General Management of Poisoned Patients

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Epidemiology

Accidental and intentional poisoning from both licit and illicit substances remains a major cause of morbidity and mortality worldwide.

In the US, AAPCC reported over two million human exposure calls in 2018.

While the overall mortality rate reported by AAPCC was just under 0.07%, 31% of cases required managements at the healthcare facility, and 8.4% of cases required hospital admission.

Most cases involving children under age six involved nonintentional ingestion, whereas most fatalities in adults (age 20 and older) were suicidal.

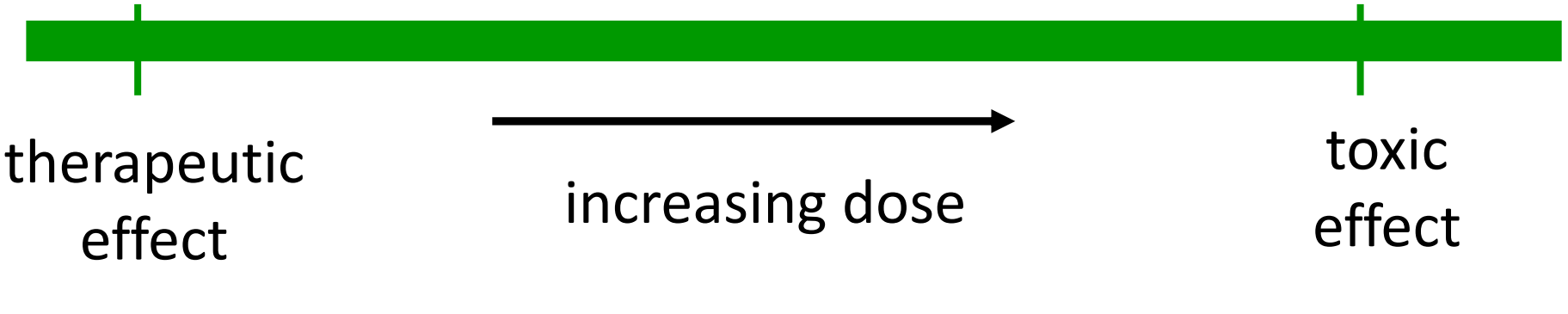
While females account for slightly more than one-half of all human exposures reported to US poison control centers, males account for just over one-half of all fatal ingestion.

Prevention is the key to reducing unintentional poisoning deaths. Pharmacists can that ensure medications are labeled correctly, anticipate potential drug interactions, and educate patients to use medications safely.

Paracelsus (1493-1541)
'Grandfather of Toxicology'

"All things are poison and nothing is without poison, only the dose permits something not to be poisonous."

"The dose makes the poison"



Cause of poisoning

- ✓ Accidental (46%)
  children less than 5 years and elderly
  inhalation of organophosphorus pesticides
- ✓ Deliberate (54%)
  suicidal attempts
- ✓ Homicidal (<1%)

Exposures routs

- ✓ Ingestion
- ✓ Inhalation
- ✓ Insufflation
- ✓ Injection
- ✓ Cutaneous and mucous membrane exposure

Substance most frequently involved in human poisoning

- Drugs : 61%
  - analgesics and pain killers (acetaminophen, aspirin, naproxen, celecoxib)
  - antidepressants (TCA)
  - sedative/hypnotics (Benzodiazepines)
  - cardiovascular dugs
  - opioids
- Cleaning substance: 12%
- Cosmetics and personal care products: 10%
- Foreign bodies: 5%
- Plants: 5%
- Bites and environments: 4%

Prevention

Key to reducing unintentional poisoning deaths:

Pharmacists can ensure that medication are **labeled correctly**, anticipate **potential drug interactions**, and **educate** patients to use medication safely.

Parents have the responsibility to ensure that poisons are placed in **childproof**, labeled containers stored in adult-only accessible areas to reduce pediatric exposures. **Nonfood storage.**

Teachers and healthcare providers can provide age-appropriate education to children about the dangers of poisons.

Criteria used to determine whether the exposure is nontoxic are:

- ✓ An **unintentional exposure** to a clearly identified single substance
- ✓ An **estimate of the dose** is known
- ✓ A **recognized information source** (e.g., a poison control center) confirms the substance as nontoxic in the reported dose.

TOXIDROMES

Substances belonging to **a particular pharmaceutical/chemical class** often produce **a cluster of symptoms and signs, or "toxidrome"**

Enabling the identification of potential toxins when a clear history is unavailable.

Toxidrome	Examples of Agents	Examination Findings (most common in bold)
Anticholinergic	Atropine, *Datura* spp., antihistamines, antipsychotics	**Altered mental status, mydriasis, dry flushed skin, urinary retention, decreased bowel sounds, hyperthermia, dry mucous membranes** Seizures, arrhythmias, rhabdomyolysis
Cholinergic	Organophosphate and carbamate insecticides Chemical warfare agents (Sarin, VX)	**Salivation, lacrimation, diaphoresis, vomiting, urination, defecation, bronchorrhea, muscle fasciculations, weakness** Miosis/mydriasis, bradycardia, seizures
Opioid	Codeine Heroin Morphine	**Miosis, respiratory depression, central nervous system depression** Hypothermia, bradycardia
Sedative/hypnotic	Benzodiazepines Barbiturates	**Central nervous system depression, ataxia, dysarthria** Bradycardia, respiratory depression
Serotonin	SSRIs MAOIs Tricyclic antidepressants Amphetamines Fentanyl St. John's wort	**Altered mental status, hyperreflexia and hypertonia (>lower limbs), clonus, tachycardia, diaphoresis** Hypertension, flushing, tremor
Sympathomimetic	Amphetamines Cocaine Cathinones	**Agitation, tachycardia, hypertension, hyperpyrexia, diaphoresis** Seizures, acute coronary syndrome

DIAGNOSTIC TESTING

A serum acetaminophen concentration is a routine screening test in poisoned patients. Early acetaminophen poisoning is often asymptomatic and does not have a readily identifiable toxidrome at the time when antidotal treatment is most efficacious.

An electrocardiogram is a useful test to detect cardiac conduction abnormalities and identify patients at increased risk of toxin-induced adverse cardiovascular events.

Measurement of **drug or toxin concentrations** in body fluids is not required in most poisonings, but in some exposures, measurement of serum drug concentrations does influence management.

Toxicologic screening tests of the **urine and/or blood** can be done in a central laboratory or performed with point-of-care drug screening assays.

Toxicological screening tests of urine

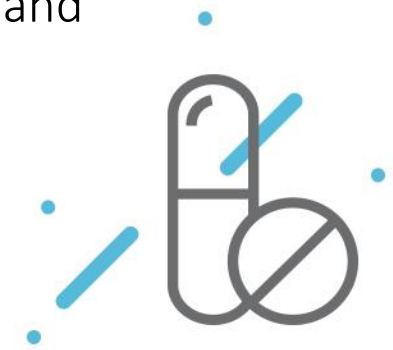
Urine drug screens most often use **enzyme immunoassays** to detect typical drugs within each class.

Cross-reactivity is common and some drugs within the class may not be detected.

Dilute urine can make it difficult to detect low levels.

