

SHOCK

CHAPTER

5

LEARNING OBJECTIVES

After the completion of this chapter, you should be able to,

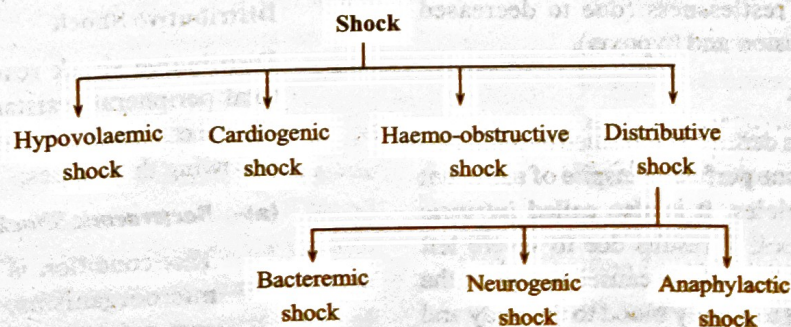
- ◆ Define shock and explain its various types
- ◆ Discuss the pathogenesis of different types of shock
- ◆ Outline the various intravenous fluids given for the treatment of shock
- ◆ Provide a brief note on dextran and its types
- ◆ Summarize the treatment procedures of hypovolaemic and cardiogenic shocks.

1. INTRODUCTION

Shock may be defined as the resultant effect of failure of the circulatory system in supplying adequate amounts of blood (and hence oxygen) to the tissues and organs of the body. This in turn results in insufficient supply of oxygen and nutrients which impairs the normal cellular functioning. It is generally manifested by hypotension and hypoperfusion, but shock may also occur even when the vital body signs are normal. If the treatment is not provided at appropriate time then both hypotension and hypoperfusion may result in impaired cellular metabolism and eventually death. Circulatory shock, also known as true or secondary shock is the outcome of failure of circulatory system thereby creating an imbalance between the supply and requirement of oxygen at cellular level. Initial or primary shock, on the other hand, is a transient attack observed due to emotional outburst such as surprise, fear, sadness etc., which is caused due to neurogenic vasodilation that decreases the venous return to the heart and also results in peripheral pooling of blood. Primary shock may last from few seconds to minutes and is manifested by weakness, pale and cold limbs, weak pulse, hypotension, falling sensation, loss of consciousness etc. However, anaphylactic shock does not involve the circulatory system rather it occurs due to type-I immunologic reaction. Basically shock is not a disease, it is a syndrome that may be encountered during the course of many other life-threatening conditions or diseased states.

Various reasons for shock include severe blood loss, excessive loss of body fluids, acute myocardial dysfunctioning, severe infection, congestion of capacitance vessels (veins), allergens etc.

Types of Shock



1. Hypovolaemic Shock

Hypovolaemic shock, also called *oligemic shock* results due to decrease in intravascular blood volume or insufficient volume of circulating blood, which decreases preload and hence the cardiac output.

Aetiology

- (a) Dehydration, diarrhoea and vomiting
- (b) Acute blood loss during accidents
- (c) Fluid loss during burns
- (d) Diabetic ketoacidosis (seen in type-I diabetes) leads to chemical imbalance in the body leading to high blood glucose levels and low circulatory blood volume.
- (e) Diabetes insipidus contributes to excess thirst and frequent passing of urine due to failure of pituitary gland to secrete antidiuretic hormone.
- (f) GI bleeding, pancreatitis, intestinal obstruction and cirrhosis.

Signs and Symptoms

- (a) Hypotension (due to decrease in intravascular blood volume)
- (b) Tachycardia i.e., heart rate above 100 beats/min
- (c) Weak or rapid pulse (due to decreased blood flow)
- (d) Fast breathing (due to excess CO₂)
- (e) Sweating and hypothermia (due to inadequate perfusion)
- (f) Dry mouth and thirst (due to depletion of body fluids)
- (g) Oliguria i.e., decreased production of urine (<30 ml/hr)
- (h) Fatigue (due to less O₂ supply)
- (i) Cool and clammy skin (due to vasoconstriction) and mottled skin (due to inadequate skin perfusion)
- (j) Anxiety and restlessness (due to decreased cerebral perfusion and hypoxia).

2. Cardiogenic Shock

Cardiogenic shock is defined as sustained hypotension with inadequate tissue perfusion inspite of sufficient filling of left ventricles. It is also called *intrinsic or compression shock*. It results due to severe left ventricular dysfunction which causes defect in the functioning of heart to supply blood to the body and failure of the Na⁺ - K⁺/ATPase pump of the heart.

Aetiology

- (a) Defects in myocardium such as in myocardial ischaemia, myocardial infarction (MI) and cardiomyopathy
- (b) Cardiac valvular insufficiency
- (c) Aortic stenosis (narrowing of aortic walls) which leads to obstruction of blood flow
- (d) Septal defects
- (e) Arrhythmias
- (f) Congestive heart failure (CHF).

Signs and Symptoms

It has similar signs and symptoms as that of hypovolaemic shock. Other symptoms include absence of pulse (due to tachyarrhythmia), distended jugular veins (due to decreased jugular venous pressure) and pulmonary oedema (due to insufficient pumping of the heart).

3. Haemo-Obstructive Shock

Haemo-obstructive shock results due to incomplete filling of blood in the ventricles during diastole.

Aetiology

- (a) Cardiac tamponade or pericardial tamponade (condition where fluid accumulates within the pericardium). This increases the pressure on the heart, leading to incomplete filling of ventricles.
- (b) Constrictive pericarditis (inflammatory condition of pericardium) seen in the later stages.
- (c) Aortic stenosis which leads to obstruction of blood flow.
- (d) Massive pulmonary embolism.

Signs and Symptoms

It has same symptoms as that of hypovolaemic shock. Other symptoms include distended jugular veins, paleness of skin (pallor) and extremities of the body become cold.

