedent hematologic disorders
2. Congenital disorders
3. Familial syndromes
4. Environmental exposures
5. Previous exposure to chemotherapeutic agents for another malignancy

**Mortality/Morbidity**

In adults, treatment results are generally analyzed separately for younger (18-60 y) and older (>60 y) patients with acute myelogenous leukemia (AML). With current standard chemotherapy regimens, approximately 30-35% of adults younger than 60 years survive longer than 5 years and are considered cured. Results in older patients are more disappointing, with fewer than 10% of surviving over the 1 yr.

Symptoms of bone marrow failure are related to anemia, neutropenia, and thrombocytopenia

The most common symptom of anemia is fatigue. Patients often retrospectively note a decreased energy level over past weeks. Other symptoms of anemia include dyspnea upon exertion, dizziness, and, in patients with coronary artery disease, anginal chest pain. In fact, myocardial infarction may be the first presenting symptom of acute leukemia in an older patient.

Patients often have decreased neutrophil levels despite an increased total white blood cell (WBC) count.

Patients with acute myelogenous leukemia (AML) present with fever, which may occur with or without specific documentation of an infection. Patients with the lowest absolute neutrophil counts (ANCs) (ie, <500 cells/µL, especially <100 cells/µL) have the highest risk of infection.

Patients often have a history of upper respiratory infection symptoms that have not improved despite empiric treatment with oral antibiotics. Patients present with bleeding gums and multiple ecchymoses. Bleeding may be caused by thrombocytopenia, coagulopathy that results from [disseminated intravascular coagulation (DIC)](http://emedicine.medscape.com/article/199627-overview), or both.

Potentially life-threatening sites of bleeding include the lungs, gastrointestinal tract, and the central nervous system. Symptoms may be the result of organ infiltration with leukemic cells;**The most common sites of infiltration include the spleen, liver, gums, and skin. Infiltration occurs most commonly in patients with the monocytic subtypes of acute myelogenous leukemia (AML). Patients with** [**splenomegaly**](http://emedicine.medscape.com/article/206208-overview) **note fullness in the left upper quadrant and early satiety. Patients with gum infiltration often present to their dentist first. Gingivitis due to neutropenia can cause swollen gums, and thrombocytopenia can cause the gums to bleed.**

**Patients with markedly elevated WBC counts (>100,000 cells/µL) can present with symptoms of leukostasis (ie, respiratory distress and altered mental status). Leukostasis is a medical emergency that requires immediate intervention. Patients with a high leukemic cell burden may present with bone pain caused by increased pressure in the bone marrow.**

**Treatment**

**Induction of Remission:** The most widely used remission-induction regimen includes treatment with an anthracycline (usually doxorubicin) and cytarabine with or without thioguanine or etoposide. Afterwhich consolidation therapy to eliminate leukemic cells is given.

BMT. Aggressive chemotherapy regimen given with or radiation therapy when a suitable tissue match (donor) is available. Hematopoietic function is destroyed and infusion of donor stem cells done.

Supportive care alone is given to patients with significant comorbidity and occasionally hydroxyurea given to control the increase of blast cells.

Complication of treatment

Tumor lysis syndrome; release of ICF and electrolytes into the circulation with increasing uric acid, potassium and phosphate levels.

GI problems

Significant neutropenia, thrombocytopenia.

**3. Chronic Myelogenous Leukemia**

**Background:**

Chronic myelogenous leukemia (CML) is a myeloproliferative disorder characterized by increased proliferation of the granulocytic cell line without the loss of their capacity to differentiate. Consequently, the peripheral blood cell profile shows an increased number of granulocytes and their immature precursors, including occasional blast cells.It accounts for approximately 2 to 4% of cases of leukemia among children and it includes the adult type of Philadelphia chromosome-positive CML and a rare hematopoietic malignant disease of childhood called *juvenile myelomonocytic leukemia* (formerly juvenile CML).

**Pathophysiology**

CML is an acquired abnormality that involves the hematopoietic stem cell. It is characterized by a cytogenetic aberration consisting of a reciprocal translocation between the long arms of chromosomes 22 and 9; t(9;22). This translocation relocates an oncogene called *abl* from the long arm of chromosome 9 to the long arm of chromosome 22 in the *bcr* region. The resulting *bcr-abl* fusion gene encodes a chimeric protein with strong tyrosine kinase activity. The expression of this protein leads to the development of the CML phenotype through processes that are not yet fully understood.

**Epidemiology**

**Frequency:** Internationally: Increased incidence was reported among individuals exposed to radiation in Nagasaki and Hiroshima after the dropping of the atomic bomb.