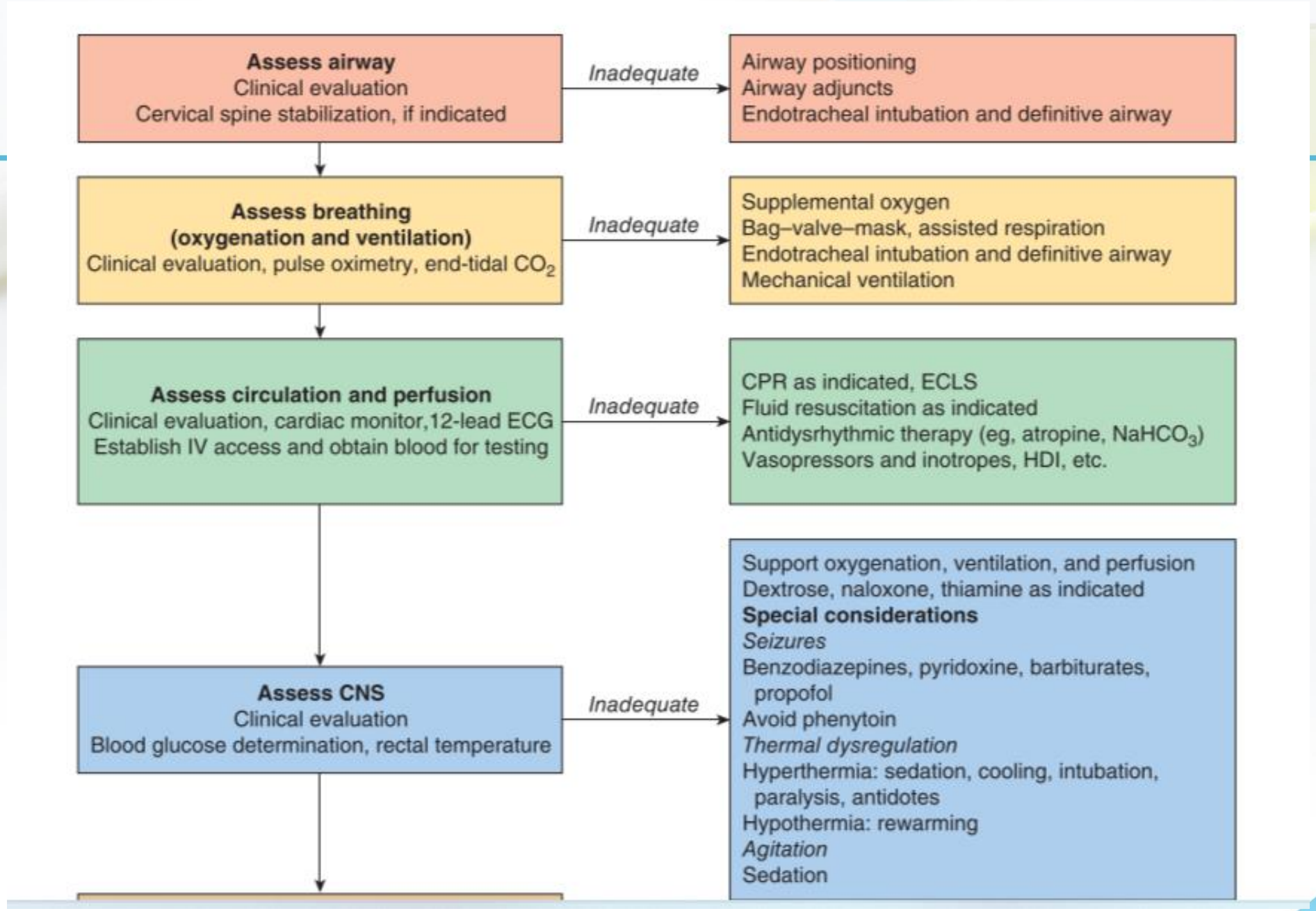
Because some drugs are present in urine for an extended period of time , the **positive test** may **not be** related to the current clinical condition.

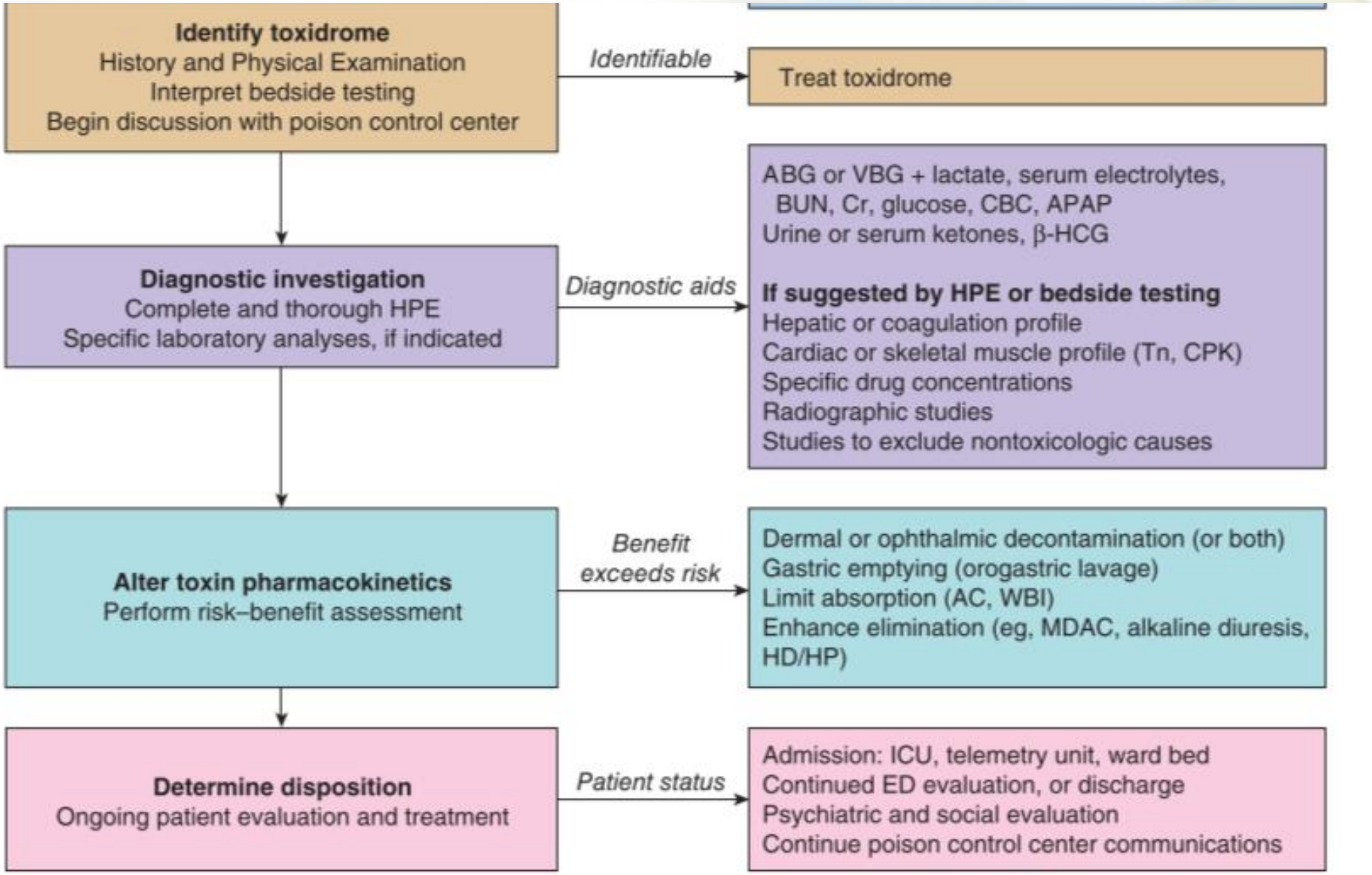
Urine drug screen results **seldom** influence patient management in most adult overdoses and poisoning.