4. Distributive Shock

Distributive shock results due to decrease in the total peripheral resistance (TPR) and decrease in the functioning of myocardium. It is divided into following three types.

(a) Bacteraemic Shock (Endotoxic or Septic Shock)

This condition is seen during infection with microorganisms, which releases exotoxins and endotoxins. The endotoxins released by Gram-negative bacteria leads to an increase

in the body temperature. These toxins in blood causes the release of cell-derived mediators of inflammation like tumour necrosis factor (TNF- α), interleukin-1 (IL-1) and platelet activating factor (PAF) which further releases inflammatory substances like eicosanoids (i.e., PG, LT and TXA₂). These eicosanoids cause,

- (i) Disrupt the vascular endothelial membrane
- (ii) Increase the membrane permeability
- (iii) Release fluid from the body causing hypovolaemia
- (iv) Damage the myocardium in later stage.

The above changes contribute to hypoxia and further damage, leading to multiple organ failure.

Aetiology

- (i) Toxins from microorganisms like Gram-negative bacteria (E.g: *E.coli* and *Klebsiella pneumoniae*), Gram-positive bacteria (E.g: Cocci like *Pneumococci* and *Streptococci*), fungi and rarely viruses.
- (ii) Infections during surgery or during disease conditions like peritonitis, cholangitis (inflammation of bile duct due to bacterial infection), meningitis, wet gangrene etc.
- (iii) Risk factors which contribute to the aetiology of bacteremic shock include immunity weakening diseases (E.g: AIDS), diseases affecting the genito-urinary system (E.g: Pyelonephritis, a bacterial infection of the kidney), lymphoma, leukaemia and prolong usage of antibiotics.

Signs and Symptoms

It has same signs and symptoms as that of hypovolaemic shock. The other symptoms include pyrexia due to release of toxins in the body by microorganisms, vasodilation and paleness of extremities.

(b) *Neurogenic Shock (Vasogenic Shock)*

Neurogenic shock, also called *vasogenic shock* results due to congestion of blood within the post capillary capacitance vessels. This leads to loss of autonomic innervation of the cardiovascular system, vascular tone and reflexes.

Aetiology

- (i) Imbalance of the autonomic nervous system (which is responsible for maintaining arteriolar resistance, venous return and cardiac output).
- (ii) Injury of the spinal cord leads to loss of autonomic and motor reflexes.
- (iii) Abdominal and testicular trauma.
- (iv) Administration of spinal anaesthesia.
- (v) Patients on antihypertensive therapy may experience vasomotor collapse.
- (vi) Cortisol deficiency leads to shock syndrome.
- (vii) Neurological disorders.

Signs and Symptoms

The signs and symptoms of neurogenic shock are similar to hypovolaemic shock. The other symptoms include dry and warm skin, vasodilation and hypotension (due to decreased TPR), bradycardia, venous pooling (congestion of blood vessels), poikilothermia (irregularity in body temperature) and priapism

(c) *Anaphylactic Shock*

Anaphylactic shock results due to allergens, drugs, foreign matter etc. This leads to antigen-antibody reaction which releases inflammatory mediators like histamine, PGs and LTs from the mast cells. These mediators result in vasodilation which is responsible for hypotension and increased capillary permeability.

Aetiology

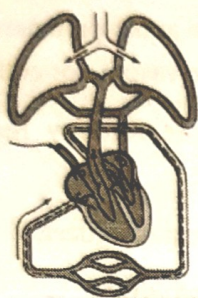
Allergens (E.g: Pollen, pet fur etc), certain drugs, foreign matter and horse serum used to make vaccines are the common causative agents of anaphylactic shock.

Signs and Symptoms

Skin eruptions, localized oedema, breathlessness (due to constriction of airways), dyspnoea (difficulty in breathing), cough, weak and rapid pulse, abdominal pain, vomiting and diarrhoea.



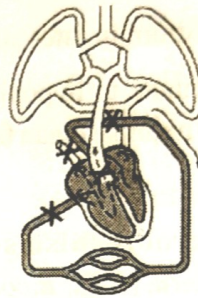
Normal Blood Circulation



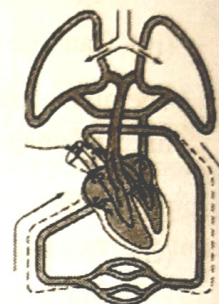
Hypovolaemic Shock



Cardiogenic Shock



Haemo-obstructive Shock



Distributive Shock

Figure: Types of Shock

2. PATHOGENESIS OF SHOCK

All the types of shock are associated with hypotension, hypoperfusion which induces cellular injury. These injured cells in turn release toxins and inflammatory mediators. In response to such derangements, body initiates few compensatory mechanisms that eventually worsen the condition, if treatment is not provided.

1. Hypotension

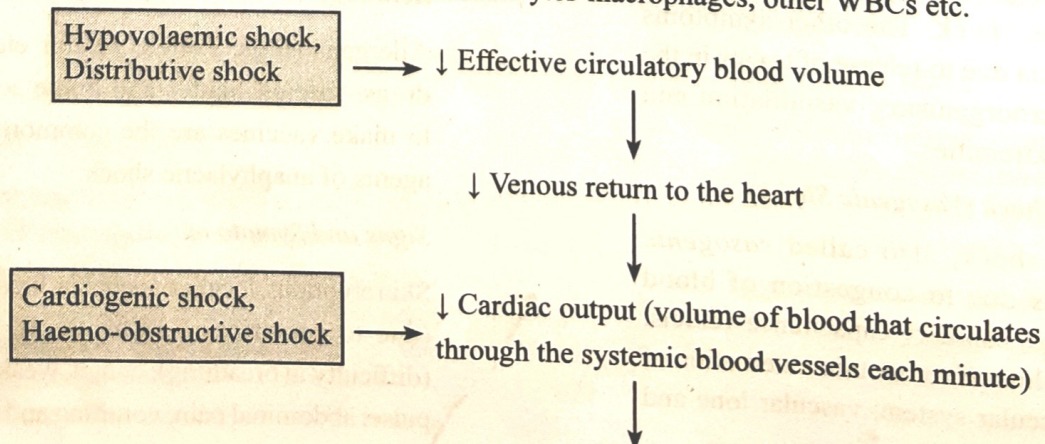
Hypotension refers to a decrease in the effective circulatory blood volume which may be due to drastic blood loss (as seen in hypovolaemic shock) or due to decreased cardiac output (as seen in septic and cardiogenic shock) in spite of absence of any loss of blood.

