INHERITED DISODERS OF BLOOD COAGULATION

Although there are many different types of bleeding disorders, there are inherited coagulations disorders such as hemophilia A (factor VIII deficiency), hemophilia B (factor IX deficiency) Factor XI def.(Hemophilia C), Von Willebrand disease, and others rare factor deficiencies including I, II, V, VII, X, XII and XIII.

Hemophilia A, (factor VIII deficiency):

It is the most common hereditary disorder of blood coagulation after Von Willebrand Disease . It is due to the absent or decreased function of coagulation factor VIII. Hemophilia A is an X-linked inherited disorder caused by deficiency of functional plasma clotting factor VIII (FVIII), which may be inherited or arise from spontaneous mutation. Because the gene for factor VIII is present on the X chromosome, females are usually not affected because they carry only one defective gene. Children of a female carrier have a 50% chance of inheriting the abnormal X chromosome Hemophilia A occurs in approx. 1 in 10,000 persons.

Signs and symptoms:

Excess bleeding is relatively uncommon at birth. The first bleeding problems usually start when a child starts crawling, and this may be from 9 mo to 1 yr of age. Bleeding, however, can occur after surgery, i.e., circumcision. The first signs that parents may notice are large skin bruises.
Depending on the level of FVIII activity, patients with hemophilia may present with easy bruising, inadequate clotting of traumatic injury or—in the case of severe hemophilia—spontaneous hemorrhage.

Signs of hemorrhage include the following:

General: Weakness, postural Hypotension from significant blood loss , tachycardia, tachypnea
Musculoskeletal (joints): Tingling, cracking, warmth, pain, stiffness, and refusal to use joints
CNS: Headache, stiff neck, vomiting, lethargy, irritability, and spinal cord syndromes
Gastrointestinal: Hematemesis, melena, frank red blood per rectum, and abdominal pain
Genitourinary: Hematuria, renal colic, and post circumcision bleeding.
Other: Epistaxis, oral mucosal hemorrhage, hemoptysis, dyspnea (hematoma leading to airway obstruction), compartment syndrome symptoms, excessive bleeding with routine dental procedures.

Diagnosis: Laboratory studies for suspected hemophilia include the following
Complete blood cell count to rule out other hematological problems
Coagulation studies.
FVIII assay: Normal values for FVIII assays are 50-150%. Values in hemophilia are as follows
Mild: >5%
Moderate: 1-5%
Severe: < 1%

Expected laboratory values are as follows:

Hemoglobin/hematocrit: Normal or low

Platelet count: Normal

Bleeding time and prothrombin time: Normal

Clotting time prolong > 8 minutes

Activated partial thromboplastin time (aPTT): Significantly prolonged in severe hemophilia, but may be normal in mild or even moderate hemophilia.

Hemophilia B(Fac. IX):

The inheritance X linked the clinical features of hemophilia B (factor IX deficiency, Christmas disease) are identical to those of hemophilia A. The incidence is one-fifth of that of hemophilia A. The two disorders can only be distinguished by coagulation factor assays.

CLINICAL PRESENTATION:

The same as of hemophilia A, Excess bleeding is relatively uncommon at birth. The first bleeding problems usually start when a child starts crawling, and this may be from 9 mo to 1 yr of age. Bleeding, however, can occur after surgery, i.e., circumcision. The first signs that parents may notice are large skin bruises. Abnormal and recurrent bleeding can then occur from any part of the body. A dominant feature of the severe form of the disorder is recurrent painful bleeding into the joints (hemarthrosis) and into the muscles (muscle hematomas). Joint bleeding usually involves the large joints (knees, ankles, ellbows), and the accumulation of blood in the joint space leads to severe pain. If left untreated, the recurrence of the bleeding episodes will lead to progressive deformity and crippling in severely affected patients. Soft tissue and intramuscular bleeding may lead to considerable blood loss, particularly in the retroperitoneum and the thigh. Repeated subperiostal hemorrhage with bone destruction, new bone formation. Bleeding in the pharyngeal area may be life-threatening because of potential airway obstruction. Minor head traumas may cause serious CNS bleeding leading to death or permanent disability.

