Unit-2
Pharmacology- II

B.Pharma 5th Sem Notes

Unit: 2

- **Pharmacology of drugs acting on cardio vascular system**
  - Drug used in the therapy of shock.
  - Hematinics, coagulants and anticoagulants.
  - Fibrinolytics and anti-platelet drugs
  - Plasma volume expanders
- **Pharmacology of drugs acting on urinary system**
  - Diuretics
  - Anti-diuretics.

Pharmacology of drugs acting on cardio vascular system:

Drug used in the therapy of shock:

Shock:

- Shock is a life-threatening condition that occurs when the body isn't getting enough blood flow. This deprives organs of oxygen and nutrients, potentially leading to damage.

Types of Shock:

1. **Hypovolemic Shock:** Caused by blood or fluid loss (e.g., bleeding, dehydration).
2. **Cardiogenic Shock:** Heart problems (e.g., heart attack, heart failure) prevent adequate blood pumping.
3. **Septic Shock:** Overwhelming infection triggers a widespread inflammatory response.
4. **Anaphylactic Shock:** Severe allergic reaction.
5. **Neurogenic Shock:** Damage to the nervous system (e.g., spinal cord injury).
6. **Obstructive Shock:** Something blocks blood flow (e.g., blood clot in the lungs).

Symptoms:

- Rapid, weak pulse
- Low blood pressure
- Rapid, shallow breathing
- Confusion or disorientation
- Cold, clammy skin
- Dizziness or fainting
- Thirst
- Nausea or vomiting

1. Hypovolemic Shock

Cause:

- Hypovolemic shock occurs when there is a significant loss of blood or fluids from the body, leading to a decrease in blood volume.
- This reduction in blood volume impairs the heart's ability to pump enough blood to vital organs, resulting in oxygen deprivation and potential organ failure.

Common Causes:

- **Trauma**: Injuries that lead to substantial blood loss (e.g., fractures, deep cuts).
- **Severe dehydration**: Excessive loss of fluids due to vomiting, diarrhea, or sweating.
- **Burns**: Severe burns can result in fluid loss through the skin.

- **Gastrointestinal bleeding**: Conditions like peptic ulcers, varices, or gastrointestinal bleeding can lead to significant blood loss.

Symptoms:

- Rapid, weak pulse
- Low blood pressure (hypotension)
- Cool, clammy skin
- Pale or ashen skin
- Confusion or disorientation
- Dizziness or fainting
- Rapid, shallow breathing
- Thirst

Treatment:

- Fluid replacement with intravenous (IV) saline or blood transfusions
- Addressing the underlying cause, such as controlling bleeding or rehydration

2. Cardiogenic Shock

Cause: Cardiogenic shock occurs when the heart is unable to pump effectively, causing insufficient blood flow to the body. This is typically due to a severe cardiac event or heart condition.

Common Causes:

- **Myocardial infarction (Heart attack)**: Damage to the heart muscle from a blockage in the coronary arteries.
- **Heart failure**: A condition where the heart is weak and cannot pump blood efficiently.
- **Arrhythmias**: Abnormal heart rhythms, especially those that are very rapid or irregular.
- **Myocarditis**: Inflammation of the heart muscle.
- **Cardiac tamponade**: Pressure on the heart due to fluid buildup in the pericardium (the sac surrounding the heart).

Symptoms:

- Chest pain or discomfort
- Weak, rapid pulse
- Low blood pressure
- Shortness of breath (dyspnea)
- Cold, clammy skin
- Confusion or altered mental status
- Decreased urine output (oliguria)
- Cyanosis (bluish tint to skin, lips, or extremities)

Treatment:

- Medications to improve heart function (e.g., inotropes)
- Mechanical support (e.g., intra-aortic balloon pump)
- Revascularization procedures like angioplasty or coronary artery bypass grafting (CABG) after a heart attack
- Oxygen therapy

3. Septic Shock

Cause: Septic shock is a severe infection that triggers a widespread inflammatory response, leading to a significant drop in blood pressure and impaired circulation. It is a result of an infection that spreads throughout the body, often causing organ dysfunction.

Common Causes:

- **Bacterial infections**: Often due to infections like pneumonia, urinary tract infections, or abdominal infections.
- **Viral infections**: In some cases, viruses can also lead to sepsis.
- **Fungal infections**: Though less common, fungal infections like candidiasis can cause septic shock.

