Antidotes

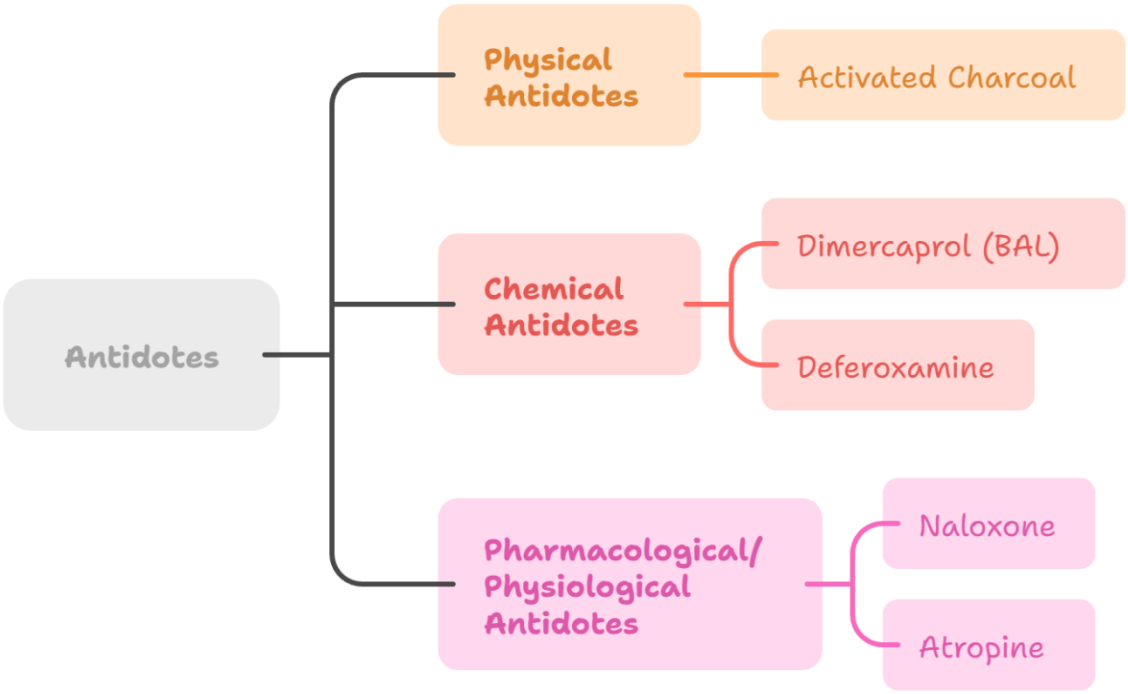
Antidotes and Their Clinical Applications

Introduction

- An antidote is an agent used to counteract or neutralize the toxic effects of a poison.
- The management of poisoning often depends on the timely use of specific antidotes, which may act by:
    - neutralizing the poison,
    - preventing its absorption,
    - enhancing its elimination, or
    - antagonizing its effects at receptor or enzyme levels.
- While supportive care remains the cornerstone of poisoning management, antidotes play a critical role in specific toxic exposures where they can significantly reduce morbidity and mortality.

Classification of Antidotes

Antidotes can be broadly classified based on their mechanism of action:



1. Physical Antidotes

- **Mechanism:** Prevent absorption of the poison by adsorbing or inactivating it locally within the gastrointestinal tract.
- **Example:**
    - **Activated Charcoal:** Adsorbs a wide range of toxins in the GI tract, preventing systemic absorption.

2. Chemical Antidotes

- **Mechanism:** React chemically with the poison to form a non-toxic compound that can be excreted from the body.
- **Examples:**
  - **Dimercaprol (BAL):** Binds heavy metals like arsenic, gold, and mercury forming stable, excretable complexes.
  - **Deferoxamine:** Chelates free iron to form ferrioxamine, which is water-soluble and excreted in urine.

3. Pharmacological / Physiological Antidotes

- **Mechanism:** Counteract or antagonize the physiological effects of poisons at the receptor or enzyme level.
- **Examples:**
  - **Naloxone:** Reverses opioid-induced respiratory depression by competitively blocking opioid receptors.
  - **Atropine:** Blocks muscarinic effects of acetylcholine in organophosphate poisoning.

