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PHARMACOLOGY - III

UNIT 5

TOPIC :

- **Principles of toxicology**

  a. Definition and basic knowledge of acute, subacute and chronic toxicity.

  b. Definition and basic knowledge of genotoxicity, carcinogenicity, teratogenicity and mutagenicity

  c. General principles of treatment of poisoning

  d. Clinical symptoms and management of barbiturates, morphine,
  organophosphosphorus compound and lead, mercury and arsenic poisoning.

Principles of Toxicology

Toxicology

Toxicology is the branch of science that studies the harmful (adverse) effects of chemicals, drugs, poisons, and other substances on living organisms, including humans, animals, and plants. It also deals with the prevention, diagnosis, and treatment of poisoning.

The word Toxicology is derived from:

- Greek word: *Toxikon* = Poison
- Logos = Study

Therefore, Toxicology means "the study of poisons."

Father of Modern Toxicology

- Paracelsus (1493–1541) – Introduced the principle: "The dose makes the poison."
- Mathieu Joseph Bonaventure Orfila (1787–1853) – Known as the Father of Modern Toxicology because he established toxicology as a scientific discipline.

Importance of Toxicology

- Studies the harmful effects of chemicals and drugs.
- Helps prevent poisoning.
- Ensures the safe use of medicines.
- Assists in environmental protection.
- Used in forensic investigations.
- Protects workers from occupational hazards.
- Helps regulatory agencies determine safe exposure limits.

Principles of Toxicology

The basic principles of toxicology include:

1. Dose–Response Relationship

- The toxic effect of a substance depends on the **dose** received.
- A low dose may be harmless, while a high dose can be toxic.
- As the dose increases, the severity of toxic effects also increases.

Example:

- Paracetamol is safe at the recommended dose but can cause severe liver damage in overdose.

2. Route of Exposure

Toxic substances can enter the body through different routes:

- **Inhalation** – Breathing toxic gases or dust.
- **Ingestion** – Swallowing contaminated food, water, or medicines.
- **Skin Absorption** – Chemicals entering through the skin.
- **Injection** – Through needles, insect bites, or animal bites.

3. Toxicity

Toxicity is the ability of a substance to produce harmful effects on living organisms.

The degree of toxicity depends on:

- Dose
- Duration of exposure
- Route of exposure
- Age
- Body weight
- Health condition
- Individual sensitivity

4. Combined Effects of Chemicals

Sometimes two or more toxic substances act together and produce greater toxicity.

Types include:

- **Additive Effect:** Total effect equals the sum of both substances.
- **Synergistic Effect:** Combined effect is greater than the sum.
- **Antagonistic Effect:** One substance reduces the toxicity of another.

TOXICITY

→ Toxicity is the ability of a substance to cause harmful effects, injury, illness, or death in living organisms.

A substance becomes toxic depending on:

- Amount (dose)
- Frequency of exposure
- Duration of exposure
- Route of entry
- Individual susceptibility

Examples:

- Pesticides
- Heavy metals
- Alcohol
- Certain medicines in overdose

Types Of Toxicity

1. Acute Toxicity

→ Acute toxicity refers to harmful effects that occur after a single exposure or multiple exposures within 24 hours, producing symptoms immediately or within a few days.

Causes

- Drug overdose
- Poisonous chemicals
- Toxic gas inhalation
- Accidental poisoning

Symptoms

- Nausea
- Vomiting
- Dizziness
- Headache
- Difficulty in breathing
- Skin irritation
- Loss of consciousness
- Convulsions
- Death (in severe cases)

Examples

- Mercury poisoning
- Pesticide poisoning
- Snake venom
- Drug overdose

Treatment

- Immediate medical attention
- Remove the poison source
- Gastric lavage (when indicated)
- Activated charcoal
- Antidotes (if available)
- Supportive care (oxygen, IV fluids)

2. Sub-Acute Toxicity

→ Sub-acute toxicity refers to harmful effects produced by repeated exposure to a toxic substance for about 14–28 days (up to 30 days).

