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PHARMACOLOGY - II

UNIT 2

TOPIC :

- **Pharmacology of drugs acting on cardio vascular system**
 - a. Drug used in the therapy of shock.
 - b. Hematinics, coagulants and anticoagulants.
 - c. Fibrinolytics and anti-platelet drugs
 - d. Plasma volume expanders



Drugs Used in the Therapy of Shock

- Shock is a life-threatening medical emergency characterized by a sudden fall in blood pressure (BP) and inadequate tissue perfusion, resulting in impaired oxygen and nutrient delivery to vital organs such as the brain, heart, and kidneys.
- If untreated, shock can lead to multiple organ failure and death. Hence, immediate and appropriate therapy is essential to restore circulatory stability and tissue perfusion.
- Shock is defined as an acute circulatory failure that results in inadequate tissue perfusion and cellular oxygenation, leading to metabolic and organ dysfunction.

Types of Shock

Type	Cause / Mechanism	Examples
1. Hypovolemic shock	Due to loss of blood or plasma volume	Hemorrhage, burns, dehydration
2. Cardiogenic shock	Due to failure of the heart to pump blood effectively	Myocardial infarction, arrhythmia, heart failure
3. Septic shock	Due to severe infection leading to vasodilation and capillary leakage	Bacterial endotoxins (e.g., Gram-negative sepsis)
4. Anaphylactic shock	Due to severe allergic reaction (IgE-mediated)	Drug allergy, insect bite
5. Neurogenic shock	Due to loss of sympathetic tone	Spinal cord injury, anesthesia
6. Obstructive shock	Due to mechanical obstruction of circulation	Pulmonary embolism, cardiac tamponade

General Principles of Treatment

The main goals in shock therapy are:

1. Restore circulating blood volume
2. Improve cardiac output and tissue perfusion
3. Maintain adequate blood pressure
4. Correct underlying cause

Treatment involves:

- Fluid replacement therapy
- Oxygen therapy
- Use of vasoactive (pressor) drugs
- Treatment of the underlying cause (infection, allergy, etc.)

Drugs Used in the Therapy of Shock

Drugs used are mainly those that increase blood pressure, improve cardiac output, or counteract vasodilation.

A. Sympathomimetic (Adrenergic) Drugs

These drugs stimulate α - and β -adrenergic receptors and are the most important agents in emergency management of shock.

Drug	Receptor Action	Effect / Use
1. Dopamine	Acts on D_1 , β_1 , and α_1 receptors (dose-dependent)	$\uparrow$ Renal blood flow (low dose), $\uparrow$ Cardiac output (moderate dose), $\uparrow$ BP (high dose). Used in cardiogenic and septic shock
2. Noradrenaline (Norepinephrine)	Strong α_1 , moderate β_1	Potent vasoconstrictor $\rightarrow \uparrow$ BP; maintains perfusion. Used in septic and neurogenic shock
3. Adrenaline (Epinephrine)	α and β agonist	$\uparrow$ Cardiac output, vasoconstriction, bronchodilation. Drug of choice in anaphylactic shock
4. Dobutamine	Predominantly β_1 agonist	$\uparrow$ Myocardial contractility without much effect on HR; used in cardiogenic shock
5. Isoproterenol	Non-selective β agonist	$\uparrow$ Heart rate and contractility; causes vasodilation. Used in heart block and cardiac arrest, rarely in shock
6. Phenylephrine	Pure α_1 agonist	Vasoconstrictor; used in neurogenic shock or when BP is low

B. Vasodilators

- In some forms of cardiogenic shock, excessive vasoconstriction increases afterload, worsening the condition.
- Controlled vasodilation may improve tissue perfusion.

Examples:

- Nitroglycerin – Reduces preload; used in cardiogenic shock with myocardial ischemia.
- Sodium nitroprusside – Potent vasodilator; used under strict monitoring.

C. Glucocorticoids

Examples: Hydrocortisone, Dexamethasone

Mechanism & Role:

- Restore vascular responsiveness to catecholamines.
- Reduce capillary permeability.
- Suppress inflammation in septic or anaphylactic shock.

Uses:

- Anaphylactic shock (as adjunct to adrenaline)
- Septic shock (in low doses)
- Adrenal insufficiency-related shock

D. Plasma Expanders and Fluid Therapy

These restore circulating volume in hypovolemic shock.

Type	Examples	Use / Mechanism
1. Crystalloids	Normal saline, Ringer's lactate, Dextrose solution	Replace fluid and electrolytes
2. Colloids	Dextran, Gelatin, Hydroxyethyl starch	Maintain oncotic pressure and plasma volume
3. Blood / Blood	Whole blood, packed RBCs,	Used in hemorrhagic

products	plasma	shock
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E. Antibiotics

Used in septic shock to eliminate infection.