The severity of the bleeding manifestations depends on the remaining activity of factors VIII or IX measured in clotting assays .

The laboratory diagnosis of the hemophilia's is straightforward, as often the family history and the clinical manifestations suggest the only the activated partial thromboplastin time (aPTT) is prolonged. With the severe form of hemophilia.

A prolongation in the range of 90–100 s can be expected. (The reference normal range of the aPTT is 30-40 seconds).

Diagnosis:

Subsequent testing with a specific, factor VIII- or IX-deficient plasma can prove the suspected diagnosis of hemophilia A or B. The bleeding time, the prothrombin time, and also the VWF activity should be normal.

Normal values for FIX assays are 50-150%. Values in hemophilia B as A: are as follows

Mild: >5%

Moderate: 1-5%

Severe: < 1%

TREATMENT of Hemophilia (A and B):

Acute bleeding episodes are treated with concentrates of clotting factor VIII in hemophilia A and clotting factor IX in hemophilia B.

Spontaneous bleeding (joints, muscles) is usually controlled if the patient’s factor level is raised to 20% of the normal level.

If the hemorrhage is occurring at critical sites (CNS, Nasopharyngeal area), before major surgery, or after serious posttraumatic bleeding, the factor VIII or IX level should be elevated to 100% and then maintained above 50% until healing has occurred.

DDAVP(deamino-8-D arginine-vasopresssin:(desmopressin) generic name (desmopressin acetate): provides an alternative treatment for increasing the factor VIII levels in patients with a mild form of hemophilia and administration of systemic nonspecific drugs such as antifibrinolytic agents (e.g., tranexamic acid), which may be helpful in prevention or treatment of mucocutanous hemorrhage and after dental procedures.

A Local supportive measures in treating hemoarthrosis and hematomas include resting the affected extremity.

Coagulation factor activity (%)	Clinical manifestations
<1 Severe disease	Recurrent spontaneous bleeding episodes
	Joint deformities and crippling, if insufficiently treated
1–5 Moderate disease	Occasional spontaneous bleeding
	Postsurgical or posttraumatic bleeding
5–20 Mild disease	Postsurgical or posttraumatic bleeding
The amount of clotting factor needed can be calculated as follows:	
1 unit of factor VIII/kg will raise the blood level by 2%	
1 unit of factor IX/kg will raise the blood level by 1%	

Hemophilia C (Fact. XI def.):

Mutations in the factor XI gene(on the distal arm of chromosome 4 cause the congenital deficiency of factor XI clotting activity. The inheritance pattern of factor XI is autosomal recessive.

is a mild form of hemophilia affecting both sexes. However, it predominantly occurs in Jews of Ashkenazi descent. It is the fourth most common coagulation disorder after von Willebrand's disease and hemophilia A and B. the bleeding risk is not always influenced by the severity of the deficiency. Treatment is usually not necessary, except in relation to operations, leading to many of those having the condition not being aware of it. In these cases, fresh frozen plasma or recombinant factor XI may be used, but only if necessary. The afflicted may often suffer epistasis , and females can experience heavy menstrual bleeding.

Von Willebrand Disease:

VWF is a protein synthesized by endothelial cells(Weibel-Palade bodies) and megakaryocytes, which is involved in both platelet function and coagulation.

VWD is characterized by an abnormal platelet adhesion with or without a low factor VIII activity. VWF promotes platelet adhesion and is also the carrier for factor VIII, protecting the latter from premature destruction. This explains the combination of defective platelet adhesion and reduced levels of factor VIII. VWD is a bleeding disorder inherited in an autosomal dominant disorder.

Types of von Willebrand Disease:

Type1.. Type2(A, B, M and N).. Type3…a quantitative (types 1 and 3) or qualitative(type 2) deficiency of von Willebrand factor (vWF).