Management principles

- ✓ Supportive care
- ✓ Gastrointestinal decontamination
- ✓ Urinary alkalization
- ✓ Hemodialysis and hemoperfusion
- ✓ antidotes


Assess airway
Clinical evaluation
Cervical spine stabilization, if indicated
Inadequate
Airway positioning
Airway adjuncts
Endotracheal intubation and definitive airway
Assess breathing
(oxygenation and ventilation)
Clinical evaluation, pulse oximetry, end-tidal CO_2
Inadequate
Supplemental oxygen
Bag–valve–mask, assisted respiration
Endotracheal intubation and definitive airway
Mechanical ventilation
Assess circulation and perfusion
Clinical evaluation, cardiac monitor,12-lead ECG
Establish IV access and obtain blood for testing
Inadequate
CPR as indicated, ECLS
Fluid resuscitation as indicated
Antidysrhythmic therapy (eg, atropine, $NaHCO_3$)
Vasopressors and inotropes, HDI, etc.
Assess CNS
Clinical evaluation
Blood glucose determination, rectal temperature
Inadequate
Support oxygenation, ventilation, and perfusion
Dextrose, naloxone, thiamine as indicated
Special considerations
Seizures
Benzodiazepines, pyridoxine, barbiturates, propofol
Avoid phenytoin
Thermal dysregulation
Hyperthermia: sedation, cooling, intubation, paralysis, antidotes
Hypothermia: rewarming
Agitation
Sedation


Identify toxidrome
History and Physical Examination
Interpret bedside testing
Begin discussion with poison control center
Identifiable
Treat toxidrome
Diagnostic investigation
Complete and thorough HPE
Specific laboratory analyses, if indicated
Diagnostic aids
ABG or VBG + lactate, serum electrolytes, BUN, Cr, glucose, CBC, APAP
Urine or serum ketones, β-HCG
If suggested by HPE or bedside testing
Hepatic or coagulation profile
Cardiac or skeletal muscle profile (Tn, CPK)
Specific drug concentrations
Radiographic studies
Studies to exclude nontoxicologic causes
Alter toxin pharmacokinetics
Perform risk–benefit assessment
Benefit exceeds risk
Dermal or ophthalmic decontamination (or both)
Gastric emptying (orogastric lavage)
Limit absorption (AC, WBI)
Enhance elimination (eg, MDAC, alkaline diuresis, HD/HP)
Determine disposition
Ongoing patient evaluation and treatment
Patient status
Admission: ICU, telemetry unit, ward bed
Continued ED evaluation, or discharge
Psychiatric and social evaluation
Continue poison control center communications

Resuscitation

The first priority in any poisoned patient.

After resuscitation, **a structured risk assessment** is used to identify patients who may be nefit from an **antidote**, **decontamination**, or **enhance elimination techniques**.

Most patients only require provision of good **supportive care** during a period of **observation** in an appropriate environment.

Supportive care

- ✓ Vital signs, mental status, and pupil size
- ✓ ABC: airway, breathing, circulation
- ✓ cardiac monitoring, ECG
- ✓ Intravenous access
- ✓ cervical immobilization if suspect trauma
- ✓ Rule out hypoglycaemia

Hypotension

Compromised airway patency or reduced respiratory drive may lead to inadequate ventilation; provision of **a mechanical airway** and **assisted ventilation** is vital in these circumstances.

IV crystalloid bolus (10-20 ml/Kg) is fist line treatment of hypotension.

Since most patients without toxin induced fluid loss are generally not fluid depleted, avoid administration of excess fluid.

Persisting hypotension:

- May respond to a specific antidote.
- Administration of an inotropic agents

*inotrope choice is guided by knowledge of the **toxin's toxicodynamic** properties and assessment of **circulatory status** (e.g., cardiac pump failure vs. vasodilatory shock)

Hypoglycemia

IV dextrose

Patients at risk of Wernicke's encephalopathy also require **thiamine**, but do not require t hat it be administered before the dextrose.

*Altered mental status when hypoglycemia can not be excluded is an indication for IV dextrose.

"Coma Cocktail"

- ✓ D- 50% dextrose
- ✓ O- oxygen at high flow
- ✓ N- naloxone: 0.4 to 2 mg IV
- ✓ T- thiamine: 100 mg IV

Cardiac arrhythmias

In general, **antidysrhythmic drugs** are **not first-line treatment** for toxin-induced dysrhythmias, as most antidysrhythmic drugs have pro-dysrhythmic and **negative inotropic properties.**

Most toxin-induced dysrhythmias responded to correction of hypoxia, metabolic/acid-base abnormalities, and administration of antidote (e.g., digoxin Fab)

Sodium bicarbonate is administered for sodium channel blocker toxicity (e.g., TCA toxicity) with cardiovascular complications, such as wide QRS complex.

Pace maker

Seizures

First line: Titrated doses of **IV benzodiazepines**

*exception: Isoniazide-induced seizure: **pyridoxine**

Correction of metabolic disorders, such as hypoglycemia and hyponatremia.

Second line agents for benzodiazepine-resistance seizures : **Propofol, barbiturates**

A small study provided evidence for safety of **Levetiracetam** for treatment of toxin-induced seizures.

No role for Phenytoin in the treatment of toxin-induced seizure

Agitation

Physical restrained

First line: **Titrated doses of benzodiazepines** (large doses may be required, in monitored setting)

Second line: **antipsychotic agents** (disadvantages: anticholinergic and extrapyramidal effects)

Hyperthermia and Hypothermia

Patients with core temperatures of > 39°C require **aggressive active cooling measures** to prevent complications such as rhabdomyolysis, organ failure, and DIC.

Sedation, neuromuscular paralysis, and intubation are required if active cooling measures are ineffective.

Several **toxidromes** associated with hyperthermia are treated with specific agents:

- ✓ Sympathomimetic (benzodiazepines)
- ✓ Serotonin (cyproheptadine)
- ✓ Neuromuscular malignant syndrome (bromocriptine)

Hyperthermia and Hypothermia

A core temperatures of < 32°C is an indication for active rewarming.

Drug induced coma with subsequent **immobility** and **environmental exposure** or **inherent drug toxicity** (opioids, phenothiazines, ethanol) may produce hypothermia.

Decontamination

Decontamination is required for toxic exposures affecting large dermal areas.

Healthcare providers **wearing personal protective equipment** (if indicated) or observing universal precautions (gown, gloves, eye protection) should assist with undressing and washing the patient using co pious amounts of water.

Contaminated clothing is collected, bagged, and properly disposed.

Decontamination ideally occurs in a separate area adjacent to the ED, minimizing cross-contamination.

Ocular decontamination

Eye exposures may require local anesthetic (e.g., 0.5% tetracaine) instillation and lid retractors to facilitate copious irrigation with crystalloid solution.