Causes

- Repeated exposure to low doses of toxic chemicals.
- Occupational exposure.
- Repeated drug administration.

Symptoms

- Headache
- Fatigue
- Skin irritation
- Nausea
- Loss of appetite
- Stomach discomfort
- Mild organ damage

Examples

- Repeated pesticide exposure
- Long-term use of certain medicines for a few weeks

Treatment

- Stop further exposure.
- Symptomatic treatment.
- Detoxification if necessary.
- Supportive therapy.
- Monitor liver and kidney function.

3. Chronic Toxicity

→ Chronic toxicity refers to harmful effects caused by continuous or repeated exposure to toxic substances for months or years (generally more than 3 months).

Causes

- Smoking
- Air pollution
- Long-term occupational exposure
- Heavy metal exposure
- Continuous use of toxic drugs

Symptoms

- Persistent fatigue
- Headache
- Weight loss
- Breathing problems
- Nerve damage
- Liver disease
- Kidney damage
- Cancer
- Reproductive disorders

Examples

- Lead poisoning
- Mercury poisoning
- Asbestos exposure
- Cigarette smoking

Treatment

- Stop exposure to the toxic substance.
- Long-term medical management.
- Chelation therapy for heavy metals (when indicated).
- Regular monitoring of affected organs.

- Rehabilitation and supportive care.

Genotoxicity

→ Genotoxicity is the ability of a chemical, drug, radiation, or other agent to damage the genetic material (DNA or chromosomes) of living cells. DNA damage may lead to mutations, cancer, or cell death if not repaired properly.

Mechanism of Genotoxicity

1. Exposure to genotoxic agents such as chemicals, radiation, viruses, or certain drugs.
2. The agent enters the body and reaches the cells.
3. DNA is damaged by:
    - Breaking DNA strands.
    - Altering DNA bases.
    - Forming DNA cross-links.
    - Causing chromosomal abnormalities.
4. The cell attempts to repair the damaged DNA.
5. If repair fails, permanent DNA mutations occur.
6. Mutated cells may:
    - Die (cell death).
    - Become cancerous.
    - Pass mutations to daughter cells.

Causes

- Industrial chemicals
- Pesticides
- Heavy metals
- Ionizing radiation
- UV radiation
- Certain anticancer drugs
- Viral infections

Risk Factors

- Exposure to chemicals
- Radiation
- Genetic susceptibility
- Increasing age
- Smoking
- Alcohol consumption
- Weak immune system
- Environmental pollution

Effects

- DNA mutations
- Chromosomal damage
- Infertility
- Birth defects
- Cancer
- Cell death

Management / Treatment

- Remove exposure to the genotoxic agent.
- Antioxidants: Vitamin C, Vitamin E, Selenium, N-acetylcysteine.
- Cytoprotective agents: Amifostine (during chemotherapy/radiotherapy).
- Experimental DNA repair enhancers (e.g., Resveratrol, Polyphenols).
- Diet rich in fruits and vegetables.
- Avoid smoking and alcohol.
- Regular exercise and healthy lifestyle.

Carcinogenicity

→ Carcinogenicity is the ability of a substance, chemical, radiation, or infectious agent to cause cancer by producing uncontrolled growth of abnormal cells.

→ A **carcinogen** is any substance capable of causing cancer.

Mechanism of Carcinogenicity

1. Exposure to carcinogens (tobacco smoke, chemicals, radiation, viruses).
2. DNA damage occurs in body cells.
3. Mutations develop in:
    - Oncogenes
    - Tumor suppressor genes
4. Loss of normal cell cycle regulation.
5. Uncontrolled cell division.
6. Tumor formation.
7. Cancer cells invade nearby tissues.
8. Cancer spreads to distant organs (Metastasis).