2. Hypoperfusion

Hypoperfusion is responsible for decreasing the venous return to the heart due to which the cardiac output also decreases. Such derangement decreases the supply of oxygen to the organs and tissues, thereby resulting in tissue anoxia.

3. Inflammatory Mediators Release

Tissue anoxia is responsible for initiating cellular injury, which in turn activates the innate immunity of the body. Such activation induces the release of inflammatory mediators such as histamine, prostaglandins etc. Release of inflammatory mediators is augmented by pro-inflammatory mediators such as cytokines, tumour necrosis factors- α (TNF- α) etc., which are derived from monocytes-macrophages, other WBCs etc.



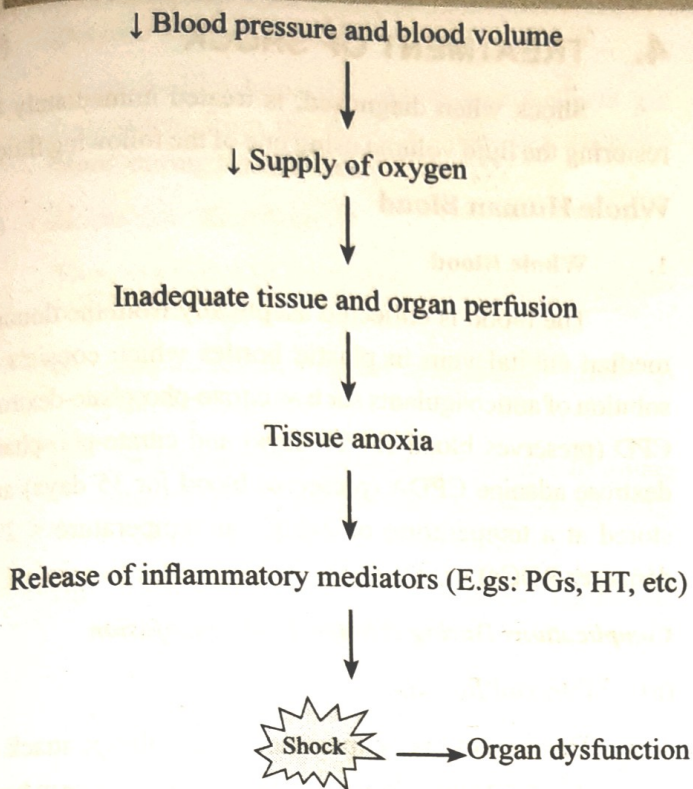


Figure: Pathogenesis of Shock

3. STAGES OF SHOCK

Shock is a progressive disorder that may have fatal consequences if the causative factor is not corrected in a timely manner. Although body tries to correct the various derangements by means of compensatory mechanisms but with time, these also become less effective, rather they worsen the condition. The following three stages have been reported in patients with shocks which is most clearly demarcated in hypovolaemic shock.

1. Non-progressive Stage

In the early stages of shock, the body initiates several compensatory mechanisms to ensure that the cardiac output and blood pressure are maintained at the normal physiological level. These include inducing the release of catecholamines and vasopressin, activation of RAA axis, baroreceptor reflexes and generalised sympathetic stimulation. All these neurohumoral mechanisms result in vasoconstriction and help in fluid conservation by the kidney. Normal circulation gets re-established by the compensatory mechanisms if underlying causative factor is adequately treated. Some of the compensatory mechanisms that are initiated by the body are described below.

- (a) Reduced blood flow and subsequent tissue anoxia induces the activation of neurohumoral factors such as RAA axis, chemoreceptors, baroreceptors, release of catecholamines etc. Such activation is responsible for cutaneous

vasoconstriction due to which the skin of the patient appear cool and pale. However the skin of patient suffering from septic shock appears warm and flushed due to cutaneous vasodilatation. Generalised vasoconstriction causes increased peripheral resistance, tachycardia and increases the blood pressure.

- (b) Hypovolaemic shock is associated with loss of effective blood volume which the body tries to compensate by renal conservation of fluid. Some of these mechanisms include activation of renin-angiotensin-aldosterone (RAA) axis which induces the release of aldosterone, release of antidiuretic hormone or vasopressin, arteriolar constriction which in turn decreases the glomerular filtration rate (GRF) and redirecting fluids from tissues to the plasma.
- (c) An attempt is made to increase the cardiac output by the release of catecholamines i.e., adrenaline and nor-adrenaline from the adrenal medulla. These amines help in increasing the heart rate and thereby cardiac output.

2. Progressive Stage

Shock progresses into the next stage which is called as the progressive stage, when the underlying causative factors are not corrected. In this stage, tissue hypoxia has become widespread due to hypotension and hyperperfusion. Due to continuous deficiency of oxygen, anaerobic glycolysis takes place rather than aerobic respiration due to which there is excessive production of lactic acid. Due to such metabolic lactic acidosis tissue, pH decreases which in turn reduces the effectiveness of the vasomotor response. Such blunting is responsible for dilatation of arterioles and pooling of blood in the microcirculation. Such pooling of blood further worsens the cardiac output and also renders the endothelial cells susceptible to anoxic cell injury. Since tissue hypoxia continues, vital organs of the body are severely affected and their functioning is impaired. Clinical manifestations of this stage of shock include mental confusion, tachypnoea and decreased urinary output.