Alkalis produce greater injury than acids due to deep tissue penetration via liquefaction so that prolonged irrigation (1-2 h) may be required.

Ten minutes after irrigation, conjunctival sac PH is tested. Irrigation continues until PH is between 7.2 and 7.4.

Ophthalmologic consultation

Gastrointestinal decontamination

Patients who have ingested potentially life threatening quantities of toxin may be considered for gastrointestinal decontamination if poisoning have been recent.

The approach to GI decontamination must be individualized. No decontamination method is completely free of risks. The indications and contraindications for GI decontamination must be well defined for each patient, and the method of choice must depend largely on what was ingested, how much was ingested, who ingested it, and when it was ingested.

Induction of **emesis (ipecac syrup)** is no longer used.

1-Activated Charcoal

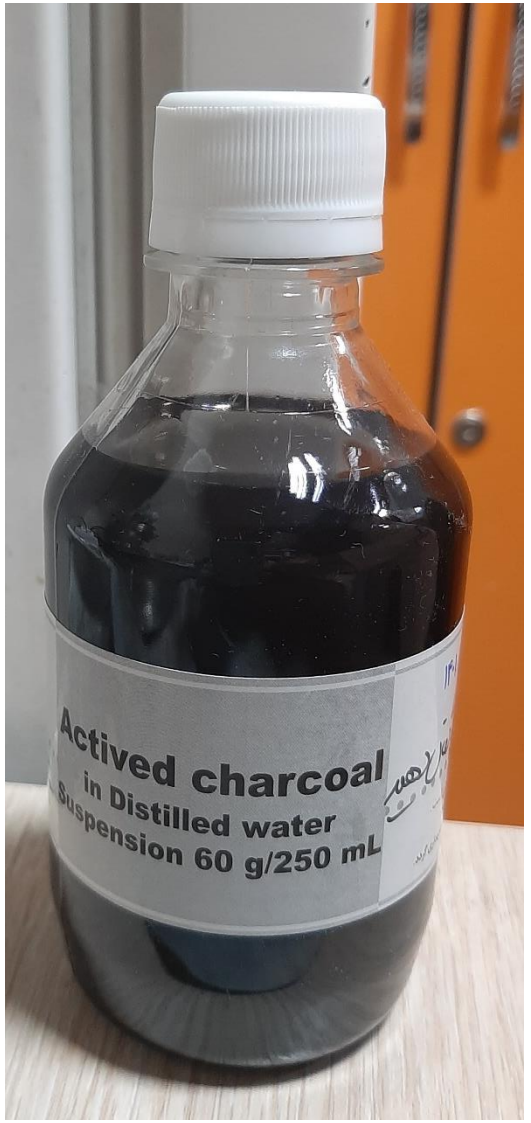
A highly porous substance, which is suspended in solution and given PO as a slurry. Toxins within the gastrointestinal lumen are adsorbed onto the activated charcoal and carried through the gastrointestinal tract, limiting absorption.

Efficacy decreases with time and current guidelines do not advocate use more than **1 hour** after overdose.

However, use after a long interval may be reasonable when a **delayed release preparation** has been taken or when **gastric emptying is delayed** (e.g., anticholinergics).

Activated charcoal does not effectively adsorb **metals, corrosives, and alcohols.**

Laxatives is generally given to reduce the risk of constipation by charcoal.



Multidose activated charcoal

Multidose activated charcoal increases elimination of toxins with enteroenteric, enterohepatic, or enterogastric recirculation. Lipophilic drugs with low volume of distribution, protein binding, and molecular weight may pass down a concentration gradient between intravascular space and activated charcoal in the gut lumen.

May also adsorb residual intraluminal toxins; this is more likely for substances slowing gastric motility or forming bezoars.

May be administered by an orogastric or nasogastric tube to intubated patients.

Regular aspiration of stomach contents helps avoid gastric distention.

Not be given when bowel sounds are absent.

Activated Charcoal	Adults 50 grams orally, children 1 gram/kg orally
Indications	Ingestion within the previous hour of a toxic substance known to be adsorbed by activated charcoal, where the benefits of administration are judged to outweigh the risks
Contraindications	Nontoxic ingestion Toxin not adsorbed by activated charcoal Recovery will occur without administration of activate charcoal Unprotected airway Corrosive ingestion Possibility of upper gastrointestinal perforation
Complications	Vomiting Aspiration of the activated charcoal Impaired absorption of orally administered antidotes

TABLE 176-8 Indications, Contraindications, and Complications of Enhanced Elimination Procedures

Multidose Activated Charcoal	Initial dose: 50 grams (1 gram/kg children), repeat dose 25 grams (0.5 gram/kg children) every 2 hours
Indications	Carbamazepine coma (reduces duration of coma) Phenobarbital coma (reduces duration of coma) Dapsone toxicity with significant methemoglobinemia Quinine overdose Theophylline overdose if hemodialysis/hemoperfusion unavailable
Contraindications	Unprotected airway Bowel obstruction Caution in ingestions resulting in reduced gastrointestinal motility
Complications	Vomiting Pulmonary aspiration Constipation Charcoal bezoar, bowel obstruction/perforation
Urinary Alkalinization	

2- Gastric aspiration and lavage

It is infrequently indicated in acute poisoning

Not effective than activated charcoal

Complication are common especially aspiration

Use is justified for poisons which are not absorbed by activated charcoal.

Orogastric Lavage	
Indications	Rarely indicated Consider for recent (<1 hour) ingestion of life-threatening amount of a toxin for which there is no effective treatment once absorbed
Contraindications	Corrosive/hydrocarbon ingestion Supportive care/antidote likely to lead to recovery Unprotected airway Unstable, requiring further resuscitation (hypotension, seizures)
Complications	Aspiration pneumonia/hypoxia Water intoxication Hypothermia Laryngospasm Mechanical injury to gastrointestinal tract Time consuming, resulting in delay instituting other definitive care

3- Whole-Bowel Irrigation

Polyethylene glycol is an osmotically balanced electrolyte solution.

Nonsurgical treatment of asymptomatic **body drug packers** using whole-bowel irrigation is increasingly common.

An **antiemetic** such as the prokinetic agent metoclopramide may be required to control polyethylene glycol–induced gastric distension and vomiting.

The endpoint of whole-bowel irrigation treatment **is clear rectal effluent** and imaging demonstrating absence of foreign bodies.

Whole-Bowel Irrigation	Polyethylene glycol 2 L/h in adults, children 25 mL/kg per hour (maximum 2 L/h)
Indications (potential)	Iron ingestion >60 milligrams/kg with opacities on abdominal radiograph Life-threatening ingestion of diltiazem or verapamil Body packers or stuffers Slow-release potassium ingestion Lead ingestion (including paint flakes containing lead) Symptomatic arsenic trioxide ingestion Life-threatening ingestions of lithium
Contraindications	Unprotected airway Gastrointestinal perforation, obstruction or ileus, hemorrhage Intractable vomiting Cardiovascular instability
Complications	Nausea, vomiting Pulmonary aspiration Time consuming; possible delay instituting other definitive care

URINARY ALKALINIZATION

Alkaline urine (PH>7.5) favors ionization of **acidotic drugs (e.g. salicylates, methotrexate)** within renal tubules, preventing resorption of the ionized drug back across the renal tubular epithelium and enhancing elimination through the urine.