VWD is clearly the most common genetic bleeding disorder to be encountered in clinical practice, although its estimated incidence varies widely from 0.1% to as high as 1% of the general population. The most common variant, type 1 VWD, characterized by a moderate quantitative deficiency of functionally normal VWF, accounts for about 70% of patients. The most common clinical features in VWD are mucocutanous episodes, including epistaxis, easy bruising, hematomas, and menorrhagia. Postoperative bleeding occurs after tooth extraction, tonsillectomy, and, naturally, following major operative procedures.

Bleeding is quite variable in each patient and within the same family, and menstrual blood loss in females varies widely in the same family. An unexplained observation is the tendency of clinical symptoms to decrease after the patient enters the second decade of life.

Laboratory Diagnosis of Von Willebrand Disease:

Initial diagnostic tests should include the bleeding time, a factor VIII assay, and measurement of the levels of VWF. Bleeding time varies from abnormal in moderately and severely affected patients to normal in patients with mild forms of VWD. Bleeding time correlates well with the clinical symptoms.

Levels of vWF increases with physiologic stress; in particular with estrogens, vasopressin, growth hormone, and adrenergic stimuli. Thus, vWF levels may intermittently be normal in patients with von Willebrand disease (vWD), and measurements should be repeated to confirm abnormal results.

Screening tests for Von Willebrand Disease: include the following:

- Prothrombin time (PT)
- Activated partial thromboplastin time (aPTT)
- Factor VIII (FVIII) coagulant activity
- Ristocetin cofactor (RCoF) activity
- Concentration of vWF antigen (vWF:Ag)

Treatment of VW Disease :

Most patients with moderate disease (usually type 1) and mild bleeding symptoms or bleeding after minor surgery will respond to DDAVP (deamino-8-D arginine-vasopresssin, desmopressin,), a synthetic analog of the natural hormone vasopressin, which releases factor VIII, VWF, and plasminogen activator from storage sites. DDAVP probably releases the very large VWF multimers from the endothelial cells or platelets and thus corrects the prolonged bleeding time. The effect extends over several hours, the response decreases if treatment is repeated over a period of several days. It is helpful to determine the response to DDAVP at diagnosis or before an elective procedure. Fibrinolytic inhibitors (tranexamic acid) have proved useful in reducing bleeding from the mouth, nose, or uterus.

Acquired bleeding disorders:

Disseminated intravascular coagulation (DIC):

It is characterized by systemic activation of blood coagulation, which results in generation and deposition of fibrin, leading to microvascular thrombi in various organs and contributing to multiple organ dysfunction syndrome (MODS). Consumption and subsequent exhaustion of coagulation proteins and platelets (from ongoing activation of coagulation) may induce severe bleeding. a patient with disseminated intravascular coagulation (DIC) can present with a simultaneously occurring thrombotic and bleeding problem.
It is always secondary to an underlying disorder and is associated with a number of clinical conditions, generally involving activation of systemic inflammation.

COMMON CAUSES OF DIC :

Sepsis and severe infection as bacterial (eg, gram-negative sepsis, gram-positive infections, rickettsial),parasitic as malaria
- Trauma (neurotrauma).
-Burn
- **Organ destruction** (eg, pancreatitis)
- **Malignancy** (solid and lymphoproliferative/myeloproliferative malignancies). Acute myelocytic leukemia M3)
- **Severe transfusion reactions**
-**Obstetric complications** - Amniotic fluid embolism; abruptio placentae; hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome; and eclampsia, Retained dead fetus syndrome
-**Severe hepatic failure**
-**Heat stroke and hyperthermia**
-**Catastrophic antiphospholipid syndrome** (rare)
-**Others as snake bite, etc…**
DIC is most commonly observed in severe sepsis and septic shock.The development and severity of DIC correlate with mortality in severe sepsis. Although bacteremia, including both gram-positive and gram-negative organisms, is most commonly associated with DIC, other organisms (eg, viruses, fungi, and parasites) may also cause DIC.
Trauma, especially neurotrauma, is also frequently associated with DIC. DIC is more frequently observed in trauma patients with the systemic inflammatory response syndrome (SIRS). Evidence indicates that inflammatory cytokines play a central role in DIC in both trauma patients and septic patients. The symptoms of DIC are often those of the underlying inciting condition . In addition, symptoms of thrombosis, embolism, organ dysfunction, or bleeding may be present.
Complications of DIC include the following:
Acute renal failure, Respiratory failure ,Hepatic failure
Change in mental status
Life-threatening thrombosis and hemorrhage (in patients with moderately severe–to–severe DIC)
Cardiac tamponade , Hemothorax ,Intracerebral hematoma
Gangrene and loss of digits
Shock and Death.