Types of Carcinogens

Physical

- X-rays
- Gamma rays
- UV radiation

Chemical

- Tobacco smoke
- Asbestos
- Benzene
- Arsenic

Biological

- Human Papillomavirus (HPV)
- Hepatitis B virus (HBV)
- Hepatitis C virus (HCV)

Risk Factors

- Smoking
- Alcohol
- Pollution
- Obesity
- Poor diet
- Family history
- Radiation
- Asbestos exposure
- Immunosuppression

Effects

- Benign tumors
- Malignant tumors
- Organ damage
- Metastasis
- Death if untreated

Management / Treatment

- Avoid exposure to carcinogens.
- Stop smoking and alcohol consumption.
- Healthy diet rich in antioxidants.
- Vaccination:
  - HPV vaccine (prevents cervical cancer)
  - Hepatitis B vaccine (reduces liver cancer risk)
- Surgery
- Chemotherapy
- Radiotherapy
- Targeted therapy
- Immunotherapy

Teratogenicity

→ Teratogenicity is the ability of a drug, chemical, infection, or radiation to produce congenital abnormalities (birth defects) in the developing fetus when exposure occurs during pregnancy.

→ A teratogen is an agent that interferes with normal fetal development.

Mechanism of Teratogenicity

1. Pregnant woman is exposed to a teratogen.
2. The teratogen enters the bloodstream.
3. It crosses the placenta.
4. Reaches the developing fetus.
5. Interferes with organ formation (organogenesis).
6. Causes abnormal fetal development.

Causes

- Certain medicines
- Alcohol
- Smoking
- Radiation
- Viral infections
- Chemical exposure
- Maternal diseases

Risk Factors

- Alcohol
- Smoking
- Radiation
- Hyperthermia (high fever)
- Hypoxia
- Obesity

- Poor nutrition

Effects

- Congenital malformations
- Neural tube defects
- Heart defects
- Limb deformities
- Growth retardation
- Brain abnormalities
- Miscarriage
- Stillbirth

Management / Treatment

- Folic acid supplementation (prevents neural tube defects).
- Iodine supplementation (prevents mental retardation due to iodine deficiency).
- Levothyroxine for maternal hypothyroidism.
- Dexamethasone for congenital adrenal hyperplasia (selected cases).
- Antiviral drugs when indicated.
- Balanced nutritious diet.
- Avoid alcohol, smoking, and unnecessary medications during pregnancy.
- Regular antenatal check-ups.

Mutagenicity

→ Mutagenicity is the ability of a substance or agent to produce permanent changes (mutations) in the DNA sequence of living cells.

→ Mutagenicity is closely related to genotoxicity, but not all genotoxic agents produce permanent mutations.

Mechanism of Mutagenicity

1. Exposure to mutagenic agents.
2. Mutagens enter the body.
3. Reach the nucleus of cells.
4. Damage DNA.
5. DNA replication or repair occurs incorrectly.
6. Permanent mutation develops.
7. Mutated cells may survive and multiply.

Causes

- Chemicals
- Radiation
- UV rays
- X-rays
- Tobacco smoke
- Industrial pollutants
- Pesticides
- Certain drugs

Risk Factors

- Radiation exposure
- Smoking
- Alcohol
- Pollution
- Pesticides

- UV radiation

Effects

- Gene mutations
- Chromosomal abnormalities
- Birth defects
- Genetic disorders
- Cancer
- Cell dysfunction

Management / Treatment

- Avoid exposure to mutagens.
- Antioxidants (Vitamin C, Vitamin E, Selenium).
- Cytoprotective agents.
- DNA repair enhancers (experimental).
- Folic acid and Vitamin B12 supplementation.
- Diet rich in fruits, vegetables, and whole grains.
- Regular physical exercise.
- Avoid smoking, alcohol, and processed foods.

