

CLINICAL TOXICOLOGY

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LEARNING OBJECTIVES

- To understand the general principles of clinical toxicology
- To know general factors that influence toxicity
- To understand the initial approach to the poisoned patient in terms of setting immediate priorities
- To appreciate the necessity to conduct, as the first order of business, those procedures that evaluate and preserve vital signs

LEARNING OBJECTIVES

- To know what aspects of the physical examination and what diagnostic tests are to be conducted to evaluate the general type as well as the specifics of the poisoning
- To understand the goals of treatment e.g. to treat the patient, not the poison, promptly
- To know and understand strategies for treatment
- To know and understand specific approaches for reducing the body burden of various poisons

LEARNING OBJECTIVES

- To know how to counteract toxicological effects at receptor sites, if possible
- To know and understand important treatment contraindications that prevent serious injury or death of patients
- To be aware of newer approaches and treatment modalities
- To know where to rapidly obtain facts, specific antidotes, or other information on poison control needed immediately to treat the patient

Pediatric poisoning

- Since 1960, there has been a 95% decline in the number of pediatric poisoning deaths
 - child resistant packaging
 - heightened parental awareness
 - more sophisticated interventions

Common Causes of Death in the Acutely Poisoned Patient

- Comatose patient:
 - ▣ Loss of protective reflexes
 - ▣ Airway obstruction by flaccid tongue
 - ▣ Aspiration of gastric contents into tracheobronchial tree
 - ▣ Loss of respiratory drive
 - ▣ Respiratory arrest
- Hypotension – due to depression of cardiac contractility

Common Causes of Death in the Acutely Poisoned Patient

- Shock – due to hemorrhage or internal bleeding
- Hypovolemia – due to vomiting, diarrhea or vascular collapse
- Hypothermia – worsened by i.v. fluids administered rapidly at room temperature
- Cellular hypoxia – in spite of adequate ventilation and O₂ admin. – due to CN, CO or H₂S poisoning

Common Causes of Death in the Acutely Poisoned Patient

- Seizures – may result in pulmonary aspiration; asphyxia
- Muscular hyperactivity resulting in hyperthermia, muscle breakdown, myoglobinemia, renal failure, lactic acidosis and hyperkalemia
- Behavioral effects –traumatic injury from fights, accidents, fall from high places. Suicides, etc

Common Causes of Death in the Acutely Poisoned Patient

- Massive damage to a specific organ system:
 - ▣ Liver (acetaminophen; amanita phylloides [poison mushroom])
 - ▣ Lungs (paraquat)
 - ▣ Brain (domoic acid)
 - ▣ Kidney (ethylene glycol)
 - ▣ Heart (cobalt salts)
 - Note: death may occur in 48 – 72 hrs