Laboratory work up:

In clinical practice, a diagnosis of DIC can often be made by a combination of the following tests : - Platelet count: which is low . - (aPTT and PT) both are prolong - Assay for D-dimer or FDPs which positive and high titer .

Management of the DIC :

The management of disseminated intravascular coagulation (DIC) should primarily be directed at treatment of the underlying disorder. DIC will resolve on its own once the underlying disorder is addressed and proper treatment . Monitor vital signs. Assess and document the extent of hemorrhage and thrombosis Correct hypovolemia Administer the following medications :

Platelet and factor replacement: should be directed not at simply correcting laboratory abnormalities but at addressing clinically relevant bleeding. administering of FFP, particularly in patients with an international normalized ratio (INR) higher than 2.0, a 2-fold or greater prolongation of the aPTT, or a fibrinogen level below 100 mg/dL.

Heparin or low-molecular-weight heparin (LMWH): should be provided to those patients who demonstrate extensive fibrin deposition without evidence of substantial hemorrhage. Heparin is appropriate to treat the thrombosis that occurs with DIC. It also has a limited use in acute hemorrhagic .

Activated protein C (drotrecogin alfa): showed benefit in subgroups of patients with sepsis who have DIC.

Patients with DIC should be treated at hospitals with appropriate critical care and subspecialty expertise, such as hematology, blood bank, or surgery.

Repeated measurement of (aPTT and PT) might be useful for monitoring the coagulation defect. In case of a vitamin K deficiency in the face of consumption, administration of vitamin K may be required.

Liver Disease:

The liver is central to hemostasis. Liver failure is associated with a high risk of bleeding due to deficient synthesis of procoagulant factors and enhanced fibrinolysis.

Thrombocytopenia is common in patients with liver disease due to congestive splenomegaly (hypersplenism), or immune-mediated shortened platelet lifespan (primary biliary cirrhosis).

Dysfibrinogenemia is a relatively common finding in patients with liver disease due to impaired fibrin polymerization.

DIC in chronic liver disease is not uncommon and may enhance the risk for bleeding.

Laboratory evaluation is mandatory for an optimal therapeutic strategy, either to control ongoing bleeding or to prepare patients with liver disease for invasive procedures.

Typically, these patients present with prolonged PT, aPTT, and TT(thrombin time or named clotting time) depending on the degree of liver damage, thrombocytopenia, and normal or slight increase of FDP.

Fibrinogen levels are diminished only in fulminant hepatitis, decompensated cirrhosis or advanced liver disease, or in the presence of DIC. The presence of prolonged TT and normal fibrinogen and FDP levels suggest dysfibrinogenemia.

FVIII levels are often normal or elevated in patients with liver failure, and decreased levels suggest superimposing DIC.

Because FV is only synthesized in the hepatocyte and is not a vitamin K–dependent protein, reduced levels of FV may be an indicator of hepatocyte failure. Normal levels of FV and low levels of FVII suggest vitamin K deficiency.

Vitamin K levels may be reduced in patients with liver failure due to compromised storage in hepatocellular disease, changes in bile acids or cholestasis that can diminish the absorption of vitamin K. Replacement of vitamin K may be desirable (10 mg given by slow intravenous injection) to improve hemostasis.

Chronic Renal failure:

Abnormal bleeding is common in patients with uremia. Bleeding time is generally very prolonged. The bleeding has the characteristics of a platelet disorder, and GI tract bleeding is the most frequent manifestation

Clinical bleeding in uremia may involve the skin, resulting in easy bruising, or the oral and nasal mucosa, gingiva, gastrointestinal and urinary tracts, and respiratory system. Excessive bleeding may also occur in response to injury or invasive procedures.