Poison

A poison is any substance that can cause injury, illness, or death when it enters the body in relatively small amounts through chemical action. Poisons interfere with normal physiological and biochemical functions of the body.

Poisons may be present as:

- Solids
- Liquids
- Gases

They may enter the body through ingestion, inhalation, skin contact, or injection.

Characteristics of Poison

- Causes harmful biological effects.
- Acts by chemical interaction with body tissues.
- Toxicity depends on the dose, route of exposure, and duration of exposure.
- Can affect one or multiple organs.

Classification of Poisons

1. Corrosive Poisons

→ Corrosive poisons destroy tissues immediately after contact.

Types & Examples

A. Strong Acids

- Sulphuric acid (H_2SO_4)
- Hydrochloric acid (HCl)
- Nitric acid (HNO_3)

B. Strong Alkalis

- Sodium hydroxide (Caustic soda)
- Potassium hydroxide (Caustic potash)

Effects

- Burns of mouth and stomach
- Severe pain
- Vomiting
- Tissue necrosis

2. Irritant Poisons

→ Irritant poisons produce inflammation and irritation of tissues.

Types

A. Inorganic Irritants

Non-metals

- Phosphorus, Chlorine
- Bromine
- Iodine

Metals

- Arsenic, Lead
- Mercury
- Antimony

B. Organic Irritants

Plant Origin

- Castor seeds, Croton oil

Animal Origin

- Snake venom

- Cantharides

C. Mechanical Irritants

- Glass powder
- Diamond dust

Effects

- Burning sensation
- Vomiting
- Diarrhea

3. Neurotic Poisons

→ Neurotic poisons primarily affect the central or peripheral nervous system.

Types

A. Cerebral Poisons

Narcotics (Sleep-producing)

- Opium, Morphine

Intoxicants

- Alcohol

General Anaesthetics

- Ether, Chloroform

Deliriants

- Datura, Belladonna

B. Spinal Poisons

- Nux vomica (Strychnine)

C. Cardiac Poisons

- Digitalis, Aconite
- Tobacco (Nicotine)

D. Peripheral Nervous System Poisons

- Carbon monoxide (CO)
- Carbon dioxide (CO_2)
- Coal gas

Effects

- Convulsions
- Paralysis

- Respiratory depression
- Cardiac arrest

Mechanism of Poisoning

→ Poisoning occurs when a toxic substance enters the body and interferes with normal physiological functions.

Mechanism

1. Poison enters the body through:
    - Oral ingestion
    - Inhalation
    - Skin absorption
    - Injection
2. Poison is absorbed into the bloodstream.
3. It is distributed to various organs.
4. It interferes with normal body functions by:
    - Blocking enzymes.
    - Damaging cells.
    - Disrupting the nervous system.
    - Affecting the heart, liver, kidneys, or lungs.
5. Symptoms appear depending on the poison and dose.
6. The body attempts to eliminate the poison by:
    - Vomiting
    - Sweating
    - Urination
    - Liver metabolism
7. Severe poisoning requires emergency medical treatment.

Symptoms of Poisoning

Symptoms vary depending on the poison but commonly include:

- Nausea
- Vomiting
- Abdominal pain
- Dizziness
- Headache
- Difficulty breathing

- Convulsions
- Confusion
- Coma

General Principles of Treatment Of Poisoning

1. Identify the Poison

- Determine the poison involved.
- Ask about:
  - Name of the poison.
  - Amount consumed.
  - Time of exposure.
  - Route of exposure (oral, inhalation, skin, injection).

2. Remove the Poison

From the Mouth

- Remove remaining poison carefully.
- Rinse the mouth with clean water (if appropriate).

From the Skin

- Wash thoroughly with plenty of soap and water.

From the Eyes

- Irrigate with clean water for **15–20 minutes**.

From Inhalation

- Move the patient to fresh air immediately.
- Remove from toxic fumes.