Common Antidotes and Their Clinical Applications

Poison / Toxin	Antidote	Mechanism / Clinical Use
Paracetamol (Acetaminophen)	**N-acetylcysteine (NAC)**	Replenishes glutathione; detoxifies toxic metabolite (NAPQI). Most effective within **8–10 hours** of ingestion.
Opioids (e.g., Morphine, Heroin)	**Naloxone**	Competitive **opioid receptor antagonist**; reverses respiratory depression and CNS depression.
Organophosphates / Carbamates	**Atropine + Pralidoxime (2-PAM)**	Atropine blocks muscarinic receptors; pralidoxime reactivates **acetylcholinesterase** inhibited by organophosphates.
Benzodiazepines	**Flumazenil**	Competitive **GABA-A receptor antagonist**; reverses excessive sedation (use cautiously in mixed overdoses).
Methanol / Ethylene Glycol	**Fomepizole or Ethanol**	Inhibit **alcohol dehydrogenase**, preventing formation of toxic metabolites (formic acid, oxalic acid).

Iron	**Deferoxamine**	Chelates free iron, forming water-soluble ferrioxamine excreted in urine.
Cyanide	**Hydroxocobalamin / Sodium Nitrite + Sodium Thiosulfate**	Hydroxocobalamin forms **cyanocobalamin (vitamin B12)**; thiosulfate donates sulfur for conversion to thiocyanate.
Heparin	**Protamine Sulfate**	Binds and neutralizes heparin, forming a stable inactive complex.
Warfarin	**Vitamin K1 (Phytonadione)**	Restores hepatic synthesis of clotting factors II, VII, IX, and X.
Digoxin	**Digoxin-specific antibody fragments (Digibind)**	Bind free digoxin, forming inactive complexes excreted renally.
Beta Blockers	**Glucagon**	Increases **cAMP** independent of β-receptors; improves cardiac contractility and rate.
Calcium Channel Blockers	**Calcium Gluconate / Glucagon / High-dose Insulin**	Stabilizes cardiac membranes and enhances myocardial contractility.
Isoniazid (INH)	**Pyridoxine (Vitamin B6)**	Replaces depleted coenzyme; prevents and treats seizures caused by INH toxicity.
Snake Bite (Viper, Cobra, etc.)	**Antivenom (Polyvalent or Monovalent)**	Neutralizes venom components; prevents systemic toxicity.
Lead	**EDTA, DMSA (Succimer)**	Chelate lead to form water-soluble complexes for renal excretion.
Arsenic, Mercury	**Dimercaprol (BAL), DMSA**	Chelating agents forming stable, excretable metal complexes.
Carbon Monoxide (CO)	**100% Oxygen / Hyperbaric Oxygen**	Displaces CO from hemoglobin; restores oxygen-carrying capacity.
Methemoglobinemia	**Methylene Blue**	Converts methemoglobin (Fe^{3+}) back to hemoglobin (Fe^{2+}).
Tricyclic Antidepressants (TCA), Salicylates	**Sodium Bicarbonate**	Alkalinizes serum and urine; narrows QRS complex in TCA toxicity.
General Oral Poisons	**Activated Charcoal**	Adsorbs toxins in GI tract; reduces systemic absorption (effective within 1 hour).

Mechanisms of Antidotal Action

1. Receptor Antagonism:

- Antidote binds to the same receptor as the poison, blocking its action.
- **Example:** Naloxone blocks opioid receptors.

2. Enzyme Reactivation:

- Restores normal enzyme activity inhibited by the poison.
- **Example:** Pralidoxime reactivates acetylcholinesterase in organophosphate poisoning.

3. Chemical Neutralization:

- Forms a non-toxic compound by direct chemical reaction with the toxin.
- **Example:** Hydroxocobalamin binds cyanide to form cyanocobalamin.

4. Chelation:

- Binds metal ions into stable, excretable complexes.
- **Examples:** Deferoxamine (iron), EDTA (lead), Dimercaprol (arsenic, mercury).

5. Replenishment of Depleted Cofactors:

- Restores essential substrates or enzymes required for detoxification.
- **Example:** N-acetylcysteine replenishes glutathione in paracetamol toxicity.

6. Physiological Antagonism:

- Produces opposite physiological effects through a different mechanism.
- **Example:** Glucagon increases heart rate and contractility in β-blocker overdose.

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