The causes of bleeding tendency in chronic renal failure , including anemia, mild thrombocytopenia and the accumulation of low molecular weight waste products (nitrogenous products), normally excreted by the kidney, which inhibit platelet function.

BLOOD PRODUCTS AND TRANSFUSION:

Blood is a tissue; transfusion from a donor to a recipient is a form of allogeneic transplant and carries some risk, including an immunological interactions between the host and blood. and transmission of infectious agents. Although there are many clinical indications for blood transfusion however there are many therapeutic circumstances, the evidence for its value is relatively low.

ABO system:

The ABO system is a group of carbohydrate antigens that project from the red cell surface. The ABO gene has three common alleles: A, B and O. The O allele encodes an inactive enzyme, leaving the ABO antigen precursor (called the H antigen).

The ABO system is regarded as the most important blood-group system in transfusion medicine because of severe hemolytic transfusion reactions and, to a lesser degree, hemolytic disease of the newborn.

The routine practice of blood typing and cross matching blood products should prevent adverse transfusion reactions caused by ABO antibodies. However, "the wrong blood" being transfused into a patient, an error which can result in the death of the patient.

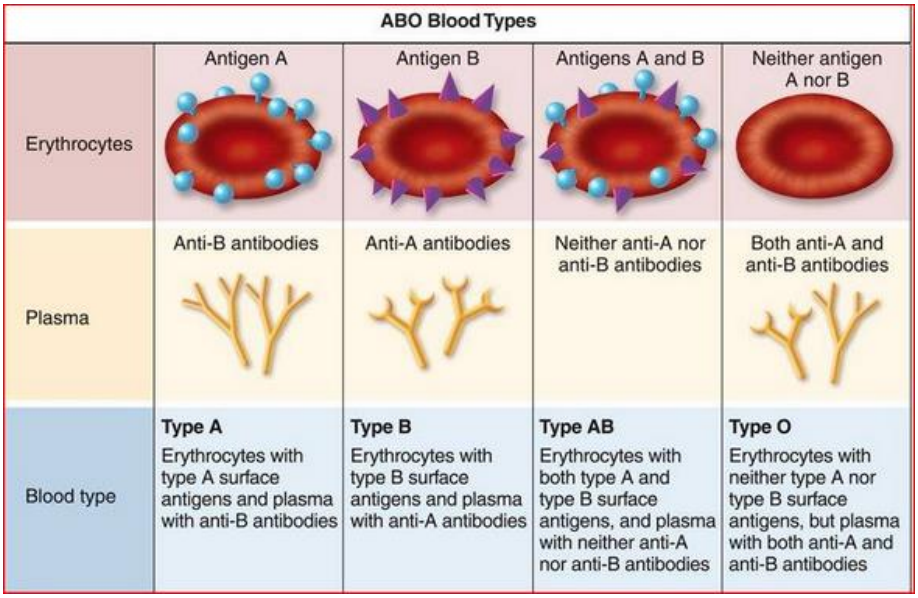
If a recipient who has blood group O is transfused with blood group(A, B, AB), the naturally occurring anti-A and anti-B in the recipient's serum binds to their corresponding antigens on the transfused RBCs. These antibodies fix complement and cause rapid intravascular hemolysis, triggering an acute hemolytic transfusion reaction that can cause disseminated intravascular coagulation, shock, acute renal failure, and death.

ABO blood group antigens and antibodies:

The genes that determine the ABO blood group antigens are found on chromosome 9 . Individuals who lack the "A" and "B" antigens are phenotypically type "O" while those who inherit both antigens A,B called type "AB."

Four main blood groups: A, B, O, or AB. Individuals have antibodies (isohemagglutinins) in their plasma that are directed against blood group antigens that their RBCs lack. These antibodies (isohemagglutinins) form early in life. ABO antigens are expressed on RBCs, platelets, and endothelial cells and are present in body fluids.