Symptoms:

- Fever or hypothermia (low body temperature)
- Rapid heart rate (tachycardia)
- Low blood pressure (hypotension)
- Warm, flushed skin that later may become cool and pale
- Confusion or altered mental status
- Rapid, shallow breathing
- Decreased urine output (oliguria)
- Nausea, vomiting, and diarrhea

Treatment:

- Antibiotics to treat the underlying infection
- Intravenous fluids to restore blood volume and stabilize blood pressure
- Vasopressor drugs to raise blood pressure (e.g., norepinephrine)
- Organ support such as dialysis for kidney failure or mechanical ventilation for respiratory failure
- Surgery to remove infected tissue or abscesses

4. Anaphylactic Shock

Cause: Anaphylactic shock is a severe allergic reaction that causes widespread blood vessel dilation, leading to a sudden drop in blood pressure and difficulty breathing. It is a life-threatening emergency.

Common Causes:

- **Allergic reactions** to foods (e.g., peanuts, shellfish), insect stings (e.g., bee stings), medications (e.g., penicillin), or latex.
- **Other triggers**: Certain environmental factors or allergic conditions like asthma.

Symptoms:

- Difficulty breathing, wheezing, or tightness in the chest
- Swelling of the face, lips, tongue, or throat (angioedema)
- Low blood pressure (hypotension)
- Dizziness, lightheadedness, or fainting
- Rapid pulse
- Hives, rash, or itching
- Nausea, vomiting, or abdominal pain
- Anxiety or a sense of impending doom

Treatment:

- Immediate administration of **epinephrine (adrenaline)** via injection
- Antihistamines or corticosteroids to reduce inflammation
- Oxygen therapy if breathing is compromised
- Fluid resuscitation to restore blood pressure

5. Neurogenic Shock

Cause: Neurogenic shock is caused by damage to the central nervous system (brain or spinal cord), leading to the loss of sympathetic nerve tone and resulting in blood vessel dilation. This dilation causes a sudden decrease in blood pressure and can lead to organ hypoperfusion.

Common Causes:

- **Spinal cord injury**, especially to the cervical or upper thoracic regions.
- **Brain injury** or severe head trauma.
- **Severe emotional stress** (in rare cases).
- **Anesthesia** or drug-induced effects on the central nervous system.

Symptoms:

- Low blood pressure (hypotension) due to dilated blood vessels
- Bradycardia (slow heart rate) due to loss of sympathetic control
- Warm, dry skin (as opposed to the cool, clammy skin seen in other types of shock)
- Dizziness or fainting
- Weakness or paralysis, especially below the level of the injury in spinal cord cases
- Respiratory distress in severe cases

Treatment:

- Stabilization of the spinal cord if injury is the cause
- Medications like vasopressors to raise blood pressure
- Fluid resuscitation
- In some cases, a pacemaker to regulate heart rate

6. Obstructive Shock

Cause: Obstructive shock occurs when there is a physical obstruction in the circulatory system, preventing blood from flowing properly. This can be due to blockages in the heart or lungs, affecting blood return or pump efficiency.

Common Causes:

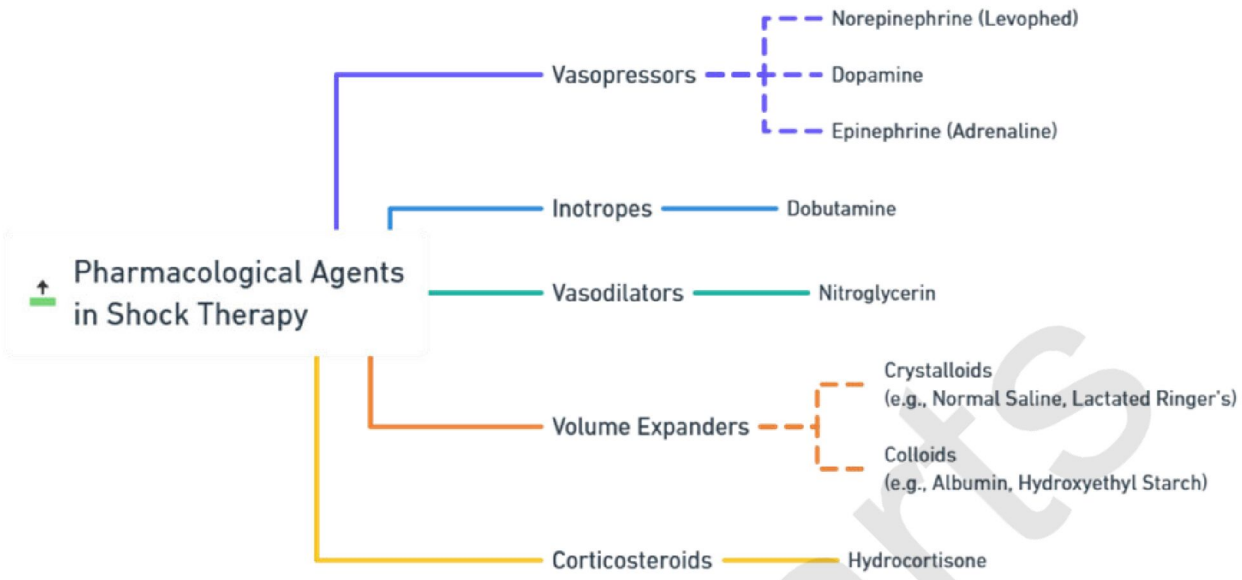
- **Pulmonary embolism (PE)**: A blood clot that blocks a pulmonary artery, reducing blood flow to the lungs and impairing oxygen exchange.
- **Tension pneumothorax**: Accumulation of air in the pleural cavity, compressing the heart and great vessels.
- **Cardiac tamponade**: Fluid buildup around the heart that compresses it, restricting its ability to pump effectively.
- **Aortic dissection**: A tear in the aorta that leads to blood leakage and reduced blood flow to vital organs.