Hypokalemia will reduce the effectiveness of urinary alkalinization.

The primary indication for urinary alkalinization is moderate to severe **salicylate toxicity** when criteria for hemodialysis have not been met.

Although urinary acidification can enhance the elimination of weak bases including amphetamines and phencyclidine, associated risks (e.g., rhabdomyolysis) outweigh potential benefit.

Urinary Alkalinization	
Indications	Moderate to severe salicylate toxicity not meeting criteria for hemodialysis Phenobarbital (multidose activated charcoal superior) Chlorophenoxy herbicides (2-4-dichlorophenoxyacetic acid and mecoprop): requires high urine flow rate 600 mL/h to be effective Chlorpropamide: supportive care/IV dextrose normally sufficient
Contraindications	Preexisting fluid overload Renal impairment Uncorrected hypokalemia
Complications	Hypokalemia Volume overload Alkalemia Hypocalcemia (usually mild)

Protocol for urinary alkalization in adults with normal renal function

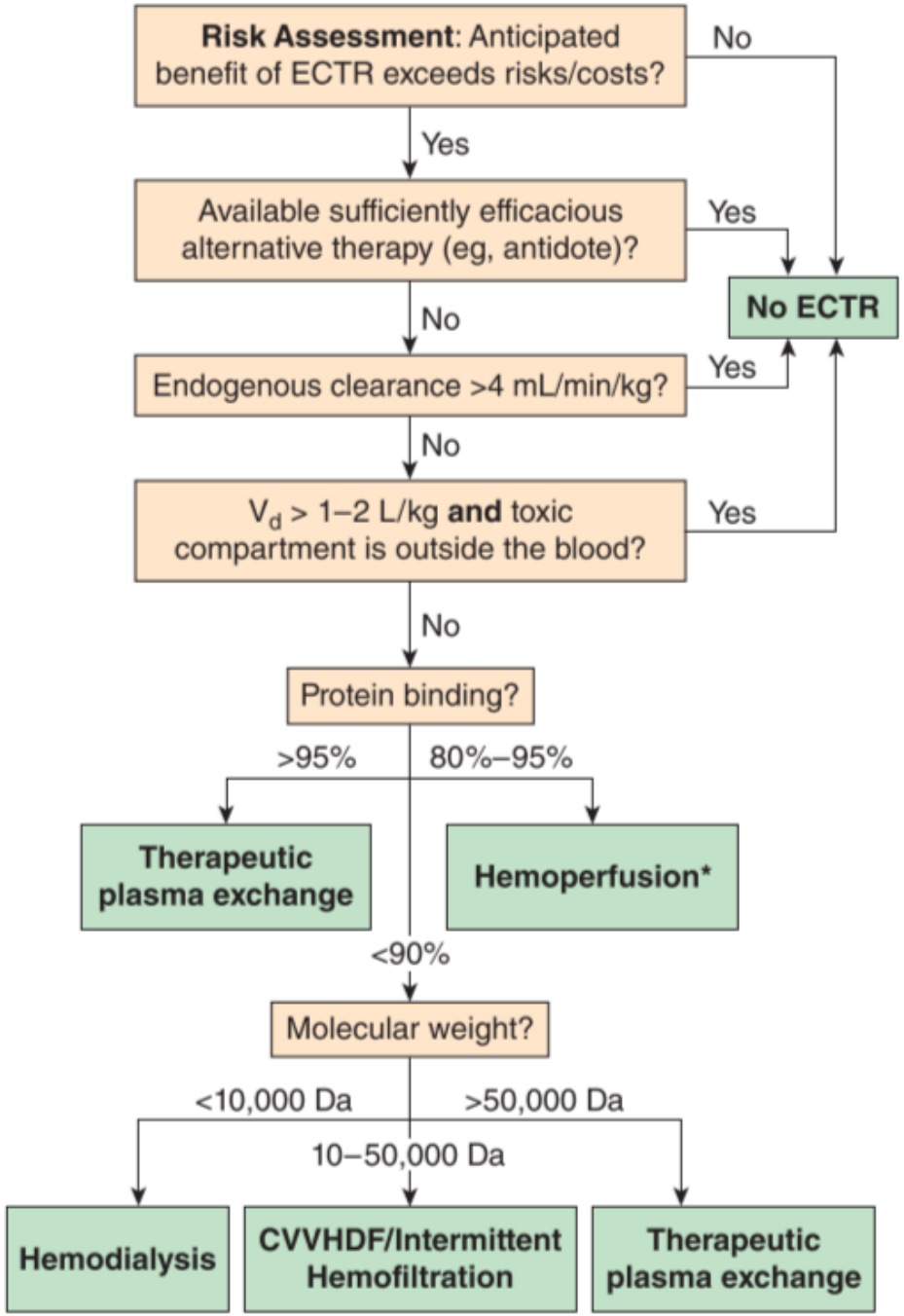
- ✓ Correct any existing hypokalemia.
- ✓ Administer a 1 to 2 mEq/kg IV sodium bicarbonate bolus.
- ✓ Infuse 100 mEq of sodium bicarbonate mixed with 1 L of D5W at 250 mL/h.
- ✓ 20 mEq of potassium chloride may be added to the solution to maintain normokalemia.
- ✓ Monitor serum potassium and bicarbonate every 2 to 4 hours to detect hypokalemia or excessive serum alkalinization.
- ✓ Check urine pH regularly (every 15 to 30 minutes), aiming for a pH of 7.5 to 8.5.
- ✓ A further IV bolus of 1 mEq/kg of sodium bicarbonate may be necessary if sufficient alkalinization of the urine is not achieved.

EXTRACORPOREAL REMOVAL

Extracorporeal removal techniques, including **hemodialysis**, **hemoperfusion**, and **continuous renal replacement therapies**, have limited indications in poisoned patients.

A toxin must possess a number of properties to be effectively removed :

- ✓ low volume of distribution (<1.0 L/kg)
- ✓ low molecular weight (<500 Da)
- ✓ relatively low protein binding
- ✓ low endogenous clearance.
- ✓ In general, extracorporeal removal must improve endogenous clearance rate by >30% to be clinically beneficial



Hemodialysis

Extracorporeal removal techniques including high-flux hemodialysis are constantly evolving, so discussion with an intensivist or nephrologist may be beneficial when this approach is considered.

Hemodialysis	Movement of solute down a concentration gradient across a semipermeable membrane	
Toxin requirements	Low volume of distribution, low protein binding, low endogenous clearance, low molecular weight	
Indications	**Life-threatening poisoning by:**	Methanol/ethylene glycol
	Lithium	Metformin-induced lactic acidosis
	Metformin lactic acidosis	Potassium salts
	Phenobarbital	Theophylline
	Salicylates	
	Valproic acid	
Contraindications	Hemodynamic instability	Poor vascular access
	Infants (generally)	Significant coagulopathy

Hemoperfusion

Hemoperfusion uses a charcoal (or other adsorbent) filter, which comes into direct contact with blood, partially overcoming molecular weight and protein-binding limitations.