ABO testing is performed in order to prevent an adverse transfusion reaction that could be caused by ABO incompatibility between the patient and a blood donor.



Rh system:

The Rh factor (Rhesus factor) is a red blood cell surface antigen that was named after the monkeys in which it was first discovered.
Rh incompatibility, also known as Rh disease, is a condition that occurs when a woman with Rh-negative blood type is exposed to Rh-positive blood cells, leading to the development of Rh antibodies.

Clinically, the Rh blood group system is almost as important as the ABO system. Unlike the ABO system, which comprises carbohydrate antigens, Rh antigens are proteins. Also unlike the ABO system, antibodies to Rh antigens are rarely present unless a person has been previously immunized by transfusion or pregnancy, or has undergone an allogeneic hematopoietic stem cell transplantation (HSCT) utilizing an Rh-alloimmunized donor or an Rh-mismatched donor.
Rh incompatibility can occur by 2 main mechanisms. The most common type occurs when an Rh-negative pregnant mother is exposed to Rh-positive fetal red blood cells secondary to fetomaternal hemorrhage during the course of pregnancy from spontaneous or induced abortion, trauma, invasive obstetric procedures, or normal delivery. Rh incompatibility can also occur when an Rh-negative female receives an Rh-positive blood transfusion. In part, this is the reason that blood banks prefer using blood type "O negative" or "type O, Rh negative," as the universal donor type in emergency situations when there is no time to type and crossmatch blood.

The Rh antigens are found on RBC membrane protein that has no defined function. Although >40 different antigens in the Rh system have been described, five determinants account for the vast majority of phenotypes.
The presence of the D antigen confers Rh "positivity," while persons who lack the D antigen are Rh negative. Two allelic antigen pairs, E/e and C/c, are also found on the Rh protein. The three Rh

genes, E/e, D, and C/c, are arranged in tandem on chromosome 1 and inherited as a haplotype, i.e., cDE or Cde. Two haplotypes can result in the phenotypic expression of two to five Rh antigens. The D antigen is a potent alloantigen. About 15% of individuals lack this antigen. Exposure of these Rh-negative people to even small amounts of Rh-positive cells, by either transfusion or pregnancy, can result in the production of anti-D alloantibody.

Other protein antigen systems:

More than 100 blood group systems are recognized, composed of more than 500 antigens. The presence or absence of certain antigens has been associated with various diseases and anomalies; antigens also act as receptors for infectious agents.
Outside the ABO and Rh systems, most clinically significant blood group alloantibodies are directed against protein based antigens, particularly antigens in the Kell, Kidd and Duffy. As is the case with the Rh system, and unlike the ABO system, these systems are defined by protein .

Red cell compatibility testing:

It is essential that all blood is tested before transfusion in order to: Ensure that transfused red cells are compatible with antibodies in the recipient's plasma.
All pre-transfusion test procedures should provide the following information about both the units of blood and the patient: ABO group, RhD type, Presence of red cell antibodies that could cause hemolysis in the recipient.
These antibodies are usually of IgM and IgG class and are normally able to hemolysis (destroy) transfused red cells.

RED CELL COMPONENTS:

In red cell transfusion, there must be ABO and RhD compatibility between the donor's red cells and the recipient's plasma.
1- Group O individuals can receive blood from group O donors only
2- Group A individuals can receive blood from group A and O donors
3- Group B individuals can receive blood from group B and O donors
4- Group AB individuals can receive blood from AB donors, and also from group A, B and O donors.

PLASMA AND COMPONENTS CONTAINING PLASMA

In plasma transfusion, group AB plasma can be given to a patient of any ABO group because it contains neither anti-A nor anti-B antibody.
1- Group AB plasma (no antibodies) can be given to any ABO group patients
2- Group A plasma (anti-B) can be given to group O and A patients
3- Group B plasma (anti-A) can be given to group O and B patients
4-Group O plasma (anti-A + anti-B) can be given to group O patients only
A direct test of compatibility (cross match) is usually performed before blood is infused. This detects a reaction between:
_Patient's serum
_Donor red cells.
The laboratory performs:

_Patient's ABO and RhD type

_Direct compatibility test or crossmatch. These procedures normally take about 1 hour to complete. Shortened procedures are possible, but may fail to detect some incompatibilities. fortunately, only the ABO and the Rh systems are important in the majority of blood transfusion.