Symptoms:

- Difficulty breathing or shortness of breath (dyspnea)
- Chest pain (especially in pulmonary embolism or aortic dissection)
- Rapid heart rate (tachycardia)
- Low blood pressure (hypotension)
- Cyanosis (bluish color of the lips or extremities)
- Swelling in the neck veins (jugular venous distention)

Treatment:

- **Pulmonary embolism**: Anticoagulants or thrombolytics to dissolve the clot.
- **Tension pneumothorax**: Needle decompression followed by chest tube placement.
- **Cardiac tamponade**: Pericardiocentesis (removal of fluid from around the heart).
- **Aortic dissection**: Emergency surgery to repair the aorta.



Vasopressors:

- **Norepinephrine (Levophed):**
  - **Mechanism:** Primarily alpha-adrenergic agonist with some beta-1 activity, causing vasoconstriction and increased cardiac contractility.
  - **Use:** First-line agent in septic shock; helps increase blood pressure and improve perfusion.
  - **Side Effects:** Arrhythmias, excessive vasoconstriction leading to peripheral ischemia.
- **Dopamine:**
  - **Mechanism:** Dose-dependent effects:
  - Low doses: Dopaminergic receptors, causing renal vasodilation.
  - Intermediate doses: Beta-1 adrenergic effects, increasing heart rate and contractility.
  - High doses: Alpha-adrenergic effects, causing vasoconstriction.
  - **Use:** Cardiogenic and hypovolemic shock; aims to improve cardiac output and blood pressure.
  - **Side Effects:** Tachycardia, arrhythmias, ischemia at high doses.
- **Epinephrine (Adrenaline):**

- **Mechanism:** Non-selective adrenergic agonist affecting alpha and beta receptors; increases heart rate, contractility, and causes vasoconstriction.
- **Use:** Anaphylactic shock, cardiac arrest; sometimes used in septic shock.
- **Side Effects:** Tachycardia, arrhythmias, increased myocardial oxygen demand.

Inotropes:

- **Dobutamine:**
  - **Mechanism:** Primarily beta-1 adrenergic agonist, increasing cardiac contractility and output with mild vasodilation.
  - **Use:** Cardiogenic shock; improves heart performance.
  - **Side Effects:** Arrhythmias, hypotension.

Vasodilators:

- **Nitroglycerin:**
  - **Mechanism:** Nitric oxide donor causing vasodilation, particularly in veins and coronary arteries.
  - **Use:** Initially in hypertensive emergencies or specific types of shock (e.g., cardiogenic shock due to myocardial infarction).
  - **Side Effects:** Hypotension, headache, reflex tachycardia.

Volume Expanders:

- **Crystalloids (e.g., Normal Saline, Lactated Ringer's):**
  - **Mechanism:** Restore intravascular volume through isotonic solutions.
  - **Use:** Hypovolemic shock due to fluid loss.
  - **Side Effects:** Fluid overload, electrolyte imbalances.
- **Colloids (e.g., Albumin, Hydroxyethyl Starch):**
  - **Mechanism:** Larger molecules remain in the intravascular space longer, providing sustained volume expansion.
  - **Use:** Similar to crystalloids but when longer-lasting volume expansion is needed.
  - **Side Effects:** Allergic reactions, coagulopathy with some colloids.

Corticosteroids:

- **Hydrocortisone:**
  - **Mechanism:** Anti-inflammatory effects; may help in septic shock by enhancing vascular responsiveness to vasopressors.
  - **Use:** Septic shock unresponsive to fluid and vasopressor therapy.
  - **Side Effects:** Immunosuppression, hyperglycemia, electrolyte disturbances.

Hematinics, coagulants and anticoagulants:

Hematinics:

Definition:

- Hematinics are substances that help in the production or increase of hemoglobin in the blood and, by extension, promote the formation of red blood cells (RBCs).
- They are essential for the treatment and prevention of anemia, especially in conditions where there is a deficiency of iron, folate, or vitamin B12, all of which are required for the proper production of red blood cells.