**Age:** In general, this disease occurs in the fourth and fifth decades of life. Younger patients aged 20-29 years may be affected and may present with a more aggressive form, such as in accelerated phase or blast crisis

**Clinical manifestations**

Chronic myeloid leukemia is characterized initially by a chronic phase (splenomegaly and extreme leukocytosis with full granulocytic maturation) that lasts 2 to 3 years followed inevitably by a blast crisis.

Juvenile myelomonocytic leukemia most often manifests before the age of 5 years and is commonly associated with;

1. Massive splenomegaly,
2. Modest leukocytosis with monocytosis,
3. Thrombocytopenia, and
4. Elevated levels of fetal hemoglobin.
5. Many children have skin rashes that include xanthoma, cafe-au-lait spots, and eczematous lesions.

**Treatment**

The current treatment recommendation for children with JMML is allogeneic BMT with or without pretransplantsplenectomy.

**Chronic Lymphocytic Leukemia**

**Background:**

Chronic lymphocytic leukemia (CLL) is a monoclonal disorder characterized by a progressive accumulation of functionally incompetent lymphocytes.

It is the most common form of leukemia found in adults in Western countries.

**Epidemiology**

**Age:** CLL is a disease that primarily affects elderly individuals, with the majority of cases reported in individuals older than 55 years.

**SICKLE CELL ANEMIA**

Sickle cell anemia is a severe hemolytic anemia that results from inheritance of the sickle hemoglobin gene that causes the hemoglobin molecule to be defective. It is an autosomal recessive condition.

(HbS) acquires a crystal-like formation when exposed to low oxygen tension. The O2 level in venous blood can be low enough to cause this change; consequently, the RBC containing (HbS) loses its round, very pliable, biconcave disk shape and becomes deformed, rigid, and sickle-shaped

These long, rigid RBCs can adhere to the endothelium of small vessels;when they pile up against each other, blood flow to a region or an organ may be reduced. If ischemia or infarction results, the patient may have pain,swelling, and fever.

The sickling process takes time; if the RBC is again exposed to adequate amounts of oxygen (eg, when it travels through the pulmonary circulation) before the membrane becomes too rigid, it can revert to a normal shape thus, the “sickling crises” are intermittent.

Sickle cell anemia is the most severe form of sickle cell disease. Less severe forms include sickle cell hemoglobin C (SC) disease, sickle cell hemoglobin D (SD) disease, and sickle cell beta-thalassemia.

*sickle cell trait* refers to the carrier state for SikcleCell diseases; it is the most benign type of SC disease, in that less than 50% of the hemoglobin within an RBC is HbS. Genetic counseling is very important.

**Clinical Manifestations**

Symptoms and complications result from chronic hemolysis or thrombosis. The sickled RBCs have a shortened life span.

1. Patients are always anemic, usually with hemoglobin values of 7 to 10 g/dL.
2. Jaundice is characteristic and is usually obvious in the sclera.
3. The bone marrow expands in childhood in a compensatory effort to offset the anemia, sometimes leading to enlargement of the bones of the face and skull.
4. The chronic anemia is associated with tachycardia, cardiac murmurs, and often an enlarged heart (cardiomegaly).
5. Dysrhythmias and heart failure may occur in adults.
6. Primary sites vulnerable to thrombosis involve those areas with slowed circulation, e.g. spleen, lungs, and central nervous system. Though any organ may be affected hence hypoxia and necrotic damage.
7. Patients unusually susceptible to infection, particularly pneumonia and osteomyelitis.

**Potential complications**

* Hypoxia, ischemia, infection, and poor wound healing leading to skin breakdown and ulcers
* Dehydration
* Cerebrovascular accident (CVA, brain attack, stroke)
* Anemia
* Renal dysfunction
* Heart failure, pulmonary hypertension, and acute chest syndrome
* Impotence
* Poor compliance
* Substance abuse related to poorly managed chronic pain

**SICKLE CELL CRISIS**

There are three types of sickle cell crisis in the adult population

1. Very painful *sickle crisis;* results from tissue hypoxia and necrosis due to inadequate blood flow to a specific region of tissue or organ. It is the most common
2. *Aplastic crisis* results from infection with the human parvovirus. The hemoglobin level falls rapidly and the marrow cannot compensate, as evidenced by an absence of reticulocytes.
3. *Sequestration crisis* results when other organs pool the sickled cells. Although the spleen is the most common organ responsible for sequestration in children, by 10 years most children with sickle cell anemia have had a splenic infarction and the spleen is then no longer functional (autosplenectomy). In adults, the common organs involved in sequestration are the liver and, more seriously, the lungs.

**Assessment and Diagnostic Findings**

The patient with sickle cell trait usually has a normal hemoglobin level, **a normal hematocrit, and a normal blood smear**. In contrast,the patient with sickle cell anemia has a **low hematocrit and sickled cells on the smear**. The diagnosis is confirmed by hemoglobin electrophoresis.