Blood Products:

Any therapeutic substance prepared from human blood

1- WHOLE BLOOD:

A 450 ml whole blood donation contains: Up to 510 ml total volume (volume may vary in accordance with local policies), 450 ml donor blood, 63 ml anticoagulant-preservative solution.

2-RED CELL CONCENTRATE (Packed red cells):

'plasma-reduced blood'150-300 ml red cells from which most of the plasma has been removed.

3-PLATELET CONCENTRATES:

(prepared from whole blood donations).

Indications :Treatment of bleeding due to Thrombocytopenia, Platelet function defects, Prevention of bleeding due to thrombocytopenia, such as in bone marrow failure

Not indicated in: Thrombotic thrombocytopenic purpura (TTP).

Give platelet concentrates that are ABO compatible, whenever possible. Each platelet unit contain about 5000

prophylactic : given when plt.counts below 10,000-20,000

prophylactic preoperative : plt.counts below 50,000

Neuro/ ocular surgery should be the platelet count > 75,000

4-FRESH FROZEN PLASMA

Pack containing the plasma separated from one whole blood donation Contains normal plasma levels of stable clotting factors, albumin and immunoglobulin. within 6 hours of collection and then rapidly frozen to –25C or colder.

Indications: Replacement of multiple coagulation factor deficiencies: e.g Liver disease, Warfarin (anticoagulant) overdose, Disseminated intravascular coagulation (DIC), Thrombotic thrombocytopenic purpura (TTP).

5-CRYOPRECIPITATE:

Prepared from fresh frozen plasma by collecting the precipitate formed during controlled thawing at +4C and resuspending it in 10–20 ml plasma. Cryoprecipitate contain high conc. Of factor VIII, fibrinogen .

Indications: As an alternative to Factor VIII concentrate in the treatment of inherited deficiencies of: Von Willebrand Factor (Von Willebrand's disease) Factor VIII (hemophilia). A), Factor XIII,As a source of fibrinogen in acquired coagulopathies: e.g. disseminated intravascular coagulation (DIC).

6-HUMAN ALBUMIN SOLUTIONS:

Prepared by fractionation of large pools of donated plasma. Albumin 5%: contains 50 mg/ml of albumin.

Indications :Replacement fluid in therapeutic plasma exchange: use albumin 5%, Treatment of diuretic-resistant edema in hypoproteinaemic patients: e.g. nephrotic syndrome or ascites.

7-COAGULATION FACTORS:

Factor VIII Concentrate:

Description: Partially purified Factor VIII prepared from large pools of donor plasma. all heated and/or chemically treated to reduce the risk of transmission of viruses

Indications :Treatment of hemophilia A.

Alternatives : Cryoprecipitate, fresh frozen plasma

Factor IX Concentrate: Indications : Treatment of hemophilia B (Christmas disease).

8-IMMUNOGLOBULINS: Indications: Idiopathic autoimmune thrombocytopenic purpura and some other immune disorders as Guillain barre syndrome, Treatment of immune deficiency states(HIV-related disease) and Hypogammaglobulinaemia.

Complication of Blood transfusion:

Transfusion reaction: is any unfavorable transfusion-related event occurring in a patient during or after transfusion of blood components.

Transfusions of blood products are associated with several complications, many of which can be due to immunological or non-immunological like infectious.

Immunological Complications:

Acute hemolytic reaction (Intravascular Hemolysis) : occur with transfusion of red blood cells, and This is due to destruction of donor erythrocytes by preformed recipient antibodies. Most often this occurs due to errors or improper typing and crossmatching.

Its occurred Within minutes, Antibodies IgM &/or IgG antibody, Complement activation release of histamine and serotonin.