Mechanism of Action: Hematinics work by providing essential nutrients (such as iron, vitamins, or folic acid) that the body needs to produce healthy red blood cells. They either:

1. Stimulate the production of hemoglobin.
2. Improve the absorption or bioavailability of essential nutrients.
3. Promote the differentiation and maturation of red blood cells.

Classification of Hematinics: Hematinics can be classified into several categories based on the specific component or nutrient that they supply. These include:

1. **Iron Preparations:** Iron is a vital component of hemoglobin and is necessary for the transport of oxygen in the blood. Iron deficiency is one of the most common causes of anemia.
    - **Oral Iron Supplements:**
        - Ferrous sulfate
        - Ferrous gluconate
        - Ferrous fumarate
        - Polysaccharide iron complex
    - **Parenteral Iron Preparations:**
        - Iron dextran
        - Iron sucrose
        - Ferric carboxymaltose These are used when oral iron is not tolerated or in more severe cases of anemia.
2. **Vitamin B12 Preparations:** Vitamin B12 is essential for the production of red blood cells and the maintenance of the nervous system. Its deficiency can cause megaloblastic anemia.

- **Cyanocobalamin (Vitamin B12)**
- **Hydroxocobalamin** Vitamin B12 can be given orally, intramuscularly, or subcutaneously depending on the severity of the deficiency.

3. **Folic Acid Preparations:** Folate (Vitamin B9) is required for DNA synthesis and red blood cell production. Folic acid deficiency can lead to megaloblastic anemia.
   - **Folic acid (oral)**
   - **Leucovorin (active form of folate)**, often used when there is a deficiency with malabsorption or as an adjunct in chemotherapy.
4. **Copper:** Copper is involved in the absorption and utilization of iron in the body. Copper deficiency can lead to anemia due to impaired iron metabolism.
   - Copper supplements may be used in cases of copper deficiency anemia.
5. **Other Hematinics:**
   - **Erythropoiesis-Stimulating Agents (ESAs):** These are synthetic forms of erythropoietin, a hormone produced by the kidneys that stimulates RBC production in the bone marrow. They are used in cases of anemia due to chronic kidney disease or cancer chemotherapy.
     - Epoetin alfa
     - Darbepoetin alfa
   - **Multivitamin Preparations:** In cases where multiple deficiencies are present, such as in certain malabsorptive conditions, multivitamins containing iron, folate, and B12 may be prescribed.

Indications for Use: Hematinics are typically prescribed to address various forms of anemia, which may include:

- **Iron-deficiency anemia**
- **Vitamin B12 deficiency anemia (pernicious anemia)**
- **Folate deficiency anemia**
- **Anemia of chronic disease** (in some cases)
- **Anemia due to malabsorption disorders**
- **Anemia related to pregnancy**
- **Anemia associated with chemotherapy or kidney disease**

Side Effects:

- **Iron supplements** can cause gastrointestinal upset, constipation, or diarrhea. Parenteral iron can sometimes lead to allergic reactions.
- **Vitamin B12 supplements** may cause mild irritation at the injection site or, rarely, an allergic reaction.
- **Folic acid** is usually well tolerated, but in very high doses, it can mask a vitamin B12 deficiency, potentially causing nerve damage if not addressed.

Coagulants:

Definition:

- Coagulants are substances that promote or facilitate the clotting of blood.
- They are primarily used to treat or prevent excessive bleeding by helping to form blood clots, especially in conditions where the body's natural clotting mechanisms are impaired.
- Coagulants are essential in managing bleeding disorders and for surgical procedures where blood loss must be controlled.

Mechanism of Action: Coagulants work by enhancing the body's natural coagulation cascade, which is a complex process involving clotting factors, platelets, and other proteins that work together to form a stable clot at the site of injury. The primary mechanism involves:

1. Activation of the clotting factors in the blood.
2. Formation of fibrin, a protein that forms the structural framework of the clot.
3. Stabilization of the clot to stop bleeding.

Classification of Coagulants: Coagulants can be classified based on their mode of action, mechanism, and specific use. Broadly, they can be categorized into:

1. Plasma-derived Coagulants:

These are products derived from human plasma and are used to replace deficient or defective clotting factors in patients with bleeding disorders such as hemophilia or von Willebrand disease.

- **Factor Concentrates:** These are specific clotting factors purified from pooled human plasma.
    - **Factor VIII concentrate** (for hemophilia A)
    - **Factor IX concentrate** (for hemophilia B)
    - **Factor XIII concentrate** (for factor XIII deficiency)

- **Fresh Frozen Plasma (FFP):** Contains all clotting factors and is used in the treatment of massive bleeding or to correct deficiencies in multiple clotting factors.
- **Cryoprecipitate:** Contains high concentrations of fibrinogen, factor VIII, von Willebrand factor, and other clotting factors. It is used in cases of fibrinogen deficiency or bleeding due to von Willebrand disease.