3. Irreversible Stage

Shock progresses into the final stage called as the irreversible or decompensated stage if both the compensatory mechanisms or therapeutic correction of the underlying causes are not able to correct the derangement. Patients in this stage of shock are generally comatose and present worsened cardiac function and renal failure. In spite of providing the best therapeutic interventions, this stage most commonly culminates into death.

- (a) This stage is characterised by progressive vasodilation. This occurs due to damage to the walls of capillaries and venules induced by anoxia and continued vasodilation of arterioles because they become unresponsive to vasoconstrictors. Vasodilation is responsible for peripheral pooling of blood which ultimately worsen the already deficient effective circulating blood volume.
- (b) Another factor which is responsible for further deteriorating the effective circulating blood volume is increased vascular permeability. This in turn is mediated by the release of inflammatory mediators from anoxic tissue cells.
- (c) Contractility of myocardium is also severely affected, partly due to the release of nitric oxide (NO). Moreover, myocardial ischaemia and coronary insufficiency also occurs due to progressively decreasing myocardial blood flow and blood pressure.
- (d) Specialized cells of vital organs such as the brain, heart and kidney are severely affected because these are heavily dependent on ATP generated by intracellular aerobic respiration. However, due to continuous tissue hypoxia, anaerobic glycolysis occurs resulting in the generation of lactic acid. Hence, such tissues experience ischaemic cell death.
- (e) Intestinal flora may gain access to the circulation due to ischaemic bowel tissue. This could worsen the condition as it may result in the development of bacteremic shock.
- (f) Continuous ischaemic injury of the kidney results in impairment of kidney function.
- (g) Shock is also responsible for activating the coagulation cascade, which induces the release of thromboplastin (promotes clotting) and ADP (promotes aggregation of platelets). These factors decrease the flow of blood in the vessels and increase the risk of vascular thrombosis.

4. TREATMENT OF SHOCK

Shock when diagnosed, is treated immediately by restoring the fluid volume using one of the following fluids.

Whole Human Blood

1. Whole Blood

The blood is collected aseptically from the donor's median cubital vein in plastic bottles which consists of solution of anticoagulants such as citrate-phosphate-dextrose CPD (preserves blood for 21 days) and citrate-phosphate-dextrose adenine CPDA (preserves blood for 35 days) and stored at a temperature of 2-6°C (as temperature < 2°C damages RBCs).

Complications During Whole Blood Transfusion

(a) Pyrexial Reaction

The patient may experience rigor (abrupt attack of shivering and cold sensation followed by rise in body temperature), if the apparatus used is improperly sterilized. This is seen due to accumulation of pyrogens in the body or stimulation of antibodies during earlier transfusions. It can be avoided by administering,

- (i) Aspirin (NSAID that relieves pain, reduces inflammation and fever).
- (ii) Antihistaminics (prevents allergy) and
- (iii) Glucocorticoids (prevents inflammation).

(b) Allergic reactions

This may occur during transfusion and can be prevented by administering,

- (i) Antihistaminics
- (ii) Adrenaline (prevents anaphylactic reaction).

(c) Air Embolism

When blood transfusion is not carried out with care, it leads to air embolism (air lock which obstructs the blood outflow from the right ventricle of the heart). This is prevented by keeping the head of the patient down and making him lie on his left side.

(d) Pulmonary Oedema

Blood transfusion when carried at a massive rate leads to overloading of the circulatory system which contributes to pulmonary oedema.

(e) *Disease Transmission*

Diseases like hepatitis, AIDS and malaria get transmitted from the donor's blood to recipient's blood during transfusion.

(f) *Haemolytic Reactions*

This occurs due to mismatched transfusion and can be prevented by,

- (i) Rapid administration of mannitol (20%) to initiate diuresis.
- (ii) Maintaining diuresis at a rate of 100 ml/hr by giving normal saline and furosemide and maintaining 100 mm Hg systolic blood pressure.
- (iii) Free haemoglobin released during haemolytic reaction is excreted by i.v administration of sodium bicarbonate (renders the urine alkaline) at a concentration of 40-50 mEq.
- (iv) In case of no diuresis, the patient is checked for acute renal failure and is treated accordingly.

(g) *Hyperkalaemia*

Blood when stored at a temperature below 6°C leads to the movement of potassium ions (intracellular ion) from the RBCs into the plasma. This condition is reversed when the blood is kept at room temperature. If the blood fails to rewarm, then hyperkalaemic condition is seen upon blood transfusion.

(h) *Graft-Versus-Host Disease*

It is a complication of allogenic bone marrow transplant in which the engrafted donor cells attack the organs and tissues of the patient. It is seen when the patient receives mismatched transplants from family members or unrelated donors. It can be prevented by using prophylactic drugs like methotrexate (immunosuppressant) and cyclosporin A (T-cell immunosuppressant).

(i) *Iron Overload*

Excess build up of iron occurs in the body during whole blood transfusion. This is prevented by chelating iron.

(j) *Complications During Massive Blood Transfusion*

These include,

- (i) The citrate used for preserving whole blood can cause intoxication (citrate intoxication) by its conversion to bicarbonate. The bicarbonate formed leads to metabolic alkalosis and cardiac irregularities.

- (ii) Low concentration of calcium ions in blood (hypocalcaemia).

- (iii) High concentration of potassium ions in blood (hyperkalaemia).

Indications

- (a) *Anaemic Conditions: Whole blood is given in the following conditions.*

(i) *In case of anaemia*

1. Aplastic anaemia (complete loss of the functioning of bone marrow).

2. Hemolytic anaemia (premature RBC destruction in 40-50 days).

E.g.s: Sickle cell anaemia, thalassaemia.

3. Severe anaemia, when the haemoglobin level falls below 20% (i.e., 2.9 g).

4. In chronic anaemia, oxygen deficiency leads to myocardial ischaemia, hence the blood is transfused at the rate of 10-15 drops/min in order to prevent cardiac failure.