**Management**

Goals of management of sickle cell anemia are;

* Management of vaso-occlusive crisis
* Management of chronic pain syndromes
* Management of chronic hemolytic anemia
* Prevention and treatment of infections
* Management of the complications and the various organ damage syndromes associated with the disease
* Prevention of stroke
* Detection and treatment of pulmonary hypertension

Medical Management

Treatment for sickle cell anemia is the focus of continued research (Steinberg, 1999). Many trials of medications that have antisickling properties are being conducted, as is research using antiadhesion treatment for vasoocclusive crises. Currently there are only three primary treatment modalities for sickle cell diseases:

* Bone Marrow Transplant,
* Hydroxyurea, and
* Longterm RBC transfusion.

**BMT**

Offers the potential for cure for this disease.

However, this treatment modality is available to only a small subset of the patient population, because of either lack of a compatible donor or severe organ damage (eg, renal, liver, lung) already present in the patient.

**PHARMACOLOGIC THERAPY**

Hydroxyurea (Hydrea), a chemotherapy agent, has been shown to be effective in increasing hemoglobin F levels in patients with sickle cell anemia, thereby decreasing the permanent formation of sickled cells

Pts appear to have fewer painful episodes of sickle cell crisis, a lower incidence of acute chest syndrome, and less need for transfusions. However, whether hydroxyurea can prevent or reverse actual organ damage remains unknown. Side Eeffects; chronic suppression of WBC formation, teratogenesis, and potential for later development of a malignancy.

Patient response to the medication varies significantly

The incidence and severity of side effects are also highly variable within a dose range

**TRANSFUSION THERAPY**

Chronic transfusions with RBCs have been shown to be highly effective in several situations:

* in an acute exacerbation of anemia (eg,aplastic crisis),
* in the prevention of severe complications from anesthesia and surgery, and
* in improving the response to infection (when it results in exacerbated anemia) (Ohene-Frempong, 2001).

Chronic transfusions have also been shown to be effective in diminishing episodes of sickle cell crisis in pregnant women though have not been shown to improve fetal survival.

May be effective in preventing complications from sickle cell disease. Although controversial, some data support the use of chronic transfusions in patients with cerebral ischemic injury to prevent more severe injury.

May also be useful in the management of severe cases of acute chest syndrome.

**Complications from transfusion**

* Iron overload, which necessitates chronic chelation therapy
* Poor venous access, which necessitates a vascular access device (and its attendant risk for infection or thrombosis)
* Infections
* Alloimmunization from repeated transfusions
* Increased viscosity of blood before the concentration of hemoglobin S is reduced. Exchange transfusion may be performed to diminish the risk of increasing the viscosity excessively

Pts require daily folic acid replacements to maintain the supply required for increased erythropoiesis from hemolysis.

Infections must be treated promptly with appropriate antibiotics; infection remains a major cause of death in these patients.

Acute chest syndrome is managed by prompt initiation of antibiotic therapy

Incentive spirometry decrease the incidence of pulmonary complications significantly and in severe cases, bronchoscopy may be required to identify the source of pulmonary disease

* Fluid restriction may be more beneficial than aggressive hydration. Corticosteroids may also be useful.
* Transfusions reverse the hypoxia and decrease the level of secretory phospholipase A2.
* patients may develop multiple autoantibodies due to repeated transfusion, making cross-matching difficult thus a hemolytic transfusion reaction may mimic the signs and symptoms of a sickle cell crisis

In hemolytic transfusion reaction, the patient becomes more anemic after being transfused. This pt is supported with corticosteroids, intravenous immunoglobulin and erythropoietin.

**SUPPORTIVE THERAPY**

**Pain management**; painful sickle cell crises is highly variable; many patients have pain on a daily basis. The severity of the pain may not be enough to cause the patient to seek assistance from health care providers but severe enough to interfere with the ability to work and function within the family.

Acute pain episodes tend to be self-limited, lasting hours to days. If the patient cannot manage the pain at home, intervention is frequently sought in the acute care setting, usually at an urgent care facility or emergency department

**Use of medication to relieve pain**

Aspirin is very useful in diminishing mild to moderate pain; it also diminishes inflammation and potential thrombosis.

(NSAIDs) are useful for moderate pain or in combination with opioid analgesics. Although no tolerance develops with NSAIDs, a “ceiling effect” does develop whereby an increase in dosage does not increase analgesia. S/E; precipitate renal dysfunction.

Opioid analgesics are used, morphine is the medication of choice for acute pain.

Patient-controlled analgesia is frequently used

Chronic pain increases in incidence as the patient ages. Here, the pain is caused by complications from the sickling, such as avascular necrosis of the hip. The principal goal is to maximize functioning; pain may not be completely eliminated without sacrificing function.