2. Vitamin K:

Vitamin K is essential for the synthesis of several clotting factors, including factors II (prothrombin), VII, IX, and X. Deficiency in vitamin K can lead to bleeding tendencies. Coagulants containing vitamin K are often used in:

- **Vitamin K deficiency** (due to malabsorption, liver disease, or use of anticoagulants like warfarin)
- **Newborns**, who may be given a prophylactic dose to prevent vitamin K deficiency bleeding.
- **Vitamin K1 (Phytonadione)**
  - Available as an oral or parenteral preparation.
  - Used to reverse the effects of anticoagulants like warfarin.
- **Vitamin K2**
  - Plays a role in bone health but is not typically used directly as a coagulant in medical settings.

3. Synthetic Coagulants:

These are manufactured synthetic agents that aid in the clotting process.

- **Desmopressin (DDAVP):**
  - A synthetic analog of vasopressin.
  - Increases the release of von Willebrand factor and factor VIII from endothelial cells, helpful in treating mild hemophilia A or von Willebrand disease.
- **Aminocaproic Acid & Tranexamic Acid:**
  - These are antifibrinolytic agents that prevent the breakdown of fibrin, thus promoting clot stability. They are used in conditions like postoperative bleeding, dental procedures in patients with bleeding disorders, or trauma.
  - **Aminocaproic Acid** (Amicar) and **Tranexamic Acid** (Cyklokapron) work by inhibiting plasminogen activation, which is responsible for breaking down fibrin clots.

4. Fibrinogen Concentrates:

Fibrinogen is the final step in the coagulation cascade. In cases of fibrinogen deficiency, fibrinogen concentrates are used.

- **Fibrinogen concentrate (Cryoprecipitate or commercially available fibrinogen preparations)** is used in the treatment of bleeding disorders related to low fibrinogen levels, such as in patients with disseminated intravascular coagulation (DIC), liver disease, or congenital fibrinogen deficiencies.

5. Platelet Transfusions:

Platelets are essential for the formation of the initial plug in the blood clotting process. Platelet transfusions are used in conditions where platelet count is low or platelets are dysfunctional, such as:

- **Thrombocytopenia** (low platelet count)
- **Bone marrow failure syndromes** (e.g., leukemia or aplastic anemia)
- **Myelodysplastic syndromes**

6. Recombinant Coagulants:

These are genetically engineered forms of clotting factors that are used in the treatment of specific bleeding disorders.

- **Recombinant Factor VIII (e.g., Kogenate, Advate):** Used for hemophilia A.
- **Recombinant Factor IX (e.g., Benefix):** Used for hemophilia B.
- **Recombinant activated Factor VII (e.g., NovoSeven):** Used for bleeding episodes in hemophilia patients with inhibitors to factor VIII or IX.

7. Prothrombin Complex Concentrates (PCC):

These are used for the treatment of major bleeding episodes in patients on vitamin K antagonists (like warfarin). PCC contains clotting factors II, VII, IX, and X, and can be used to reverse warfarin effects in emergency situations.

- **4-factor PCC** (e.g., Kcentra)
- **3-factor PCC** (e.g., Bebulin)

Indications for Use of Coagulants:

- **Hemophilia** (deficiency of clotting factors)
- **Vitamin K deficiency** (due to malabsorption, liver disease, or use of certain medications like warfarin)
- **Disseminated intravascular coagulation (DIC)**

- **Severe bleeding from trauma or surgery**
- **Platelet disorders** (thrombocytopenia)
- **Massive blood loss** requiring blood product replacement

Side Effects:

- **Allergic reactions:** Some plasma-derived coagulants may cause allergic reactions, including fever, chills, or anaphylaxis.
- **Thrombosis:** Excessive clotting can lead to the formation of harmful clots (deep vein thrombosis, pulmonary embolism, etc.), especially with the use of synthetic or recombinant coagulants.
- **Infections:** Although plasma-derived products are carefully screened, there is a small risk of transmission of blood-borne infections.
- **Iron overload:** This is a concern with repeated blood transfusions or use of large amounts of clotting factor concentrates.

Anticoagulants:

- Anticoagulants are medicines that help prevent blood clots from forming. They are often used to treat or prevent conditions like deep vein thrombosis (DVT), pulmonary embolism (PE), or stroke.
- These medicines work by slowing down the blood's clotting process, which is important for preventing dangerous clots from forming inside the blood vessels.

Mechanism of Action of Anticoagulants:

Anticoagulants typically work by inhibiting specific clotting factors in the blood. Blood clotting involves a cascade of protein interactions, known as the coagulation cascade, that leads to the formation of fibrin and a stable blood clot. By interfering with one or more of the proteins involved in this cascade, anticoagulants prevent abnormal clot formation.