Hemoperfusion	Movement of toxin from blood, plasma, or plasma proteins onto a bed of activated charcoal (or other adsorbent)	
Toxin requirements	Low volume of distribution, low endogenous clearance, bound by activated charcoal	
Indications	**Life-threatening poisoning caused by:** Theophylline (high-flux hemodialysis is an alternative) Carbamazepine (multidose activated charcoal or high-efficiency hemodialysis also effective) Paraquat (theoretical benefit only if instituted early after exposure)	
Contraindications	Hemodynamic instability Infants (generally) Poor vascular access	Significant coagulopathy Toxin not bound to activated charcoal

Continuous renal replacement therapies

Continuous renal replacement therapies (including venovenous hemofiltration and venovenous hemodiafiltration) are widely available and easily instituted in most hospitals

Continuous renal replacement therapy can be used if hemodialysis or hemoperfusion is unavailable or will not be tolerated (e.g., due to hypotension).

Continuous Renal Replacement Therapies	Movement of toxin and solute across a semipermeable membrane in response to hydrostatic gradient. Can be combined with dialysis.
Indications (potential)	Life-threatening ingestions of toxins when hemodialysis or hemoperfusion is indicated, but is unavailable, or hemodynamic instability precludes their utilization
Contraindications	Hemodialysis or hemoperfusion is available Poor vascular access Significant coagulopathy

Antidotes

TABLE 176-2 Common Antidotes Used in Resuscitation of the Acutely Poisoned Patient

Antidote	Pediatric Dose	Adult Dose	Indication
Calcium chloride 10% 27.2 milligrams/mL elemental Ca	0.2–0.25 mL/kg IV	10 mL IV	Calcium channel antagonists
Calcium gluconate 10% 9 milligrams/mL elemental Ca	0.6–0.8 mL/kg IV	10–30 mL IV	Hypermagnesemia Hypocalcemia
Cyanide antidote kit Amyl nitrite	Not typically used	1 ampule O_2 chamber of ventilation bag 30 s on/30 s off	Cyanide Hydrogen sulfide (use only sodium nitrite)
Sodium nitrite (3% solution)	0.33 mL/kg IV	10 mL IV	Cyanide
Sodium thiosulfate (25% solution)	1.65 mL/kg IV	50 mL IV	Cyanide
Dextrose (glucose)	0.5 gram/kg IV	1 gram/kg IV	Insulin Oral hypoglycemics
Digoxin Fab Acute toxicity	1–2 vials IV	5–10 vials	Digoxin and other cardioactive steroids
Flumazenil	0.01 milligram/kg IV	0.2 milligram IV	Benzodiazepines

Glucagon	50–150 micrograms/kg IV	3–10 milligrams IV	Calcium channel blockers β-Blockers
Hydroxocobalamin	70 milligrams/kg IV (maximum 5 grams). Can be repeated up to 3 times. Administer with sodium thiosulfate.		Cyanide Nitroprusside
IV lipid emulsion 20%	1.5 mL/kg IV bolus over 1 min (may be repeated two times at 5-min intervals), followed by 0.25 mL/kg per minute	100-mL IV bolus over 1 min, followed by 400 mL IV over 20 min	Local anesthetic toxicity Rescue therapy for lipophilic cardiotoxins
Methylene blue	1–2 milligrams/kg IV Neonates: 0.3–1.0 milligram/kg IV	1–2 milligrams/kg IV	Oxidizing toxins (e.g., nitrites, benzocaine, sulfonamides)
Naloxone	As much as required Start: 0.01 milligram IV	As much as required Start: 0.1–0.4 milligram IV	Opioids Clonidine
Pyridoxine	Gram for gram if amount isoniazid ingested is known		Isoniazid *Gyromitra esculenta* Hydrazine
	70 milligrams/kg IV (maximum 5 grams)	5 grams IV	
Sodium bicarbonate	1–2 mEq/kg IV bolus followed by 2 mEq/kg per h IV infusion		Sodium channel blockers Urinary alkalinization
Thiamine	5–10 milligrams IV	100 milligrams IV	Wernicke's syndrome Wet beriberi

Although the proper use of antidotes is important, only a few are indicated before cardiopulmonary stabilization:

- ✓ Naloxone for opiate toxicity
- ✓ Cyanide antidotes for cyanide toxicity
- ✓ Atropine for organophosphate poisoning

DISPOSITION

Planning for patient disposition from the ED should be part of initial risk assessment.

Admission is indicated if the patient has persistent and/or severe toxic effects or will require a prolonged course of treatment.
In most cases, a 6-hour observation period is sufficient to exclude the development of serious toxicity.

Onset of clinical toxicity can be delayed after a number of exposures, including (but not limited to) modified-release preparations of calcium channel antagonists, and selective norepinephrine reuptake inhibitors (tramadol, venlafaxine); hence a period of extended observation is indicated.

Patients who have deliberately self-poisoned require appropriate mental health assessment before - disposition.

References

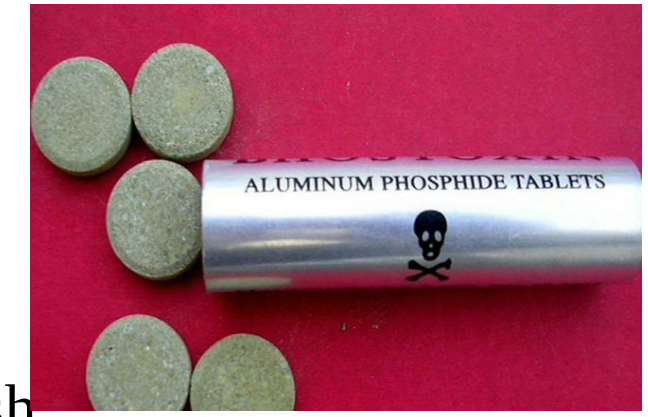
- ✓ Goldfrank's Toxicologic Emergencies, Eleventh Edition
- ✓ Tintinalli's Emergency Medicine: A Comprehensive Study Guide, 8th edition
- ✓ Critical Care Toxicology: Diagnosis and Management of the Critically Poisoned Patient
- ✓ UpTodate

- **Aluminium phosphide (ALP) Intoxicatio n**

History

The first large series describing the human health hazards of t oxic exposure to aluminum phosphide came from Northern Ind ia in 1985

Aluminium phosphide (ALP) : Pesticide (Rice Tablet)



- A greenish-gray tablet 3 g that has a garlic odor or decaying fish
- A standard 3 g tablet of ALP liberates approximately 1 g of phosphine gas
- Phosphide products have a very high mortality rate (30–100%)
- In a 70-kg individual, 150-500 mg of ALP has been reported as the lethal dose
- Air phosphine level of 50 mg/L (50 ppm) may be dangerous for health. Moreover, 40 0–600 mg/L phosphine level in the air may lead to death after 30 min

Herbal Tablet as Pesticide

Mechanisms of PH3-related Toxicity

- Interference with enzymatic function and synthesis of proteins
- Blockade of the electron transport chain and oxidative phosphorylation through noncompetitive inhibiti on of cytochrome-c oxidase.
- Phosphine gas decreases the activities of mitochondrial complexes I, II,III, IV.
- Inhibition of catalase, induction of superoxide dismutase, and reduction of the glutathione (GSH) conce ntration