Symptoms include fever, chills, chest pain, back pain or loin pain, palpitation shortness of breath, and rapid drop in blood pressure Kidney injury may occur due to the effects of the hemolytic reaction (pigment nephropathy).

When suspected, transfusion should be stopped immediately, and blood sent for tests to evaluate for presence of hemolysis. Treatment is Stop transfusion. Cardio-pulmonary support supportive care to maintain renal function by keep IV line with Normal saline Goal of urine out put 100 mL/hr. in adults for at least 18-24 hours by Low dose dopamine.

Delayed hemolytic reactions: occur due to the same mechanism as in acute hemolytic reactions. However, the consequences are generally mild and a great proportion of patients may not have symptoms. However, evidence of hemolysis and falling hemoglobin levels may still occur. Treatment is generally not needed, but due to the presence of recipient antibodies.

Febrile non hemolytic reactions :are due to recipient antibodies to donor white blood cells, and occurs in about 7% of transfusions. This may occur after exposure from previous transfusions. Fever is generally short lived and is treated with antipyretics. This is a reason for the now-widespread use of leukoreduction - the filtration of donor white cells from red cell product units.

Treatment/Prevention: stop transfusion, cold sponge antipyretic as paracetamol.

Allergic Anaphylactic reactions: may occur when the recipient has performed antibodies to certain chemicals in the donor blood, and does not require prior exposure to transfusions. Symptoms include urticaria, pruritus, and may proceed to anaphylactic shock. Treatment is the same as for any other type 1 hypersensitivity reactions. A small population of patients are deficient in the immunoglobin IgA, and upon exposure to IgA-containing blood, may develop an anaphylactic reaction.

Treatment/Prevention: stop transfusion. Adrenaline(Epinephrine: 1 ml of 1/1000 IM) and Antihistamine/steroids(hydrocortisone 100 mg IV) Washing of blood products, pretreatment, leukoreduction

Graft-versus-host disease (GVHD) Fatal complication cause by engraftment and clonal expansion of donor lymphocytes in susceptible host Attack recipient tissues may occurs 2-30 days after transfusion.

Post-transfusion Purpura (PTP): It's a rare complication Characterized by abrupt onset of severe thrombocytopenia less than 10.000.with skin purpura or bleeding in other site .mechanism due to Immune complex – platelet antibody of recipient and donor antigen.

Transfusion-related acute lung injury: Donor Ab reacts with recipient Ag, Leukocyte Ab in donor react with pt. leukocytes, Activate complements, Adherence of granulocytes to pulmonary endothelium with release of proteolytic enzyme .& toxic O2 metabolites lead endothelial damage of lung tissue (Interstitial edema and fluid in alveoli). Symptom like fever ,hypotension, tachypnea and non cardiogenic pulmonary edema.

Non immunological Complications :

1-Infection:such as HIV, hepatitis C hepatitis B, syphilis, Chagas disease, cytomegalovirus infections (in immunocompromised recipients), HTLV, and Babesia.

2-Volume overload: is a common complication simply due to the fact that blood products have a certain amount of volume. fluid overload can result in heart failure and pulmonary edema.
Too much fluid is transfused, the transfusion is too rapid and the renal function is impaired.
Treatment by diuretic with other supportive therapy.

3-Hypocalcemia can also occur with massive blood transfusions due to the complex of citrate with serum calcium

4-Metabolic alkalosis can occur with massive blood transfusions due to the breakdown of citrate stored in blood into bicarbonate

5-Iron overload:

Usually occurred when Chronic transfusion > 100 units ,lead to iron overload called hemochromatosis and deposition of iron in some organ as heart liver, endocrine glands (pancreas)treatment via Removal of Fe by Desferoxamine – Fe-chelating agent , Chronic transfusion in hemoglobinopathy as(thalassemia ,myelodysplastic syndrome ect).

Massive Blood Transfusion:

Definition: Transfusion of blood within 24 hours20 units whole blood or 10 units packed cells.

Complications: Dilutional Thrombocytopenia, Dilutional Coagulopathy ,Metabolic complications as(Acidosis, hypocalcemia, hyperkalemia) and hypothermia.