Types of Anticoagulants:

1. **Vitamin K Antagonists (VKAs)**
   These anticoagulants stop vitamin K from working, which is needed to make clotting proteins in the liver. Without vitamin K, these clotting proteins can't be produced properly, so clots are less likely to form.
   - **Example**: **Warfarin (Coumadin)**
     Warfarin is a common medicine in this group. It requires regular blood tests to make sure the dose is right because many factors, like diet and other medications, can affect how it works.

2. **Direct Oral Anticoagulants (DOACs)**
   These are newer medications that work more directly on the clotting process. They are often preferred because they don't need as much monitoring, and they tend to interact less with food or other medications.
   - **Examples**:
     - **Dabigatran (Pradaxa)**: Works directly on thrombin, a key protein in clotting.
     - **Rivaroxaban (Xarelto)**, **Apixaban (Eliquis)**: These work on another protein called factor Xa, which is involved in clotting.
3. **Heparins**
   Heparins are a type of anticoagulant that works by helping the body's natural clot-busting system. These are usually given through an injection or IV in a hospital setting.
   - **Types of Heparin**:
     - **Unfractionated Heparin (UFH)**: A fast-acting type, often used in emergencies.
     - **Low Molecular Weight Heparin (LMWH)**: More commonly used for long-term treatment, with less need for monitoring.
   - **Examples**:
     - **Enoxaparin (Lovenox)**: A commonly used LMWH.
4. **Fondaparinux**
   This is another type of anticoagulant that helps prevent clotting by working on a protein called factor Xa. It is often given by injection.
   - **Example**: **Fondaparinux (Arixtra)**

Fibrinolytics

- **Fibrinolytics** are medications that break down fibrin in blood clots, a process known as fibrinolysis.
- These drugs are primarily used in emergency situations, such as during heart attacks (myocardial infarctions), ischemic strokes, or massive pulmonary embolism, to restore blood flow by dissolving clots.

Mechanism of Action:

- Fibrinolytic drugs work by converting plasminogen, an inactive precursor, into plasmin, which is an enzyme that breaks down fibrin, the key structural protein in blood clots.
- This results in the degradation of the clot, allowing blood flow to be restored.

Examples:

1. **tPA (Tissue Plasminogen Activator)** - e.g., *Alteplase*, *Reteplase*
2. **Streptokinase**
3. **Urokinase**

Fibrinolytics

- **Mechanism**:
    1. Plasminogen → Plasmin → Breaks down Fibrin → Clot dissolution
    2. Can be administered intravenously (IV) to promote clot lysis in acute conditions.
- **Classified by Type**:
    - **Tissue Plasminogen Activators (tPA)**:
        - Examples: Alteplase, Reteplase
    - **Streptokinase**:
        - Derived from Streptococcus bacteria, activates plasminogen.
    - **Urokinase**:
        - Naturally occurring enzyme, often used in thrombolytic therapy.

Anti-Platelet Drugs

- **Anti-platelet drugs** are a class of medications that prevent platelets from clumping together and forming clots.
- These drugs are mainly used to reduce the risk of heart attacks, strokes, and other cardiovascular events by preventing platelet aggregation.

Mechanism of Action: Anti-platelet drugs work by interfering with various pathways that promote platelet activation and aggregation. They can either inhibit the formation of

thromboxane A2 (which stimulates platelet aggregation) or block receptor sites on platelets involved in clot formation.

Examples:

1. **Aspirin** - Inhibits cyclooxygenase-1 (COX-1), thus preventing thromboxane A2 production.
2. **Clopidogrel (Plavix)** - Inhibits the ADP receptor (P2Y12) on platelets, preventing platelet aggregation.
3. **Ticagrelor** - Also inhibits the ADP receptor, but is more potent than clopidogrel.
4. **Dipyridamole** - Inhibits the uptake of adenosine and enhances prostacyclin effects, leading to reduced platelet aggregation.

Anti-Platelet Drugs

- **Mechanism**:
  1. **Aspirin** - Inhibits COX-1 → Reduces thromboxane A2 → Decreases platelet aggregation.
  2. **Clopidogrel/Ticagrelor** - Inhibit ADP receptor (P2Y12) → Prevents platelet activation and aggregation.
  3. **Dipyridamole** - Inhibits adenosine uptake → Increases prostacyclin → Reduces platelet aggregation.
- **Classified by Mechanism**:
  1. **COX Inhibitors**:
     - Example: Aspirin
  2. **ADP Receptor Inhibitors**:
     - Example: Clopidogrel, Ticagrelor
  3. **Phosphodiesterase Inhibitors**:
     - Example: Dipyridamole
  4. **GPIIb/IIIa Inhibitors**:
     - Example: Abciximab, Eptifibatide (used in percutaneous coronary interventions)

Plasma Volume Expanders

Definition:

- Plasma volume expanders are intravenous fluids used to **restore blood volume** in cases of hypovolemia (e.g., hemorrhage, burns, dehydration).
- They mimic the osmotic properties of plasma to retain fluid in the intravascular space.