Examples:

- Broad-spectrum antibiotics: Piperacillin-tazobactam, Carbapenems, Cephalosporins, Aminoglycosides.

Note: Should be administered as early as possible after culture collection.

F. Antihistamines

Examples: Diphenhydramine, Chlorpheniramine

Mechanism:

- Block histamine (H_1) receptors.
- Reduce vasodilation, capillary permeability, and bronchospasm.

Use: Adjunctive therapy in anaphylactic shock (given after adrenaline).

G. Bronchodilators

Examples: Aminophylline, Salbutamol

Use: To relieve bronchospasm in anaphylactic shock and shock with respiratory distress.

H. Vasopressin (ADH)

Mechanism:

- Causes vasoconstriction via V_1 receptors.
- Retains water via V_2 receptors.

Use:

- In septic or vasodilatory shock refractory to catecholamines.

Hematinics, Coagulants, and Anticoagulants

- Blood plays a vital role in transporting oxygen, nutrients, and clotting factors.
- Certain conditions such as anemia (due to deficiency of hemoglobin or RBCs) or bleeding disorders (due to clotting abnormalities) require drugs that affect blood formation or coagulation.

These drugs are classified as:

1. Hematinics – Promote formation of blood and hemoglobin
2. Coagulants – Help in clot formation (stop bleeding)
3. Anticoagulants – Prevent clot formation (thrombosis prevention)

Hematinics

Hematinics are agents that are required for the formation of blood and in the treatment of anemia.

They promote hemoglobin synthesis and increase red blood cell (RBC) production.

Causes of Anemia

- Iron deficiency
- Folic acid deficiency
- Vitamin B₁₂ deficiency
- Chronic diseases
- Bone marrow failure

Important Hematinic Agents

Agent	Function	Examples
Iron	Essential for hemoglobin synthesis	Ferrous sulfate, ferrous fumarate
Folic acid (Vitamin B ₉)	Needed for DNA synthesis in RBC formation	Folic acid tablets
Vitamin B ₁₂ (Cyanocobalamin)	Required for maturation of RBCs	Cyanocobalamin, Hydroxocobalamin
Erythropoietin	Stimulates RBC production in bone	Epoetin alfa (in renal anemia)

Iron Preparations

(a) Oral Iron Preparations

- Ferrous sulfate
- Ferrous gluconate
- Ferrous fumarate

Mechanism:

Iron is absorbed in the duodenum and jejunum → utilized for hemoglobin synthesis in bone marrow.

Dose: 200 mg ferrous sulfate (contains 60 mg elemental iron)

Adverse Effects:

- Nausea, vomiting, epigastric pain
- Constipation or diarrhea
- Black stools

Contraindications:

Hemochromatosis, hemolytic anemia.

(b) Parenteral Iron Preparations

Used when oral iron is not tolerated or malabsorption exists.

Examples:

- Iron dextran (IM or IV)
- Iron sucrose
- Ferric carboxymaltose

Adverse Effects:

- Pain at injection site

- Fever, joint pain
- Anaphylactic reaction (rare)

Folic Acid (Vitamin B₉)

Mechanism:

- Essential for DNA and RNA synthesis → required for maturation of RBCs.
- Deficiency leads to megaloblastic anemia.

Sources: Green vegetables, liver, egg yolk.

Dose: 5 mg daily.

Uses:

- Megaloblastic anemia
- Pregnancy (to prevent neural tube defects)

Vitamin B₁₂ (Cyanocobalamin, Hydroxocobalamin)

Mechanism:

- Required for maturation of RBCs and DNA synthesis.
- Deficiency leads to pernicious anemia (megaloblastic).

Sources: Meat, fish, eggs, milk.

Dose: 100–200 µg IM every alternate day initially.

Uses:

- Pernicious anemia
- Neurological symptoms of B₁₂ deficiency

Erythropoietin (EPO)

Source: Recombinant DNA form (Epoetin alfa)

Mechanism:

- Stimulates erythropoiesis in bone marrow.

Uses:

- Anemia due to chronic kidney disease or chemotherapy

Adverse Effects:

- Hypertension

- Headache
- Thrombosis

Coagulants

→ Coagulants (Hemostatics) are agents that promote blood clotting and are used to control bleeding or prevent hemorrhage.

Mechanism of Blood Coagulation (Simplified)

- Injury → activation of platelets and clotting factors
- Conversion of prothrombin → thrombin
- Thrombin converts fibrinogen → fibrin
- Fibrin forms a clot that stops bleeding.