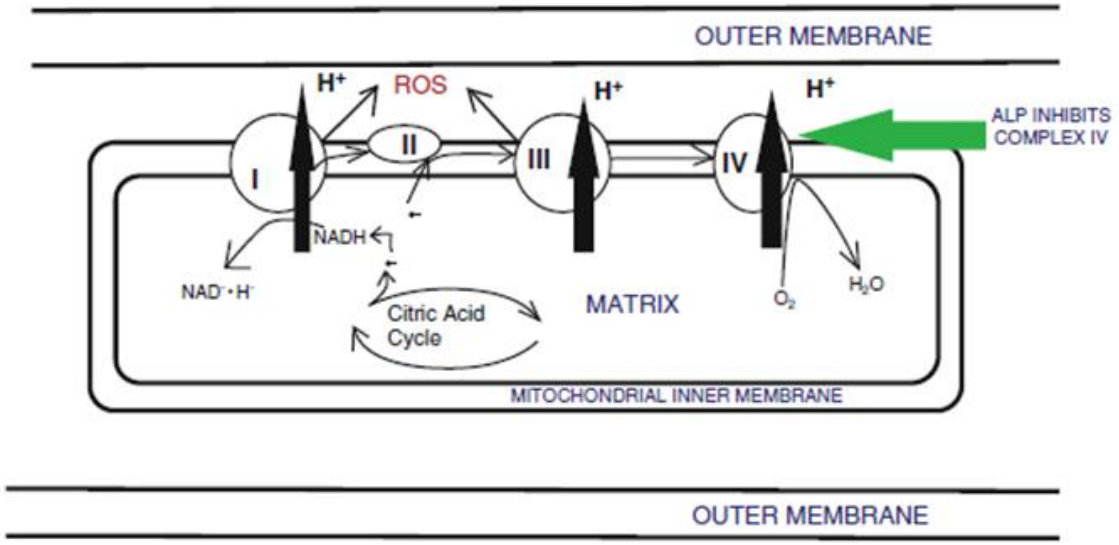


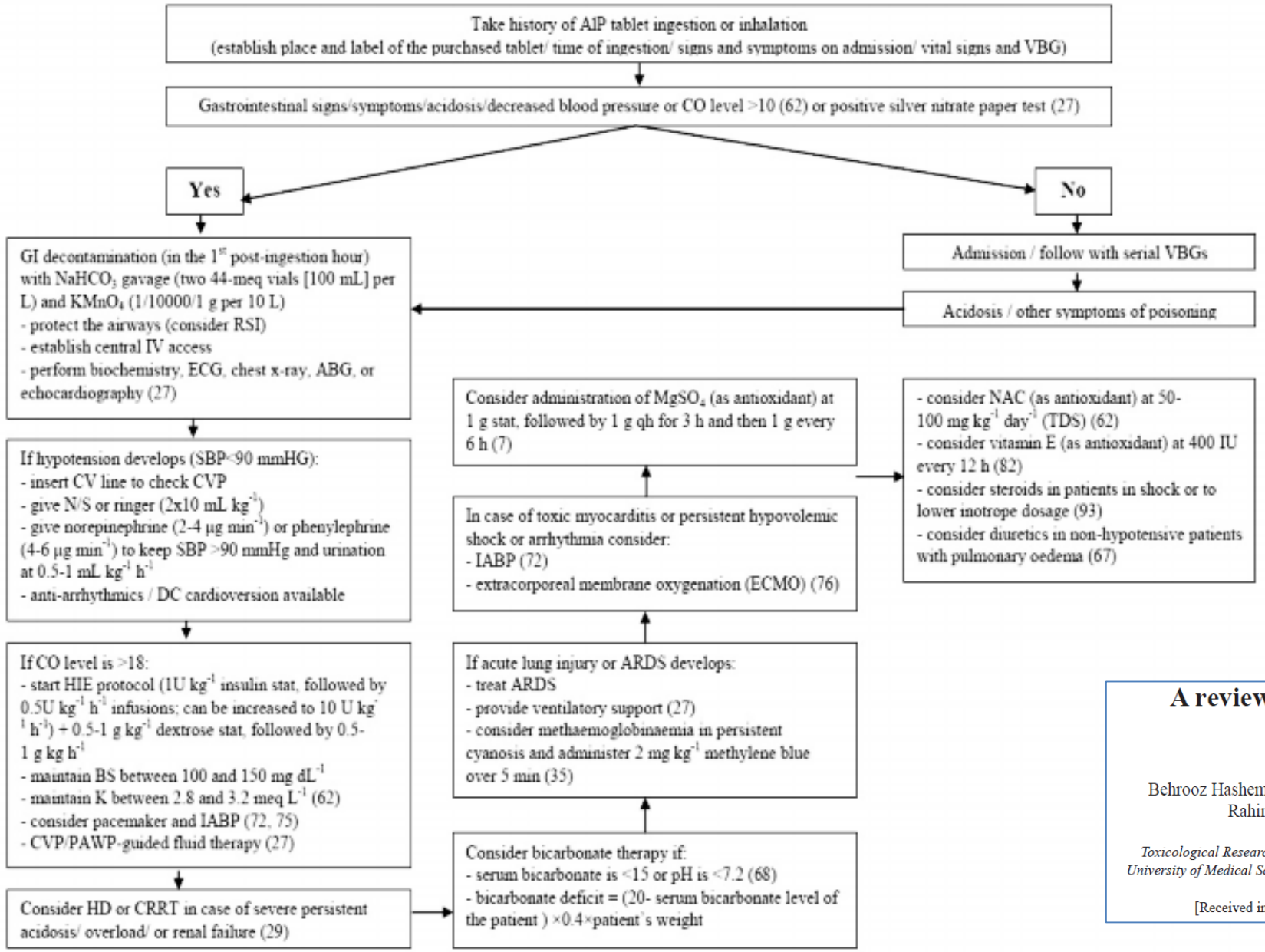
Fig. 1 Inhibition of mitochondrial respiration by ALP (From http://medcraveonline.com/JACCOA/images(Figure/JACCOA-02-00068-g001.png under a Creative Commons licence)

Clinical Manifestations ALP Intoxication

- Dependent on the dose, Route of entry, a nd Time since exposure

Table 1 Clinical features of phosphide poisoning

Following ingestion
Gastrointestinal: nausea, vomiting, epigastric discomfort, retrosternal burning, diarrhea
Cardiovascular: hypotension, shock, arrhythmias
Respiratory: tachypnea, cyanosis, adult respiratory distress syndrome
Hepatic: tender hepatomegaly, jaundice, elevated transaminases
Renal: oliguria, acute renal failure
Central nervous system: altered sensorium, restlessness, coma
Metabolic: metabolic acidosis, hypomagnesemia, hypermagnesemia, hypokalemia
Following inhalation
Chest tightness, cough, shortness of breath, and pulmonary edema if severe exposure



A review of aluminium phosphide poisoning and a flowchart to treat it

Behrooz Hashemi-Domeneh[1,2], Nasim Zamani[1,2], Hossein Hassanian-Moghaddam[1,2], Mitra Rahimi[1,2], Shahin Shadnia[1,2], Peyman Erfantalab[1,2], and Ali Ostadi[1,2]

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Melatonin

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On the Mechanisms of Melatonin in Protection of Aluminum Phosphide Cardiotoxicity