Classification and Examples

1. Colloids

- **Mechanism**: Contain large molecules (e.g., proteins, polysaccharides) that increase **oncotic pressure**, pulling fluid into blood vessels.
- **Examples**:
    - **Natural Colloids**:
        - **Human Albumin** (5%, 25%).
    - **Synthetic Colloids**:
        - **Dextrans** (Dextran 40, Dextran 70).
        - **Gelatins** (e.g., Gelofusine).
        - **Hydroxyethyl Starches (HES)** (e.g., Hetastarch – *less commonly used due to safety concerns*).

2. Crystalloids

- **Mechanism**: Electrolyte solutions that distribute across intracellular and extracellular compartments.
- **Examples**:
    - **Isotonic Solutions**:
        - **Normal Saline (0.9% NaCl)**.
        - **Lactated Ringer's (Hartmann's Solution)**.
    - **Hypertonic Solutions** (e.g., 3% NaCl – used in specific cases like cerebral edema).

Differences: Colloids vs. Crystalloids

Feature	Colloids	Crystalloids
Molecular Size	Large molecules (e.g., albumin)	Small ions (e.g., Na^+, Cl^-)
Volume Retention	Longer intravascular retention	Short-lived (rapidly distributed)
Dose Required	Smaller volume	Larger volume (3:1 rule*)
Side Effects	Allergic reactions, coagulopathy	Electrolyte imbalance, edema

Clinical Uses

1. **Colloids**:
    - Severe hypovolemia (e.g., trauma, surgery).
    - Burns (albumin preferred).
    - Hypoalbuminemia (e.g., liver cirrhosis, nephrotic syndrome).
    - *Note*: Synthetic colloids (e.g., HES) are avoided in sepsis and renal failure due to risks of AKI and mortality.
2. **Crystalloids**:
    - First-line for dehydration, mild-moderate blood loss.
    - Maintenance fluid therapy.
    - Correction of electrolyte imbalances (e.g., lactated Ringer's for acidosis).

Advantages and Disadvantages

- **Colloids**:
    - *Pros*: Efficient volume expansion, less fluid overload.
    - *Cons*: Expensive, allergic reactions, renal toxicity (HES).
- **Crystalloids**:
    - *Pros*: Cheap, readily available, minimal side effects.
    - *Cons*: Short-lived effect, risk of pulmonary/edema with overuse.

Mechanism of Action Flow Chart

1. **Colloids**:
   Administered IV → Large molecules remain in vasculature → ↑ Oncotic pressure → Draws fluid from interstitial space → ↑ Blood volume.
2. **Crystalloids**:
   Administered IV → Distribute into extracellular space → ↑ Plasma volume + Replace electrolytes → Temporary volume expansion.

Pharmacology of drugs acting on urinary system

- Diuretics
- Anti-diuretics.

Pharmacology of drugs acting on urinary system:

- Drugs acting on the urinary system are primarily used to manage fluid balance, electrolyte homeostasis, and conditions such as hypertension, heart failure, kidney disease, and edema.
- Two major classes of drugs that have significant effects on the urinary system are **diuretics** and **anti-diuretics**.

1. Diuretics

- **Diuretics** are drugs that increase the production of urine by the kidneys, helping the body excrete excess salt and water.
- They are used to treat conditions like hypertension, heart failure, kidney disease, and edema (fluid retention).
- Diuretics can be classified into several categories based on their site of action and mechanism.

Mechanism of Action:

- Diuretics increase urine output by acting on various parts of the nephron (the functional unit of the kidney), including the proximal convoluted tubule, loop of Henle, distal convoluted tubule, and collecting ducts.
- Depending on the site of action, they may inhibit sodium reabsorption, which leads to water excretion.

Types of Diuretics:

1. Thiazide Diuretics

- **Mechanism**: Thiazide diuretics act on the distal convoluted tubule to inhibit sodium chloride (NaCl) reabsorption. This leads to increased excretion of sodium and water.
- **Example**: **Hydrochlorothiazide** (HCTZ), **Chlorthalidone**, **Indapamide**
- **Indications**: Hypertension, mild edema, heart failure, nephrolithiasis (calcium-containing kidney stones).
- **Side Effects**: Hypokalemia, hyperglycemia, hypercalcemia, hyponatremia, dehydration, increased uric acid (gout).