3. Maintain Airway, Breathing and Circulation (ABC)

- Ensure airway is open.
- Provide oxygen if required.
- Support breathing.
- Maintain blood circulation.
- Perform CPR if necessary.

4. Prevent Further Absorption

Methods include:

- Activated charcoal (for many oral poisons).
- Gastric lavage (selected cases).
- Whole bowel irrigation (specific poisons).

5. Enhance Elimination

Methods include:

- Forced diuresis
- Urinary alkalinization
- Hemodialysis
- Hemoperfusion
- Chelation therapy (heavy metals)

6. Control Convulsions

- Protect the patient from injury.
- Place in the recovery position.
- Do not place objects in the mouth.
- Administer anticonvulsants (e.g., Diazepam) if indicated.

7. Fluid and Electrolyte Therapy

- Correct dehydration.
- Replace electrolytes.
- Administer IV fluids if necessary.

8. Supportive and Symptomatic Treatment

- Oxygen therapy.
- Maintain blood pressure.
- Treat shock.
- Control fever.
- Correct acid-base imbalance.
- Monitor vital signs continuously.

9. Administration of Specific Antidotes

- Use antidotes whenever a specific poison is identified.

ANTIDOTES

Antidote	Indication (Poison)	Mechanism of Action
N-Acetylcysteine (NAC)	Acetaminophen (Paracetamol) overdose	Replenishes glutathione stores and prevents liver damage.
Naloxone	Opioid overdose	Competitive opioid (μ-receptor) antagonist that rapidly reverses respiratory depression.
Atropine	Organophosphate and Carbamate poisoning	Blocks muscarinic receptors and reduces cholinergic effects.
Pralidoxime (2-PAM)	Organophosphate poisoning (with atropine)	Reactivates acetylcholinesterase by removing the phosphate group from the inhibited enzyme.
Flumazenil	Benzodiazepine overdose	Competitive antagonist at the benzodiazepine site on the GABA-A receptor.
Ethanol	Methanol and Ethylene glycol poisoning	Competes for alcohol dehydrogenase, preventing formation of toxic metabolites.
Fomepizole	Methanol and Ethylene glycol poisoning	Directly inhibits alcohol dehydrogenase and prevents toxic metabolite formation.
Deferoxamine	Iron poisoning	Chelates free iron to form a water-soluble complex excreted in urine.
Dimercaprol (BAL)	Arsenic, Mercury and Gold poisoning	Chelates heavy metals to form stable complexes for excretion.
Succimer	Lead, Arsenic and	Oral chelating agent that

(DMSA)	Mercury poisoning (especially in children)	enhances renal excretion of heavy metals.
Sodium Thiosulfate	Cyanide poisoning (adjunct therapy)	Converts cyanide into the less toxic thiocyanate, which is excreted by the kidneys.

Clinical Symptoms and Management of Poisoning

1. Barbiturate Poisoning

→ Barbiturate poisoning occurs due to overdose of barbiturate drugs, which are Central Nervous System (CNS) depressants. Excessive doses depress brain activity, resulting in respiratory depression, coma, and even death.

Mechanism of Action

1. Excess dose of barbiturates is taken.
2. Barbiturates enhance the action of GABA-A receptors.
3. Increased chloride ion influx causes excessive CNS depression.
4. Depression of respiratory and cardiovascular centers occurs.
5. Reduced heart rate, blood pressure, and body temperature.
6. Severe overdose results in respiratory failure, coma, and death.

Clinical Symptoms

Central Nervous System

- Drowsiness
- Confusion
- Slurred speech
- Poor coordination (Ataxia)
- Weak or absent reflexes
- Coma

Respiratory System

- Respiratory depression
- Slow breathing
- Apnea
- Cyanosis

Cardiovascular System

- Hypotension
- Bradycardia
- Shock (severe cases)

Other Symptoms

- Hypothermia
- Prolonged sedation
- Hyporeflexia
- Blisters (Barbiturate blisters)

Management

Supportive Treatment

- Maintain Airway, Breathing and Circulation (ABC).
- Oxygen therapy.
- Mechanical ventilation if respiratory failure occurs.
- IV fluids for hypotension.