Classification of Coagulants

Type	Examples	Mechanism / Use
1. Vitamin K and its analogues	Vitamin K ₁ (Phytonadione), Menadione	Required for synthesis of clotting factors II, VII, IX, X in liver
2. Local hemostatics	Thrombin, Fibrin, Gelatin sponge, Adrenaline	Promote local vasoconstriction and clot formation
3. Systemic hemostatics	Vitamin K, Desmopressin	Increase clotting factor activity
4. Astringents	Ferric chloride, Alum	Cause protein precipitation and vessel constriction

Vitamin K

Mechanism:

- Essential cofactor for hepatic synthesis of clotting factors (II, VII, IX, X).
- Deficiency leads to hypoprothrombinemia → prolonged bleeding.

Uses:

- Bleeding due to Vitamin K deficiency
 - Bleeding due to anticoagulant therapy (warfarin overdose)
 - Newborn hemorrhagic disease prevention

Dose: 10 mg IM or oral.

Adverse Effects:

- Flushing, dizziness
- Pain at injection site

Local Hemostatics

Examples:

- Thrombin: Topical application promotes clot formation.
- Fibrin foam / Gelatin sponge: Used surgically to stop bleeding.
- Adrenaline (epinephrine): Causes vasoconstriction to reduce bleeding.

Uses:

- Surgical bleeding, dental surgery, nasal bleeding.

Astringents

Examples: Ferric chloride, Alum, Tannic acid.

Act by precipitating proteins and constricting blood vessels to stop local bleeding.

Uses: Minor cuts, wounds, gingival bleeding.

Anticoagulants

- Anticoagulants are drugs that prevent clot formation or dissolve existing clots by interfering with the blood coagulation process.
- They are used mainly in thromboembolic disorders (e.g., deep vein thrombosis, pulmonary embolism, myocardial infarction).

Classification of Anticoagulants

Type	Examples	Mechanism / Remarks
1. Parenteral anticoagulants	Heparin, Low Molecular Weight Heparins (Enoxaparin)	Inhibit clotting factors (IIa, Xa)
2. Oral anticoagulants	Warfarin, Acenocoumarol, Dabigatran, Rivaroxaban	Inhibit synthesis of vitamin K-dependent clotting factors
3. Fibrinolytic (thrombolytic) agents	Streptokinase, Alteplase, Urokinase	Dissolve formed clots (convert plasminogen → plasmin)
4. Antiplatelet agents	Aspirin, Clopidogrel, Ticlopidine	Prevent platelet aggregation

Heparin

Source: Animal tissues (mast cells, liver, lungs).

Mechanism:

- Activates antithrombin III, which inhibits thrombin (IIa) and factor Xa → prevents clot formation.

Route: IV or SC (not oral; destroyed in GIT)

Uses:

- Deep vein thrombosis (DVT)
- Pulmonary embolism
 - During cardiac surgery or dialysis

Adverse Effects:

- Bleeding
- Thrombocytopenia
- Osteoporosis (long-term use)

Antidote: Protamine sulfate

Oral Anticoagulants

(a) Warfarin / Acenocoumarol

Mechanism:

- Inhibit vitamin K epoxide reductase, preventing activation of vitamin K → ↓ synthesis of clotting factors II, VII, IX, X.

Uses:

- Long-term prevention of thrombosis and embolism
- Atrial fibrillation, prosthetic heart valves

Adverse Effects:

- Bleeding, skin necrosis
- Teratogenic (avoid in pregnancy)

Antidote: Vitamin K₁ (phytonadione)

(b) Newer Oral Anticoagulants (NOACs)

- Dabigatran – Direct thrombin inhibitor
- Rivaroxaban, Apixaban – Direct factor Xa inhibitors

Advantages:

- Fixed dose
- No monitoring required
- Fewer food-drug interactions

Uses:

DVT, atrial fibrillation, post-surgical thromboprophylaxis.

Fibrinolytic (Thrombolytic) Agents

Examples: Streptokinase, Urokinase, Alteplase (tPA)

Mechanism:

- Convert plasminogen → plasmin, which dissolves fibrin clots.

Uses:

- Acute myocardial infarction
- Pulmonary embolism
- Ischemic stroke (Alteplase)

Adverse Effects:

- Severe bleeding
- Allergic reactions (Streptokinase)

Antiplatelet Drugs

Examples: Aspirin, Clopidogrel, Ticlopidine

Mechanism:

- Inhibit platelet aggregation → prevent thrombus formation on vessel walls.

Uses:

- Myocardial infarction prophylaxis
- Stroke prevention
- After stent placement

Adverse Effects:

- Gastric irritation (Aspirin)
- Bleeding