- (ii) To raise the haemoglobin level by 1% (i.e., 1g/100ml), whole blood (in ml) per kg of body weight is administered, which varies according to individuals.

1. Premature infants - 10 ml

2. < 25 kg weight children - 20 ml

3. Adults - 10 ml.

(b) *Blood Loss*

Blood loss is examined by checking the patients lower eyelids, finger extremities, skin paleness, blood pressure and heart rate.

- (i) Mild blood loss ($\leq 25\%$ of the total blood volume) - Administer crystalloid plasma expanders 3-4 times quantity of the estimated blood loss.

- (ii) Moderate blood loss (26-50% of the total blood volume) - Administer colloidal plasma expanders.

- (iii) Excessive blood loss - Administer crystalloid, colloidal plasma expanders and whole blood or packed blood cells.

The above transfusions are continued in patients with blood loss until,

- (i) $\geq 90\%$ of normal blood is obtained

- (ii) Level of Hb = 7g/dl

- (iii) Hematocrit = 21% (Hematocrit is the % of total blood volume comprising of erythrocytes)
- (iv) Level of total serum proteins = 60% of normal
- (v) Platelet count > 50,000/mm³
- (vi) Plasma clotting factors > 35% of normal.

(c) *Disorders of Blood*

Whole blood is given in haematological disorders to supply platelets and clotting factors and to treat agranulocytosis (deficiency of leukocytes especially neutrophils).

(d) *Other Uses*

- (i) In septicæmia, whole blood is given to increase the antibodies.
- (ii) In exsanguination transfusion, the patient's blood is removed and simultaneously replaced with the donor's blood. This is done in Kernicterus and hepatic coma as seen in acute hepatitis.
- (iii) In intrauterine transfusion, when a Rh negative mother carries a Rh positive foetus, then the Rh positive antibodies present in her blood gets stimulated. These antibodies cross the placental barrier and causes *erythroblastosis foetalis* (death of the foetus). Hence, this can be prevented by intrauterine transfusion of whole blood.

Advantage

Mismatching of blood is avoided, hence transfusion reaction does not occur.

Disadvantages

1. Re-infusion of contaminants occur when the person is infected with transmitting diseases.
2. Collected blood is mixed with an anticoagulant. This blood when administered again contributes to synergistic action of anticoagulants.
3. 44% of autologous blood donation remain unused after surgery.

2. Packed Red Cells (Red Blood Cells)

The preparation of packed red cells is made by removing 40% of the supernatant plasma by siphoning process. The remaining packed cells contains 5.5 million/mm³ of the red blood cells content (i.e., haemoglobin).

Packed red blood cells can be stored at a temperature of 10°C for ≤ 24 hrs. Transfusion of packed cells should not be more than 500 ml at a time.

Packed cells are given in severe anaemia to increase the percentage of Hb in the body. Hb level rises by 20%, when 15ml/kg of red cells are administered. This minimizes the risk of circulatory overload and pulmonary oedema. In premature infants, the amount of packed cells administered should be 10 ml/kg of body weight. In < 25 kg weight children, the amount of packed cells administered should be 15 ml/kg of body weight.

3. Dried Human Plasma

It is a straw-coloured fluid, free of blood cells. It is prepared from expired citrated whole blood (i.e., within 5 days of expiry date) which is then freeze dried and stored. It can be stored at a temperature below 25°C in atmospheric nitrogen in sterile containers. These containers should be protected from light.

This form of plasma can be used for transfusing to any category of blood group patient. It is mostly used as a substitute of whole blood.

Complications

- (a) Transmission of viral diseases (infective hepatitis and serum jaundice) is seen during preparation of dried human plasma.
- (b) Plasma agglutinins may cause haemolytic reactions. This is avoided by neutralizing it or using water soluble agglutinins (soluble in plasma and saliva). This form of plasma shows complete solubility in WFI. Hence, upon reconstitution it should be used immediately, else there are chances of it getting contaminated with hepatitis B virus.

Uses

- (a) Administered in case of hypovolaemic shock.
- (b) Administered when fibrinogen deficiency occurs in the body (lack of fibrinogen prevents clot formation).

4. Human Serum Albumin

It is prepared in the same way as that of dried human plasma, the only difference is that the dried human serum albumin is collected in dry bottles and allowed to clot. The supernatant serum is collected when the clot retracts. There is no risk of transmission of viral diseases.

Uses

- (a) Administered in case of hypovolaemic shock.
- (b) Used as a vehicle when packed red cells are transfused.
- (c) Reduces oedema, when given in undiluted form.
- (d) Raises the level of serum proteins in hypoproteinaemia.
- (e) 20% solution of human serum albumin is used in the treatment of burns.

Plasma Expanders

Plasma expanders (plasma volume expanders) are high molecular weight substances which when infused into the blood stream get retained in the vascular compartment and enhance the circulating fluid volume by exerting osmotic pressure.

Ideal Characteristics

1. Should have same osmotic pressure as that of plasma.
2. Should possess same viscosity and isotonicity as that of plasma.
3. Should be retained in the circulatory system for sufficient time period in order to exhibit its action and should be excreted slowly from the body.
4. Should have sufficient molecular weight so that it does not get diffused through the walls of the capillaries.
5. Should be free from antigenic and pyrogenic substances.
6. Should not interfere with blood groups.
7. Should be pharmacodynamically inert.
8. Should be stable on storage.
9. Should be sterilized easily and should be inexpensive.

Uses

1. In the treatment of hypovolaemic shock.
2. In cases of mild to moderate blood loss.
3. In the treatment of hypoplastic anaemia (inadequate functioning of bone marrow) and aplastic anaemia.

Types of Plasma Expanders**1. Colloidal Plasma Expanders**

These type of plasma expanders have high molecular weight so that they do not get diffused into the walls of the capillaries. This helps in retaining them in the circulatory system and in turn maintains the same osmotic pressure as that of plasma proteins.