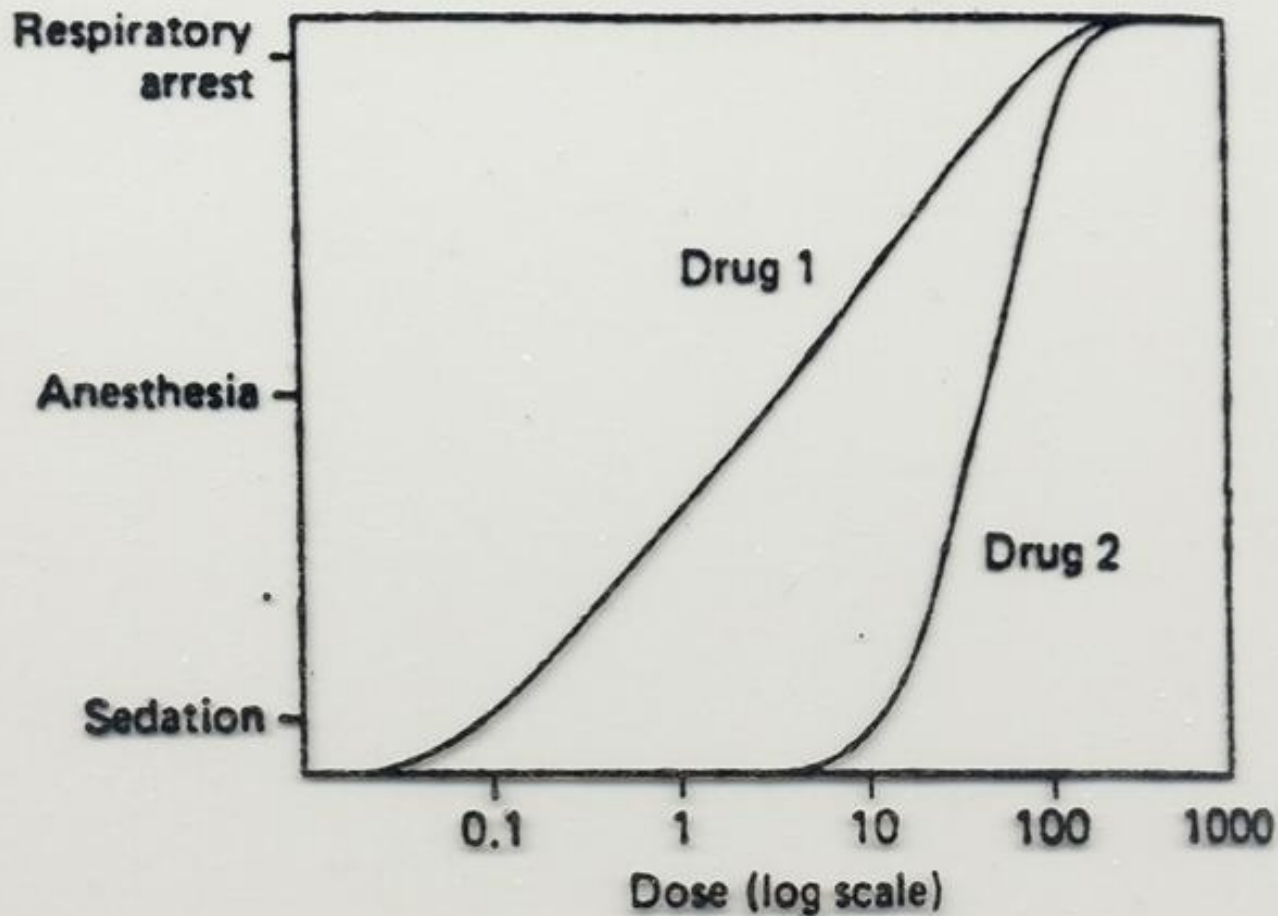


Figure Graded dose-response comparison of 2 sedative-hypnotic drugs. A much larger multiple of the normal prescription dose of drug 1 is required to cause respiratory arrest, ie, it is safer than drug 2.

APPROACH TO THE POISONED PATIENT

- History; Oral statements concerning details
- Call Poison Control Center re: drug labeling
- Initial physical examination
- Assessment of vital signs
- Eye examination
- CNS and mental status examination
- Examination of the skin
- Mouth examination
- Lab (clinical chemistry and x-ray procedures)
- Renal function tests
- Electrocardiogram (EKG or ECG)
- Other screening tests

Initial Assessment: Overview

- Treat the patient, not the poison
- Assessment triangle
 - ▣ General appearance (sleepy, obtunded, wired, etc)
 - ▣ Work of breathing (fast, slow, deep, shallow)
 - ▣ Circulation (hypertensive, hypotensive)
- ABCDs (airway, breathing, circulation, disability)
- IV access and monitors
- High Suspicion (Toxidrome: constellation of symptoms which are most likely to indicate the ingestion of a certain class of medication.)

TREATMENT OF ACUTE POISONING

- Treat the patient, not the poison", promptly
- Supportive therapy essential
- Maintain respiration and circulation – primary
- Judge progress of intoxication by:
 - Measuring and charting vital signs and reflexes

TREATMENT OF ACUTE POISONING

- - 1st Goal - keep concentration of poison as low as possible by preventing absorption and increasing elimination
- - 2nd Goal - counteract toxicological effects at effector site, if possible

PREVENTION OF ABSORPTION OF POISON

- Decontamination from skin surface
- Emesis: indicated after oral ingestion of most chemicals;
 - ▣ must consider time since chemical ingested

Contraindications of emesis:

- ingestion of corrosives such as strong acid or alkali;
- if patient is comatose or delirious;
- if patient has ingested a CNS stimulant or is convulsing
- if patient has ingested a petroleum distillate

PREVENTION OF ABSORPTION OF POISON

- Induce emesis in the following ways:
 - mechanically by stroking posterior pharynx;
 - use of syrup of ipecac, 1 oz followed by one glass of water
 - use of apomorphine parenterally

PREVENTION OF ABSORPTION OF POISON

- Gastric lavage: insert tube into stomach and wash stomach with water or $\frac{1}{2}$ normal saline to remove unabsorbed poison
- Contraindications are the same as for emesis except that the procedure should not be attempted with young children

PREVENTION OF ABSORPTION OF POISON

- Chemical Adsorption
 - activated charcoal will adsorb many poisons thus preventing their absorption
 - do not use simultaneously with ipecac if poison is excreted into bile in active form
 - adsorbent in intestines may interrupt enterohepatic circulation

PREVENTION OF ABSORPTION OF POISON

- Purgation
 - Used for ingestion of enteric coated tablets when time after ingestion is longer than one hour
 - Use saline cathartics such as sodium or magnesium sulfate
- Chemical Inactivation
 - Not generally done, particularly for acids or bases or inhalation exposure
 - For ocular and dermal exposure as well as burns on skin; treat with copious (plentiful) water

PREVENTION OF ABSORPTION OF POISON

- Alteration of biotransformation
- Interfere with metabolic conversion of compound to toxic metabolite
- Metabolism of some compounds produces highly reactive electrophilic intermediates; if nucleophiles present, toxicity is minimal; if nucleophiles depleted, toxicity results
- Increasing urinary excretion by acidification or alkalinization

PREVENTION OF ABSORPTION OF POISON

- Decreasing passive resorption from nephron lumen
- Diuresis
- Cathartics
- Peritoneal dialysis
- Hemodialysis
- Hemoperfusion

Table 1 Indications for hemodialysis (HD) and hemoperfusion (HP).

	Toxin	Procedure
Indicated immediately if significant intoxication	Ethylene glycol	HD
	Lithium	HD
	Methanol	HD
	Salicylate	HD
	Theophylline	HP
	Paraquat	HP
Indicated if supportive measures fail or if prolonged coma is expected	Digitoxin	HP
	Ethchlorvynol	HP
	Phenobarbital	HP
	Tricyclic antidepressants	HP
Not indicated	Amphetamines, PCP, cocaine	
	Benzodiazepines (chlordiazepoxide, diazepam)	
	Chlorpromazine, haloperidol, other antipsychotics	
	Digoxin	
	Glutethimide	
	Narcotics	
	Quinidine, procainamide	
	Short-acting barbiturates	

Antagonism of the absorbed poison

- If poisoning is due to agonist acting at receptors for which specific antagonist is available; antagonist may be available
- Drugs that stimulate antagonistic physiologic mechanisms may of little clinical value; titration difficult
- Use of antibodies

Strategies for Treatment of the Poisoned Patient

- Evaluate and stabilize vital signs
- Give supportive therapy, if needed
- Determine the type and specifics of the poison
- Time of exposure
- Determine the presumed current location of the poison
- Determine Volume of Distribution for the poison

Strategies for Treatment of the Poisoned Patient

- Use the drug dissociation constant, presumed pH based on location and the Henderson-Hasselbach equation to determine the ratio of ionized to non-ionized poison
- Determine the immediate (real time) risk or hazard for absorption
- Initiate body burden reduction procedures or specific antidotes based on the above information

Strategies for Treatment of the Poisoned Patient

- If volume of distribution is very large; do not waste time on any type of dialysis
- X-ray for location of enteric coated pills and use cathartics if in the stomach
- Use hypocholesteremics for poisons trapped in enterohepatic biliary system

SPECIFIC ANTIDOTES

Poison

Acetaminophen

Acetylcholinesterases, OP's,
physostigmine

Iron salts

Methanol, Ethylene glycol

Mercury, lead

Narcotic drugs

Anti/muscarinics-cholinergics

OP anticholinergics

Antidote

Acetylcysteine

Atropine

Deferoxime

Ethanol

Metal Chelators

Naloxone

Physostigmine

Praladoxime (2-PAM)