

## مقدمه

- از علل مهم مرگ ناشی از آسیب
- اكثريت موارد با بلع اتفاق مي افتد
- شایعترین داروهای بلعیده شده: مسکن ها-داروهای موضعی-ویتامین ها وآنتی هیستامین ها
  - پیشگیری از مسمومیت

### Common Agents Potentially Toxic to Young Children (<6 yr) in Small Doses\*

SUBSTANCE	TOXICITY
Aliphatic hydrocarbons (e.g., gasoline, kerosene, lamp	Acute lung injury
oil)	
Antimalarials (chloroquine, quinine)	Seizures, dysrhythmias
Benzocaine	Methemoglobinemia
β-Adrenergic receptor blockers †	Bradycardia, hypotension
Calcium channel blockers	Bradycardia, hypotension, hyperglycemia
Camphor	Seizures
Caustics (pH <2 or >12)	Airway, esophageal and gastric burns
Clonidine	Lethargy, bradycardia, hypotension
Diphenoxylate and atropine (Lomotil)	CNS depression, respiratory depression
Hypoglycemics, oral (sulfonylureas and meglitinides)	Hypoglycemia, seizures
Laundry detergent packets (pods)	Airway issues, respiratory distress, altered mental status
Lindane	Seizures
Monoamine oxidase inhibitors	Hypertension followed by delayed cardiovascular
	collapse
Methyl salicylate	Tachypnea, metabolic acidosis, seizures
Opioids (especially methadone, buprenorphine)	CNS depression, respiratory depression
Organophosphate pesticides	Cholinergic crisis
Phenothiazines (especially chlorpromazine,	Seizures, dysrhythmias
thioridazine)	
Theophylline	Seizures, dysrhythmias
Tricyclic antidepressants	CNS depression, seizures, dysrhythmias, hypotension

# Approach:

- ABC
  - Airway-breathing-circulation
- BS check
- Maybe naloxone
- A targeted history and physical examination

## History

- Intentional poisonings are typically more severe than unintentional, exploratory ingestions
- determining exactly what the child was exposed to and the circumstances surrounding the exposure
- names and specific ingredients, along with their concentrations
- a list of all medications in the child's environment