(a) Dextran

It is one of the most widely used colloidal plasma expanders. It is obtained from the bacteria *Leuconostoc mesenteroides* grown in sucrose media.

Dextran so produced is subjected to sterilization by autoclaving or by filtration. It can be stored up to 10 years.

Dextran is available in different molecular weights like 70,000 (Dextran 70), 40,000 (Dextran 40) etc. These dextrans are prepared from native dextran (mol.wt 40 millions) by the process of acid hydrolysis, thermal degradation or UV disintegration.

Table: Types of Dextran

Dextran type	Molecular weight	Properties	Advantages	Disadvantages	Uses
Dextran-40 (Low molecular weight dextran)	40,000	- Available as 10% solution with isotonic saline or 5% dextrose. - Reduces the viscosity of blood. Improves micro circulation. - Rapidly excreted by the kidneys - Stable plasma expander.	- Acts more rapidly than dextran-70. - Prevents venous thrombosis. - Improves capillary microcirculation by desludging action. - Low molecular weight. - Low plasma viscosity.	Produces platelet dysfunction, bleeding tendency and acute renal failure.	- Used in the prevention of venous thrombosis. - Used in cases of severe burns.
Dextran-60	60,000	—	—	- Rapidly excreted in urine. - Loss in tissue fluids causing adverse osmotic pressure.	—
Dextran-70	70,000	- Available as 6% solution (Dose = 50 ml i.v. at the rate of 20-40 ml/min). - Expands plasma volume for 24 hrs. - Gets retained in the body (in liver and reticuloendothelial system).	- Widely available. - Does not show any incompatibility. - Does not transmit any viral diseases.	Causes allergic reactions	Restores and maintains the blood volume.
Dextran-75	75,000	Available as 6% solution (Dose = 50 ml i.v. at the rate of 20-40 ml/min).	Same as above	Same as above	Same as above
Dextran-150 (High molecular weight dextran)	1,50,000	Replaced by dextran-110	—	- Leads to Rouleaux formation (clumping of RBCs). - Causes sludging	—

Advantages

1. Possess similar osmotic pressure as that of plasma proteins.
2. Half-life of dextran is around 24 hours, hence they get retained in the plasma.
3. Inhibits Rouleaux formation.
4. Prevents sludging action and improves microcirculation by decreasing the viscosity of blood.
5. Used in hypovolaemic shock to expand the plasma volume.

Disadvantages

1. Interferes with the functioning of platelets and coagulation factors, hence prolongs bleeding time.
2. Causes haemorrhage when used in large doses.
3. Sometimes it causes anaphylactic shock when administered in small doses by subcutaneous route. This is avoided by administering dextran by i.v. route.

4. Dextran-40 leads to clogging of the renal tubules, hence it should not be used in,
 - (a) > 1 litre (20 ml/kg/day) quantity on first day and subsequently 10 ml/kg/day on second day
 - (b) Conditions where urinary output is < 1500 ml/day
 - (c) Conditions where blood urea is ≥ 60 mg/dl.
5. Dextran should be used within 5 days of unsealing to avoid contamination.

Contraindications

1. Allergic patients.
 2. Patients with heart failure.
 3. In case of oliguric renal failure.
 4. In patients having fibrinogen deficiency (hypofibrinogenaemia), clot formation does not occur. Hence if dextrans are used, then the condition gets worsened as dextran itself prolongs the bleeding time by interfering with the functioning of coagulation factors.
 5. In thrombocytopenic conditions (reduction of platelet count in the blood).
- (b) *Hydroxyethyl Starch (Hetastarch or Hespan)*

It is one of the cheapest plasma colloidal expanders which is obtained from amylopectin. It is available as 6% solution in 0.9% of NaCl injection. Dose = 500 - 1000 ml; maximum of 1500 ml/day.

Adverse Effects

Fever, chills, itching, swelling of salivary glands and anaphylactic reactions (rarely).

Advantages

1. The volume of blood is maintained for a longer duration in comparison to dextran.
2. Non-allergenic.
3. Does not cause coagulation disturbances.
4. Does not cause acute renal failure.

Uses

1. Used to treat hypovolaemic shock.
Example: Expan (preparation of hetastarch) with a molecular weight of 4,50,000.
2. Used effectively as a colloidal plasma expander.

(c) *Polyvinyl Pyrrolidone (PVP)*

It is a water soluble polymer whose molecular weight ranges from 35,000-40,000.

Properties

1. It is given as 40% solution in buffered normal saline by i.v route and is available as amber-coloured clear solution.
2. Rapidly excreted from the body.

Disadvantages

1. Not widely used due to its interference in the blood group matching.
2. Raises the erythrocyte sedimentation rate (ESR).
3. Binds to drugs like insulin, penicillin and causes agglutination (clumping) of RBCs.
4. Interferes with the formation of antibodies.

(d) *Gelatin Polymer*

It is a plasma colloidal expander available in the form of degraded gelatin. Example of commercially available gelatin is Haemaccel whose molecular weight ranges from 30,000-35,000.

Properties

1. Available as 3.5% solution in 500 ml infusion.
2. Possess osmotic pressure similar to that of albumin.
3. pH of the infusion when dissolved in the electrolyte ranges from 7.2-7.3.
4. Remains stable for 3 years at room temperature.
5. Mean serum half-life of gelatin polymers is around 4-5 hours.
6. Around 60-80% of gelatin administered gets excreted unchanged by the kidneys.

Advantages

1. Non-antigenic.
2. Does not interfere with coagulation.
3. Does not interfere with the blood group tests.

Disadvantages

1. Expensive when compared to dextran.
2. Causes bronchospasm, hypotension, flushing, urticaria and rigors (rarely).

2. *Crystalloid Plasma Expanders*

These type of plasma expanders are less superior than colloidal plasma expanders in maintaining the blood volume during shock conditions. These expanders are less expensive in comparison to colloidal plasma expanders.