Prevent Further Absorption

- Activated charcoal (within 1–2 hours if airway is protected).
- Gastric lavage in selected cases.

Enhance Elimination

- Urinary alkalinization (Sodium bicarbonate) for phenobarbital poisoning.
- Hemodialysis in severe poisoning.

2. Morphine Poisoning

→ Morphine poisoning occurs due to overdose of morphine or other opioids, causing severe depression of the CNS and respiratory center.

Mechanism of Action

1. Excess morphine binds to μ-opioid receptors.
2. CNS activity is markedly depressed.
3. Respiratory center becomes less responsive to carbon dioxide.
4. Slow and shallow breathing develops.
5. Reduced oxygen supply leads to coma and death if untreated.

Clinical Symptoms

Central Nervous System

- Drowsiness
- Pinpoint pupils (Miosis)
- Confusion
- Coma
- Seizures (rare)

Respiratory System

- Respiratory depression

- Slow, shallow breathing
- Apnea

Cardiovascular System

- Bradycardia
- Hypotension
- Shock

Gastrointestinal

- Nausea
- Vomiting
- Constipation

Skin

- Flushing
- Pruritus (Itching)
- Cyanosis

Management

Supportive Care

- Maintain ABC.
- Oxygen therapy.
- Mechanical ventilation if required.
- IV fluids to maintain blood pressure.

Prevent Absorption

- Gastric lavage (selected early cases).
- Activated charcoal when appropriate.

Specific Antidote

- Naloxone (Opioid receptor antagonist) – rapidly reverses respiratory and CNS depression.

3. Organophosphorus Poisoning

→ Organophosphorus poisoning occurs after exposure to organophosphate insecticides, pesticides, or nerve agents that inhibit **acetylcholinesterase (AChE).**

Mechanism of Action

1. Organophosphate enters the body.
2. Irreversibly inhibits acetylcholinesterase.
3. Acetylcholine accumulates at synapses.
4. Continuous stimulation of muscarinic, nicotinic, and CNS receptors.
5. Respiratory failure may occur due to paralysis of respiratory muscles.

Clinical Symptoms

SLUDGE Symptoms

- **S** – Salivation
- **L** – Lacrimation
- **U** – Urination
- **D** – Defecation/Diarrhea
- **G** – Gastrointestinal cramps
- **E** – Emesis (Vomiting)

Nervous System

- Anxiety
- Headache
- Confusion
- Dizziness
- Seizures
- Coma

Muscular

- Muscle twitching
- Muscle weakness
- Paralysis

Cardiovascular

- Bradycardia
- Hypotension

Respiratory

- Bronchospasm
- Excessive bronchial secretions
- Respiratory distress

Management

Decontamination

- Remove contaminated clothes.
- Wash skin thoroughly with soap and water.
- Irrigate eyes if exposed.

Specific Antidotes

- **Atropine** – Blocks muscarinic effects.

- **Pralidoxime (2-PAM)** – Reactivates acetylcholinesterase.
- **Diazepam** – Controls seizures.

Supportive Care

- Oxygen therapy.
- Mechanical ventilation if needed.
- IV fluids.
- ECG and electrolyte monitoring.

4. Lead Poisoning

→ Lead poisoning is caused by excessive accumulation of lead in the body through contaminated water, paint, dust, batteries, or industrial exposure.

Mechanism of Action

1. Lead enters the bloodstream.
2. Deposits in bones, brain, kidneys, and liver.
3. Inhibits enzymes involved in heme synthesis.
4. Produces anemia and neurological damage.
5. Causes kidney dysfunction and developmental delay.