SIGN	TOXIN
ODOR	
Bitter almonds	Cyanide
Acetone	Isopropyl alcohol, methanol, paraldehyde, salicylates
Rotten eggs	Hydrogen sulfide, sulfur dioxide, methyl mercaptans (additive to natural gas)
Wintergreen	Methyl salicylate
Garlic	Arsenic, thallium, organophosphates, selenium
OCULAR SIGNS	
Miosis	Opioids (except propoxyphene, meperidine, and pentazocine), organophosphates and other cholinergics, clonidine, phenothiazines, sedative-hypnotics, olanzapine
Mydriasis	Anticholinergics (e.g., antihistamines, TCAs, atropine), sympathomimetics (cocaine, amphetamines, PCP), post–anoxic encephalopathy, opiate withdrawal, cathinones, MDMA
Nystagmus	Anticonvulsants, sedative-hypnotics, alcohols, PCP, ketamine, dextromethorphan
Lacrimation	Organophosphates, irritant gas or vapors
Retinal hyperemia	Methanol
CUTANEOUS SIG	GNS
Diaphoresis	Cholinergics (organophosphates), sympathomimetics, withdrawal syndromes
Alopecia	Thallium, arsenic
Erythema	Boric acid, elemental mercury, cyanide, carbon monoxide, disulfiram, scombroid, anticholinergics, vancomycin
Cyanosis	Methemoglobinemia (e.g., benzocaine, dapsone, nitrites, phenazopyridine), amiodarone,
(unresponsive to	silver
oxygen)	
ORAL SIGNS	
Salivation	Organophosphates, salicylates, corrosives, ketamine, PCP, strychnine
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Oral burns	Corrosives, oxalate-containing plants		
Gum lines	Lead, mercury, arsenic, bismuth		
GASTROINTESTINAL SIGNS			
Diarrhea	Antimicrobials, arsenic, iron, boric acid, cholinergics, colchicine, opioid withdrawal		
Hematemesis	Arsenic, iron, caustics, NSAIDs, salicylates		
Constipation	Lead		
CARDIAC SIGNS			
Tachycardia	Sympathomimetics, anticholinergics, antidepressants, antipsychotics, methylxanthines (theophylline, caffeine), salicylates, cellular asphyxiants (cyanide, carbon monoxide, hydrogen sulfide), withdrawal (ethanol, sedatives, clonidine, opioids), serotonin syndrome, neuroleptic malignant syndrome, MDMA, cathinones		
Bradycardia	β-Blockers, calcium channel blockers, digoxin, clonidine, organophosphates, opioids, sedative-hypnotics		
Hypertension	Sympathomimetics, anticholinergics, monoamine oxidase inhibitors, serotonin syndrome, neuroleptic malignant syndrome, clonidine withdrawal		
Hypotension	β-Blockers, calcium channel blockers, cyclic antidepressants, iron, antipsychotics, barbiturates, clonidine, opioids, arsenic, amatoxin mushrooms, cellular asphyxiants (cyanide, carbon monoxide, hydrogen sulfide), snake envenomation		
RESPIRATORY S	RESPIRATORY SIGNS		
Depressed respirations	Opioids, sedative-hypnotics, alcohol, clonidine, barbiturates		
Tachypnea	Salicylates, sympathomimetics, caffeine, metabolic acidosis, carbon monoxide, hydrocarbon aspiration		
CENTRAL NERV	OUS SYSTEM SIGNS		
Ataxia	Alcohols, anticonvulsants, sedative-hypnotics, lithium, dextromethorphan, carbon monoxide, inhalants		
Coma	Opioids, sedative-hypnotics, anticonvulsants, antidepressants, antipsychotics, ethanol, anticholinergics, clonidine, GHB, alcohols, salicylates, barbiturates		
Seizures	Sympathomimetics, anticholinergics, antidepressants (especially TCAs, bupropion, venlafaxine), cholinergics (organophosphates), isoniazid, camphor, lindane, salicylates, lead, nicotine, tramadol, water hemlock, withdrawal		
Delirium/psychosis	Sympathomimetics, anticholinergics, LSD, PCP, hallucinogens, lithium, dextromethorphan, steroids, withdrawal, MDMA, cathinones		
Peripheral neuropathy	Lead, arsenic, mercury, organophosphates, nicotine		

	SIGNS					
TOXIDROME	Vital Signs	Mental Status	Pupils	Skin	Bowel Sounds	Other
Sympathomimetic	Hypertension, tachycardia, hyperthermia	Agitation, psychosis, delirium, violence	Dilated	Diaphoretic	Normal to increased	
Anticholinergic	Hypertension, tachycardia, hyperthermia	Agitated, delirium, coma, seizures	Dilated	Dry, hot	Diminished	Ileus urinary retention
Cholinergic	Bradycardia, BP, and temp typically normal	Confusion, coma, fasciculations	Small	Diaphoretic	Hyperactive	Diarrhea, urination, bronchorrhea, bronchospasm, emesis, lacrimation, salivation
Opioids	Respiratory depression bradycardia, hypotension, hypothermia	Depression, coma, euphoria		Normal	Normal to decreased	
Sedative- hypnotics	Respiratory depression, HR normal to decreased, BP normal to decreased, temp normal to decreased	Somnolence, coma	Small or normal	Normal	Normal	

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### Mini-Toxidromes

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TOXIDROME	SYMPTOMS AND SIGNS	EXAMPLES
α <sub>1</sub> -Adrenergic	CNS depression, tachycardia,	Chlorpromazine, quetiapine, clozapine, olanzapine,
receptor	miosis	risperidone
antagonists		
α <sub>2</sub> -Adrenergic	CNS depression, bradycardia,	Clonidine, oxymetazoline, tetrahydrozoline, tizanidine,
receptor agonist	hypertension (early),	dexmedetomidine
	hypotension (late), miosis	
Clonus/myoclonus	CNS depression, myoclonic	Carisoprodol, lithium, serotonergic agents, bismuth,
	jerks, clonus, hyperreflexia	organic lead, organic mercury, serotonin or neuroleptic
		malignant syndrome
Sodium channel	CNS toxicity, wide QRS	Cyclic antidepressants and structurally related agents,
blockers		propoxyphene, quinidine/quinine, amantadine,
		antihistamines, bupropion, cocaine
Potassium channel	CNS toxicity, long QT interval	Antipsychotics, methadone, phenothiazines
blockers		
Cathinones,	Hyperthermia, tachycardia,	See Chapter 140 .
synthetic	delirium, agitation, mydriases	
cannabinoids		
•		