(a) Normal Saline

It is one of the most widely used intravenous crystalloid plasma expanders.

Properties

1. Available as 0.9% solution.
2. As the osmolality of normal saline (308 m osm/kg) is equal to that of serum, it is considered as an excellent crystalloid plasma expander for replacing the volume of lost body fluids.
3. 1 litre of normal saline when infused in the body raises the volume of blood by 300 ml.

Disadvantages

1. Short duration of action.
2. Rapid i.v administration leads to pulmonary oedema.
3. Sometimes febrile reaction occurs due to pyrogens.

Uses

1. Replaces the volume of lost body fluids and electrolytes during dehydration.
2. Acts as a vehicle for drugs which are given by i.v drip.

(b) Dextrose**Properties**

1. Available as 5% in water.
2. 1 litre of dextrose in water when infused in the body raises the volume of blood by 100 ml.

Disadvantages

1. As the osmolality of dextrose (253 m osm/kg) is less than that of serum, it is not considered as a suitable crystalloid plasma expander for replacing the volume of lost body fluids.
2. Phenytoin should not be infused along with fluids containing glucose.

Uses

1. Supplies nutrition to the body.
2. Acts as a vehicle for drugs, especially noradrenaline (NA) as its acidic solution helps to maintain the stability of NA.
3. Used in case of renal impairment.

Procedures for Treatment of Shock**1. Hypovolaemic Shock**

- (a) The blood volume is immediately restored by administering suitable fluids.
- (b) Electrolyte imbalance is corrected by administering electrolytes.
- (c) Sodium bicarbonate is administered to neutralize the acidic condition in the body seen due to acidosis.
- (d) Based on the aetiology, treatment is given.
- (e) Intravenous administration of morphine helps to relieve pain. This is avoided if there is any head injury.
- (f) In case of hypotension, vasopressor agents like dopamine are given. Noradrenaline is not used in spite of being a vasoconstrictor because the catecholamines circulating in blood are in high concentration. Vasopressor agents are added only when fluid volume is maintained, else they decrease the blood flow to kidneys and brain and increase the myocardial oxygen demand.
- (g) Excess vasoconstriction is avoided by using α -blockers along with adequate amounts of fluid volume enhancers, as blood pressure may fall drastically. These α -blockers prevent vasoconstriction which is produced by the reflex overactivity of sympathetic nervous system. This mechanism occurs without raising the central venous pressure.

Examples

- (i) Phenoxybenzamine is administered by i.v. infusion at the rate of 1 mg/kg along with 500 ml of 5% dextrose solution.
 - (ii) Phentolamine is also used but has a shorter duration of action.
- (h) Arterial hypoxemia (decrease O_2 in arterial blood) is corrected by giving oxygen.

2. Cardiogenic Shock

The main cause of cardiogenic shock is acute myocardial infarction (MI) which is treated as follows in a stepwise manner.

(a) Relief of Pain

- (i) In case of mild pain, nitroglycerine is administered sublingually in doses of 0.4 mg for every 5 mins (maximum dose: 3 mg).

(ii) In case of severe pain, morphine hydrochloride is administered intravenously in a dose of 10 mg at a slow rate (i.e., 1 mg/min). If necessary, the dose is repeated after every 30 minutes.

(iii) Oxygen is provided artificially for 2-3 days to counteract hypoxia and patient is advised strict bed rest.

(b) *Relief from Anxiety*

Diazepam is administered in doses of 2-5 mg twice or thrice daily.

(c) *Maintenance of Normal Blood Pressure*

Blood pressure is maintained in case of hypotension to restore perfusion to vital organs.

(i) Dopamine hydrochloride is administered by i.v. drip in a dose of 200 mg in 5% dextrose solution at a rate of 2.5 µg/kg/min.

In case of no response with dopamine hydrochloride, hydrocortisone hemisuccinate is given intravenously in doses of 200 mg, so as to protect the tissues from the damage caused by hypoxia.

(ii) Dobutamine may also be given as it exerts positive inotropic effect and is a peripheral vasoconstrictor.

(iii) Acidic conditions of the body are restored to normal by administering NaHCO_3 by intravenous drip.

(d) *Diagnosis of Myocardial Infarction (MI)*

MI when diagnosed should be treated with aspirin.

(e) *Prevention and Treatment of Arrhythmias*

(i) In case of ventricular arrhythmia

1. Lignocaine is administered by i.v. infusion at a rate of 1-2 mg/min, or

2. Procainamide is given intravenously in doses of 100 mg (total dose = 1 g) for every 5 min. This is given alternatively with lignocaine intramuscularly in doses of 400 mg.

(ii) In case of ventricular tachycardia, lignocaine is given by intravenous infusion.

(iii) In case of sinus or nodal bradycardia

1. Atropine sulphate intravenously in doses of 0.3 - 2 mg, or isoprenaline in doses of 0.05 mg.

2. Intravenous administration of propranolol is used exclusively for supraventricular arrhythmia which is not associated with the left ventricular failure.

3. Digoxin should be administered intravenously in supraventricular arrhythmia which is associated with left ventricular failure.

(f) *Prevention and Treatment of Thrombus Formation*

(i) Venous thrombosis is treated by anticoagulants. Heparin is given along with oral anticoagulants.

(ii) Coronary artery thrombosis is treated by the following drugs,

1. Streptokinase is administered intravenously or by intracoronary route in the form of infusion within 3 hrs of the arousal of symptoms.

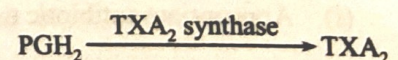
2. Urokinase is infused into the occluded coronary artery.