Mohammad Hossein Asghari [1 2], Milad Moloudizargari [3], Maryam Baeeri [4], Amir Baghaei [5], Mahban Rahimifard [4], Reza Solgi [6], Abbas Jafari [7], Hamed Haghi Aminjan [1], Shokoufeh Hassani [4], Ali Akbar Moghadamnia [2], Seyed Nasser Ostad [1], Mohammad Abdollahi [8 9]

- Mitochondria are the main target of AlP
- Ameliorate AlP-induced cardiotoxicity associated with mitochondrial dysfunction

- Antioxidant activity (reactive oxygen species (ROS) scavenger)
- Increased ATP production
- Prevention of cardiomyocyte apoptosis (cardioprotective)

- Animal study: at doses of 10 - 50 mg/kg

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JPP Journal of Pharmacy And Pharmacology
Review

A review of the protective role of melatonin during phosphine-induced cardiotoxicity: focus on mitochondrial dysfunction, oxidative stress and apoptosis

Mohammad Hossein Asghari[a,c], Mohammad Abdollahi[b,c], Marcos Roberto de Oliveira[d] and Seyed Mohammad Nabavi[e]

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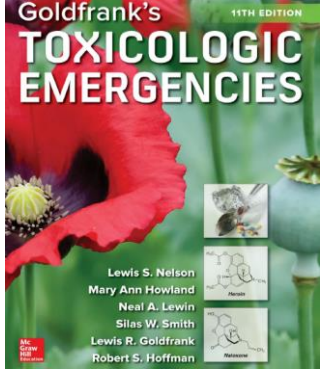
Liothyronine



Article

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Therapeutic effects of oral liothyronine on aluminum phosphide poisoning as an adjuvant therapy: A clinical trial

MH Goharbari[1], F Taghaddosinejad[2], M Arefi[3], M Sharifzadeh[1], M Mojtahedzadeh[4], S Nikfar[5], M Baeeri[1], M Rahimifard[1] and M Abdollahi[1,6]

- 50 μg oral in the first 6 hours of AlP-poisoning (Clinical trial 2017 baharloo)
  - ❑ Decrease lipid peroxidation & improvement other oxidative stress parameters & increase anti oxidant capacity
  - ❑ Improve systolic blood pressure & hemodynamic status in cardiogenic shock
  - ❑ Improve arterial blood pH
  - ❑ There is inadequate evidence to recommend routine utilization at this time

RBC in ALP-intoxication

RESEARCH ARTICLE

Fresh red blood cells transfusion protects against aluminum phosphide-induced metabolic acidosis and mortality in rats

Nastaran Rahimi[1,2], Amir Hossein Abdolghaffari[1,3], Alireza Partoazar[1], Nina Javadian[1,2], Tara Dehpour[4], Ali R. Mani[5], Ahmad R. Dehpour[1,2]*

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Table 2. Effects of fresh packed red blood cells (RBC) on blood pH, P_{CO2}, plasma electrolytes and troponin I. Values are expressed as mean ± S.E.M.

	pH	P_{CO2} (mmHg)	HCO_3^- (mM)	Na^+ (mM)	K^+ (mM)	Ca^{2+} (mM)	Troponin I (ng/ml)
Control	7.38 ± 0.02	50.1 ± 1.7	21.01 ± 1.41	148.3 ± 2.7	4.8 ± 0.4	0.98 ± 0.08	0.03 ± 0.002
AlP	6.77 ± 0.06***	40.8 ± 1.8**	7.75 ± 1.53***	139.0 ± 1.4***	4.6 ± 0.5	0.88 ± 0.07*	1.03 ± 0.02***
AlP + RBC	7.33 ± 0.07###	47.7 ± 2.1#	20.5 ± 3.08###	147.1 ± 4.5###	4.9 ± 0.7	1.02 ± 0.07##	0.03 ± 0.003###

* $P < 0.05$;

** $P < 0.01$;

*** $P < 0.001$ compared to control group;

# $P < 0.05$;

$P < 0.01$;

for $P < 0.001$ compared to AlP-treated group.

Conclusions

Our results showed that fresh RBC transfusion could ameliorate metabolic acidosis and enhance survival in AlP-poisoned rat. We assume that an increase in pool of RBCs may modulate acid-base balance or potentially chelate AlP-related toxic intermediates via phosphine-hemoglobin interaction.

The main mechanism of phosphine- induced cytotoxicity was by depletion of energy content of the cell

DHA (a non-toxic sugar) as an ATP supplier prevented AlP cytotoxicity by

Dihydroxyacetone

- Elevation of ATP production in glycolysis process
- Improve blood pressure
- Prevent cellular damage through improvement of cardiovascular f unction
- Restore mitochondrial respiration
- Trap phosphine

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Dihydroxyacetone as a definitive treatment for aluminium phosphide poisoning in rats

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- Lead poisoning is one of the oldest intoxications known to medicine. The ancient Greek physician Galen warned that consumption of water transported through lead pipes rendered individuals “subject to disorders in the intestines”.

❖**Protein Binding**

At low-to-moderate concentrations of lead in whole blood, >99% of the lead is associated with the erythrocyte.

The polymorphic enzyme δ-aminolevulinic acid dehydratase is the principal binding site for erythrocyte lead [11], and genetic polymorphisms in δ-aminolevulinic acid dehydratase seem to influence the toxicokinetics of lead and susceptibility to its toxic effects

❖Mechanisms of Clearance

Approximately 70% of total lead clearance occurs through the urine, with the balance excreted mostly in the feces and to a minor extent in sweat, hair, and nails [9, 14, 15]. Clearance from the blood is greater after acute exposure than with chronic exposure; in both cases, clearance increases exponentially with increasing blood lead concentration

- Lead Encephalopathy
- Lead encephalopathy is a potentially lifethreatening disturbance of central nervous system function associated with an altered sensorium, ataxia or incoordination, seizures, and coma. Because lead encephalopathy usually occurs in the context of recurrent lead exposure and a progressive increase in blood lead concentration, it often is preceded by several weeks or more of prodromal neurologic and constitutional symptoms, including severe headache, fatigue, sleep disturbance, anorexia, irritability, or loss of libido. Although rare, lead encephalopathy may occur after a single high-dose lead exposure [38]. An altered level of consciousness, which is expressed variably as delirium, hallucinations, lethargy, or stupor, may follow abruptly the prodromal symptoms. Isolated or recurrent seizures are common, affecting three quarters of the subjects in one survey [39]. Generalized seizures are most typical, but focal motor seizures also may occur. In some cases, convulsions may precede any evidence of an altered sensorium. Delirium, when it occurs, may persist or intensify over days to a week, even after the patient has been removed from lead exposure. Rarely the encephalopathic patient may lapse into a coma, and death may occur in the setting of progressive cerebral edema and increased intracranial pressure.

❖ **Lead colic**

Although lead colic is not life-threatening, it manifests as severe abdominal pain and usually warrants intensive care for prompt parenteral chelation, pain control, and monitoring for the possible development of lead encephalopathy. Painful lead colic generally emerges in patients with blood lead concentrations greater than 80 µg/dL (>3.9 µmol/L). Milder, nonspecific gastrointestinal discomfort and constipation may appear at blood lead concentrations greater than 60 µg/dL (>2.9 µmol/L) in some individuals.

THANK YOU