## **Physical Examination**

- assessing and stabilizing the airway, breathing, circulation, and mental status
- **key features** of the physical exam are vital signs, mental status, pupils (size, reactivity), nystagmus, skin, bowel sounds, and muscle tone

## **Laboratory Evaluation**

- A basic chemistry panel (electrolytes, renal function, glucose)
- liver transaminases
- creatinine kinase
- acetaminophen level

# Laboratory Clues in Toxicologic Diagnosis

Anion Gap Metabolic Acidosis (Mnemonic = Mudpiles Cat)

**M** ethanol, metformin

U remia

D iabetic ketoacidosis

P ropylene glycol

I soniazid, iron, massive ibuprofen

L actic acidosis

E thylene glycol

S alicylates

C ellular asphyxiants (cyanide, carbon monoxide, hydrogen sulfide)

A lcoholic ketoacidosis

**T** ylenol (clinical significance depends upon presence or absence of liver injury)



### Elevated Osmolar Gap

Alcohols: ethanol, isopropyl, methanol, ethylene glycol

### Hypoglycemia (Mnemonic = Hobbies)

**H** ypoglycemics, oral: sulfonylureas, meglitinides

O ther: quinine, unripe ackee fruit

**B** eta **B** lockers

I nsulin

E thanol

S alicylates (late)

### Hyperglycemia

Salicylates (early) Calcium channel blockers Caffeine

### Hypocalcemia

Ethylene glycol Fluoride

### Rhabdomyolysis

Neuroleptic malignant syndrome, serotonin syndrome Statins

Mushrooms (Tricholoma equestre )

Any toxin causing prolonged immobilization (e.g., opioids, antipsychotics) or excessive muscle activity or seizures (e.g., sympathomimetics)

## Radiopaque Substance on Kub (Mnemonic = Chipped)

C hloral hydrate, calcium carbonate

**H** eavy metals (lead, zinc, barium, arsenic, lithium, bismuth)

I ron

**P** henothiazines

P lay-Doh, potassium chloride

E nteric-coated pills

 ${f D}$  ental amalgam, drug packets

# quantitative blood concentrations:

salicylates, some anticonvulsants, acetaminophen,
 iron, digoxin, methanol, ethanol, lithium, ethylene
 glycol, theophylline, CO, lead



## urine drug-of-abuse screens:

- altered mental status of unknown etiology
- persistent unexplained tachycardia
- acute myocardial ischemia or stroke at a young age
- neglected or abused child

# Additional Diagnostic Testing

• ECG

Chest radiography

Abdominal radiography

## **Principles of Management**

supportive care, decontamination, directed therapy

(antidotes, ILE), and enhanced elimination

Antidotes

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POISON	ANTIDOTE	DOSAGE	ROUTE	ADVERSE EFFECTS, WARNINGS, COMMENTS
Acetaminophen	N -Acetylcysteine (Mucomyst)	140 mg/kg loading, followed by 70 mg/kg q4h	PO	Vomiting (patient-tailored regimens are the norm)
	N -Acetylcysteine (Acetadote)	150 mg/kg over 1 hr, followed by 50 mg/kg over 4 hr, followed by 100 mg/kg over 16 hr	IV	Anaphylactoid reactions (most commonly seen with loading dose) (Higher doses of the infusion are often recommended depending on acetaminophen level or degree of injury)
Anticholinergics	Physostigmine	0.02 mg/kg over 5 min; may repeat q5-10 min to 2 mg max	IV/IM	Bradycardia, seizures, bronchospasm Note: Do not use if conduction delays on ECG.
Benzodiazepines	Flumazenil	0.2 mg over 30 sec; if response is inadequate, repeat q1min to 1 mg max	IV	Agitation, seizures from precipitated withdrawal (doses over 1 mg) Do not use for unknown or polypharmacy ingestions.
β-Blockers	Glucagon	0.15 mg/kg bolus followed by infusion of 0.05-0.15 mg/kg/hr		Vomiting, relative lack of efficacy
Calcium channel blockers	Insulin	1 unit/kg bolus followed by infusion of 0.5-1 unit/kg/hr		Hypoglycemia Follow serum potassium and glucose closely.
	Calcium salts	Dose depends on the specific calcium salt	IV	