Clinical Symptoms

Central Nervous System

- Headache
- Irritability
- Fatigue
- Poor concentration
- Seizures
- Coma (severe)

Blood

- Microcytic hypochromic anemia
- Pallor

Gastrointestinal

- Abdominal pain
- Constipation
- Nausea
- Vomiting

- Loss of appetite

Other Signs

- Blue line on gums (Burton's line)
- Muscle and joint pain
- Growth retardation in children

Management

Remove Exposure

- Identify and eliminate lead source.

Chelation Therapy

- **Dimercaprol (BAL)** – Severe poisoning.
- **Calcium disodium EDTA** – Moderate to severe poisoning.
- **Succimer (DMSA)** – Mild to moderate poisoning, especially in children.
- **Penicillamine** – Alternative oral chelator.

Supportive Care

- Treat anemia.
- Nutritional support.
- Monitor neurological development.

5. Mercury Poisoning

→ Mercury poisoning results from excessive exposure to elemental, inorganic, or organic mercury through inhalation, contaminated food, or occupational exposure.

Mechanism of Action

1. Mercury enters the bloodstream.
2. Distributes to brain, kidneys, and nervous system.
3. Binds to sulfhydryl (-SH) groups of enzymes.
4. Produces oxidative stress.
5. Causes cellular injury and organ dysfunction.

Clinical Symptoms

Acute Poisoning

Respiratory

- Cough
- Breathlessness
- Pneumonitis

Gastrointestinal

- Metallic taste
- Vomiting
- Bloody diarrhea
- Abdominal pain

Kidneys

- Acute renal failure

CNS

- Tremors
- Headache
- Irritability

Chronic Poisoning

CNS

- Memory loss
- Tremors
- Insomnia
- Emotional instability

Peripheral Nervous System

- Paresthesia
- Muscle weakness

Oral

- Excess salivation
- Gingivitis
- Stomatitis

Skin

- Rashes
- Peeling
- Discoloration

Fetal Exposure

- Developmental delay
- Cerebral palsy
- Mental retardation

Management

Remove Source

- Stop mercury exposure.
- Avoid contaminated seafood.

Chelation Therapy

- Dimercaprol (BAL)
- Succimer (DMSA)
- Penicillamine (alternative)

Supportive Care

- IV fluids.
- Dialysis if renal failure develops.
- Long-term neurological monitoring.

6. Arsenic Poisoning

→ Arsenic poisoning occurs after ingestion, inhalation, or skin exposure to arsenic present in contaminated groundwater, pesticides, industrial chemicals, or traditional medicines.

Mechanism of Action

1. Arsenic enters the bloodstream.
2. Inhibits cellular enzymes involved in ATP production.
3. Increases oxidative stress.
4. Causes multi-organ damage.
5. Long-term exposure increases cancer risk.

Clinical Symptoms

Acute Poisoning

Gastrointestinal

- Severe abdominal pain
- Vomiting
- Diarrhea
- Dehydration

Cardiovascular

- Hypotension
- Tachycardia
- Shock

Central Nervous System

- Headache
- Confusion
- Seizures

Kidneys

- Acute kidney injury

Blood

- Hemolysis
- Pancytopenia

Chronic Poisoning

Skin

- Hyperpigmentation

- Hyperkeratosis

Nervous System

- Peripheral neuropathy
- Weakness
- Numbness

Blood

- Anemia
- Leukopenia
- Thrombocytopenia

Liver

- Hepatomegaly
- Cirrhosis

Cancer

- Skin cancer
- Lung cancer
- Bladder cancer

Management

Remove Exposure

- Avoid contaminated water and food.
- Remove occupational exposure.

Chelation Therapy

- **Dimercaprol (BAL)** – Acute severe poisoning.
- **Succimer (DMSA)** – Mild to moderate or chronic poisoning.

Supportive Care

- IV fluids for dehydration.
- Treat vomiting, diarrhea, and shock.
- Monitor liver and kidney function.
- Correct electrolyte imbalance.