3. Tissue-type plasminogen activator is given intravenously.

(g) *Treating the Infarct Size by Limiting it and Preventing Secondary Infarction*

(i) *Prevention of Platelet Aggregation*

1. Aspirin in low doses of 75-100 mg/day is given as it has potent and long lasting effect (1-2 weeks) on the functioning of platelets and acts by inhibiting TXA_2 synthesis of COX pathway.



2. Dipyridamole in doses of 100-200 mg twice a day also inhibits platelet aggregation. It is given alone or in combination with aspirin.

3. Sulphinpyrazone in doses of 200 mg four times a day decreases platelet aggregation.

(ii) Limitation of Infarct Size

The infarct size can be limited by administering β -blockers intravenously within 24 hours of onset of symptoms and orally after 24 hours.

1. Propranolol is given intravenously in doses of 0.1 mg/kg thrice a day with an interval of 5-10 minutes. This is followed by its oral administration in doses 24-40 mg every 6-8 hours.
2. Atenolol is also given intravenously in doses of 5-10 mg. This is followed by its oral administration in doses of 100 mg once a day.
3. Metoprolol is given intravenously in doses of 5 mg thrice a day (i.e., for 2 min and then for 5 min). This is followed by its oral administration in doses of 50-100 mg every 12 hours.

Administration of calcium channel blockers should be avoided in case of myocardial infarction as they are responsible for further exacerbating the hypotension.

(h) Treating Hyperlipidaemia

Administer antihyperlipidaemic drugs to reduce the plasma levels of low density lipoproteins (LDL) and cholesterol.

3. Haemo-Obstructive Shock

The treatment of haemo-obstructive shock is similar to that of cardiogenic shock.

4. Distributive Shock

(a) Bacteremic Shock

- (i) Appropriate antibiotic therapy is initiated.
- (ii) The blood circulatory volume is restored.
- (iii) Administration of sodium bicarbonate helps in correcting the acid-base imbalances in the body.
- (iv) Hypotension is corrected and tissue perfusion is improved by administering sympathomimetics.

(v) Hypoxia is corrected using oxygen.

(vi) Endotoxins released by Gram-negative bacteria are responsible for systemic reactions which are suppressed by giving corticosteroids.

(vii) Protein C is given by i.v infusion in doses of 24 $\mu\text{g/kg/hr}$ for 96 hours. It acts by inhibiting coagulation. This drug causes intracranial bleeding, hence it is used only in patients who are severely sick.

(b) Neurogenic Shock/Vasogenic Shock

(i) Treatment of neurogenic shock is similar to that of hypovolaemic shock.

(ii) Vasopressor agents are administered intravenously.

Example: Administration of dopamine intravenously is alternated with ephedrine (as a prophylactic drug) intramuscularly in doses of 0.5 - 1 ml of the total dose of 45 mg/ml

(c) Anaphylactic Shock

The patient should be immediately treated for laryngeal oedema, bronchospasm and hypotension in case of anaphylactic shock.

(i) The patient is laid flat and his/her legs are raised.

(ii) Blood oozing from the area is stopped by applying a tourniquet.

(iii) Administration of adrenaline intramuscularly reverses the condition of laryngeal oedema, bronchospasm and hypotension. If necessary, the drug is re-administered after 15-20 minutes, but with caution.

Severely ill patients are administered adrenaline intravenously at a slow rate of 100 $\mu\text{g/min}$ (total dose 500 μg).

In Children: Adrenaline is administered intramuscularly in doses of 0.01 ml of 1:1000 solution/kg, or intravenously in a dose of 0.1 ml of 1:10,000 solution/kg.

In Adults: Adrenaline is given intramuscularly in a dose of 0.5 ml of 1:1000 solution.

When the patient is on non-selective β -blockers, then adrenaline does not show any response to anaphylactic shock. Hence, salbutamol is administered intravenously.

(iv) In case of Hypotension

Colloidal plasma expanders are administered intravenously in large quantities, dopamine or noradrenaline by intravenous infusion, (if necessary) and cimetidine in refractory cases.

(v) The early phase of anaphylaxis is corrected by administering adrenaline (drug of choice).

(vi) The late phase of anaphylaxis is inhibited by administering,

Antihistaminics : Chlorpheniramine is given intravenously in a dose of 10-20 mg for 1 min. This is repeated for 24 or 45 hrs. Antihistaminics are administered after administering adrenaline.

Glucocorticoids : Hydrocortisone hemisuccinate is administered intravenously in a dose of 100 mg. This is followed by giving prednisolone orally.

H₂ Blockers

(a) Cimetidine is given intravenously in a dose of 500 mg for 3-5 minutes or

(b) Ranitidine is given intravenously in a dose of 50 mg for 3-5 minutes.

(vii) Bronchospasm is treated by administering bronchodilators like aminophylline intravenously or nebulized salbutamol.

Management of Shock

First-Aid

The following first-aid measures are helpful in management of shock.

1. The patient should be moved to a well-ventilated place.
2. Any crowd surrounding the patient should be dispersed tactfully to aid in proper ventilation.
3. The person administering first-aid should communicate with the patient to remove any fear or anxiety.
4. The patient should be made to calm down and lie down in a flat position with head lowered and turned to one side and the legs raised slightly by means of a support (pillow) to enhance blood circulation.
5. The patient's breathing should be checked and the airway should be made free from any obstructions. If there are disturbances in breathing, the head and chest of the person should be raised and the clothing should be loosened.
6. The patient should be kept warm using a blanket.
7. Arrangement should be made to take the patient immediately to a hospital.

Management and Prevention

Management includes the following.

1. Patients who are at a risk of developing shock should be identified and their medical history should be taken. They are to be examined physically and clinically to diagnose any such condition
2. Appropriate measures should be taken to control or eliminate the cause of decreased perfusion
3. All protective measures should be taken for safeguarding the target and distal organs from dysfunction
4. A multisystem supportive care is to be provided.

Shock can be prevented by identifying susceptible individuals and keeping a check on their fluid balance and maintenance of hygiene.