Pts need repeated explanations and support from nonjudgmental health care providers

Nonpharmacologic approaches to pain management are crucial in this setting e.g.physical and occupational therapy, physiotherapy cognitive and behavioral intervention and support groups.

Pts experience severe and unpredictable pain. Such pain is disruptive to the person’s level of functioning, including social functioning, and may result in a feeling of helplessness.

Patients with inadequate social support systems may have more difficulty coping with chronic pain.

Adequate hydration is important during a painful sickling episode. Oral hydration is acceptable if the patient can maintain adequate amounts of fluids; intravenous hydration with dextrose 5% in water (D5W) or dextrose 5% in 0.25 normal saline solution (3 L/m2/24 hours) is usually required for sickle crisis.

Supplemental oxygen may also be needed.

**LYMPHOMAS**

This is a group of neoplastic diseases that arise from the lymphoid and hemopoeitic systems. They are divided into:

1. Hodgkin disease
2. Non hodgkin lymphoma

In children, non hodgkin disease is more common. Hodgkin disease is rare before 5 years

**1. Hodgkin disease**

This is a cancer that affects the lymphatic system especially the lymph nodes and other organs of the immune and blood forming systems. It affects about 5 in 1 million children. Its common in adolescents

It predictably metastasizes to non-nodal or extra lymphatic sites especially the spleen, liver, bone marrow, lungs and mediastinum. It can be classified into 4 histological types:

1. Lymphocytic predominance
2. Nodular sclerosis
3. Mixed cellularity
4. Lymphocytic depletion

**STAGES OF HODGKIN DISEASE**

**Stage I:** Lesions are limited to one lymph node area or only one extra lymphatic site such as the lungs, kidney or intestine

**Stage II:** Two or more lymph node regions on the same side of the diaphragm or one additional extra lymphatic site or organ on the same side of the d is involved

Stage III; Lymph node regions on both sides of the d are involved, or one extra lymphatic site, spleen or both

Stage IV: Cancer metastasizes diffusely throughout the body to one or more extra lymphatic sites with or without involvement of associated lymph nodes

**Clinical manifestations**

* Hodgkin has no known cause but is associated with infections e.g. the virus that causes glandular disease and the Red-stern berg cells which are malignant B- cell lymphocytes
* It presents with:

1. Painless enlarged lymph nodes especially in the supra clavicle or cervical area
2. Other signs depend on the extent and location of involvement:

- Mediastinallympadenopathy causes persistent non productive cough

* Enlarged retro peritoneal nodes may produce unexplained abdominal pain
* Systemic symptoms include low grade or intermittent fever, anorexia, nausea, weight loss, night sweats and pruritus

**DIAGNOSTIC EVALUATION**

1. History and physical examination
2. Lab works: CBC, uric acid levels, liver function tests, ESR, T cell function studies and urinalysis
3. Radiographic tests: CT scan, Gallium scan( identifies metastatic and recurrent disease, chest XY and a bone scan
4. Lymphangiography a special procedure that involves the intradermal injection of a contrast material (usually alphazurine) in the first interdigital space of each foot for visualization of lymphatic vessels to determine the presence of disease in various lymph node regions
5. Lymph node biopsy to establish histological diagnosis and staging (the presence of Sternberg-Reed cell is diagnostic)
6. A bone marrow aspiration or biopsy

**Management**

* Primary modalities of therapy are irradiation and chemotherapy
* Each may be used alone or in combination based on clinical staging
* The goal of treatment is to cure
* Radiation involves involved field (IF), Extended field radiation ( involved areas plus adjacent nodes) or total nodal irradiation (the entire axial lymph node system) depending on the extent of involvement
* In stage IV chemotherapy is the primary form of treatment although limited irradiation may be given to areas of bulky disease
* The most effective combination of chemotherapy is:
* MOPP: mechlorethaminen (mustargen), Vincristine (oncovin), Predisone&Procarbazine
* The above alternates with ABVD: Adriamycin, Bleomycin, Vinblastine &Darcarbazine
* This therapy causes severe effects like secondary malignancies
* Other drug combination is BEACOPP- Doxorubicin, Cyclophosphamide, Etoposide, Procarbazine,

Prednisone, Vincristine and Bleomycin

**Nursing management**

This involves:

1. Preparation for diagnostic and operative procedures
2. Explanation of treatment side effects like nausea, vomiting, hair loss, lowered immunity, fatigue Mucosal ulceration and diarrhea. The most common side effects of extensive irradiation is malaise which may result from damage of the thyroid gland causing hypothyroidism. Another area of concern following chemotherapy and irradiation is sterility and altered or delayed appearance of secondary Characteristics

3. Child and family support