2. Loop Diuretics

- **Mechanism**: Loop diuretics act on the thick ascending limb of the loop of Henle. They inhibit the sodium-potassium-chloride (Na+/K+/Cl-) co-transporter, preventing sodium reabsorption and thus promoting water excretion.
- **Example**: **Furosemide**, **Bumetanide**, **Torsemide**
- **Indications**: Severe edema (e.g., in heart failure, cirrhosis), pulmonary edema, chronic kidney disease.
- **Side Effects**: Hypokalemia, hypomagnesemia, dehydration, hypotension, ototoxicity (especially with rapid intravenous administration).

3. Potassium-Sparing Diuretics

- **Mechanism**: These diuretics act on the collecting ducts and distal tubules, blocking sodium channels or antagonizing aldosterone receptors. They help the body excrete sodium while conserving potassium.
- **Example**: **Spironolactone** (aldosterone antagonist), **Eplerenone** (aldosterone antagonist), **Amiloride**, **Triamterene** (sodium channel blockers).
- **Indications**: Hypertension, heart failure, primary aldosteronism, prevention of hypokalemia (often used in combination with other diuretics).
- **Side Effects**: Hyperkalemia, gynecomastia (with spironolactone), acidosis.

4. Carbonic Anhydrase Inhibitors

- **Mechanism**: Carbonic anhydrase inhibitors reduce the reabsorption of bicarbonate in the proximal convoluted tubule, leading to a diuretic effect. They also decrease the production of aqueous humor in the eye and are used in the treatment of glaucoma.
- **Example**: **Acetazolamide**, **Methazolamide**
- **Indications**: Glaucoma, metabolic alkalosis, altitude sickness, epilepsy (adjunct therapy).
- **Side Effects**: Metabolic acidosis, hypokalemia, kidney stones, paresthesia.

5. Osmotic Diuretics

- **Mechanism**: Osmotic diuretics work by increasing the osmolarity of the renal filtrate, which prevents water reabsorption in the proximal tubule and loop of Henle.
- **Example**: **Mannitol**
- **Indications**: Increased intracranial pressure, increased intraocular pressure, renal protection during surgery.
- **Side Effects**: Dehydration, hypernatremia, hypotension, renal failure in high doses.

2. Anti-Diuretics

- Anti-diuretic drugs are used to reduce the production of urine or promote water retention.
- These drugs can be useful in conditions where excessive urination (diuresis) is a concern, such as diabetes insipidus, dehydration, or in some cases of heart failure.

Mechanism of Action:

- Anti-diuretic drugs typically enhance water reabsorption in the kidneys, either by mimicking or enhancing the action of the hormone **vasopressin (antidiuretic hormone, ADH)**, or by inhibiting diuresis at various points in the renal system.

Types of Anti-Diuretics:

1. Vasopressin (ADH) Analogues

Vasopressin (also known as **antidiuretic hormone**, or **ADH**) promotes water reabsorption by the kidneys by acting on the V2 receptors in the collecting ducts. Drugs that mimic vasopressin or enhance its action are used to reduce urine output.

- **Example**: **Desmopressin** (synthetic analogue of vasopressin), **Vasopressin**.
- **Indications**: Diabetes insipidus (central), nocturnal enuresis, bleeding disorders (e.g., von Willebrand disease, hemophilia).
- **Side Effects**: Hyponatremia, headache, nausea, water retention, and possible overhydration.

2. Aquaretics (V2 Receptor Antagonists)

Aquaretics are drugs that act as **vasopressin receptor antagonists** to promote water excretion without sodium loss (aquaresis). These drugs block vasopressin's action at the V2 receptors in the kidneys.

- **Example**: **Tolvaptan**, **Conivaptan**
- **Indications**: Hyponatremia (especially in heart failure or syndrome of inappropriate antidiuretic hormone secretion - SIADH), cirrhosis with ascites.
- **Side Effects**: Thirst, hypernatremia, liver toxicity (with long-term use of Tolvaptan).

3. Diuretics with Anti-Diuretic Effects

Certain diuretics, like **spironolactone**, can also have anti-diuretic effects due to their influence on aldosterone, which plays a role in regulating sodium and water balance. Spironolactone, as a potassium-sparing diuretic, can reduce the need for water excretion in some cases, though its main use is for reducing potassium loss.

Comparison Between Diuretics and Anti-Diuretics

Property	Diuretics	Anti-Diuretics
Effect on Urine Output	Increases urine output (diuresis)	Reduces urine output or promotes water retention
Mechanism	Acts on different sites of the nephron to increase water and electrolyte excretion.	Mimics or enhances ADH effects, or blocks diuresis pathways.
Indications	Hypertension, heart failure, edema, kidney disease, glaucoma, etc.	Diabetes insipidus, SIADH, nocturnal enuresis, hyponatremia.
Examples	Hydrochlorothiazide, Furosemide, Spironolactone	Desmopressin, Tolvaptan, Vasopressin