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Carbon monoxide	Oxygen	100% FIO 2 by non- rebreather mask (or ET if intubated)	Inhalation	Some patients may benefit from hyperbaric oxygen (see text).
Cyanide	Hydroxocobalamin (Cyanokit)	70 mg/kg (adults: 5 g) given over 15 min	IV	Flushing/erythema, nausea, rash, chromaturia, hypertension, headache
Digitalis	Digoxin-specific Fab antibodies (Digibind, DigiFab)	1 vial binds 0.6 mg of digitalis glycoside; #vials = digitalis level × weight in kg/100	IV	Allergic reactions (rare), return of condition being treated with digitalis glycoside
Ethylene glycol, methanol	Fomepizole	15 mg/kg load; 10 mg/kg q12h × 4 doses; 15 mg/kg q12h until ethylene glycol level is <20 mg/dL	IV	Infuse slowly over 30 min. If fomepizole is not available, can treat with oral ethanol (80 proof)
Iron	Deferoxamine	Infusion of 5-15 mg/kg/hr (max: 6 g/24 hr)	IV	Hypotension (minimized by avoiding rapid infusion rates)



Opioids	Naloxone	1 mg if patient not likely to be addicted. 0.04-0.4 mg if possibly addicted; repeated as needed; may need continuous	IV, intranasal, IO, IM, nebulized	May also be useful for
		infusion		

## Supportive Care

- airway, breathing, and circulation
- Hypotensive patients often are not hypovolemic but are poisoned
- IV fluids+vasopressor
- Seizures

### Medications to Maintain Cardiac Output and for Postresuscitation Stabilization\*

MEDICATION	DOSE RANGE	COMMENT
Inamrinone	0.75-1 mg/kg IV/IO over 5 min; may repeat	Inodilator
	2×; then: 2-20 μg/kg/min	
Dobutamine	2-20 μg/kg/min IV/IO	Inotrope; vasodilator
Dopamine	2-20 μg/kg/min IV/IO in low doses; pressor	Inotrope; chronotrope; renal and splanchnic
	in higher doses	vasodilator
Epinephrine	0.1-1 μg/kg/min IV/IO	Inotrope; chronotrope; vasodilator in low doses;
		vasopressor in higher doses
Milrinone	$50-75 \mu g/kg$ IV/IO over $10-60$ min then $0.5-$	Inodilator
	0.75 μg/kg/min	
Norepinephrine	0.1-2 μg/kg/min	Inotrope; vasopressor
Sodium	1-8 μg/kg/min	Vasodilator; prepare only in D5W
nitroprusside		

<sup>\*</sup> Alternative formula for calculating an infusion: Infusion rate (mL/hr) = [weight (kg)  $\times$  dose ( $\mu$ g/kg/min)  $\times$  60 (min/hr)]/concentration  $\mu$ g/mL).

## Example:

- 6\*wt+100cc DW
  - $-1 drop=1 \mu g/kg$

## Decontamination

- to minimize absorption of the toxic substance
- Decontamination should not be routinely employed for every poisoned patient
- Dermal and ocular decontamination
- Gastrointestinal (GI) decontamination strategies are most likely to be effective in
  - the 1 or 2 hours after an acute ingestion



## Gastric Lavage

- in most clinical scenarios, the use of gastric lavage is no longer recommended
- Single-Dose Activated Charcoal
  - Charged molecules (i.e., heavy metals, lithium, iron) and liquids do not bind well to activated charcoal

## Activated charcoal

- Charcoal is most likely to be effective when given within 1 hr of ingestion
- 1 g/kg in children or 50-100 g in adolescents and adults
- the patient's airway is intact or protected and that the patient has a benign abdominal examination
- adding flavorings

## Whole-bowel irrigation (WBI)

- large volumes (35 mL/kg/hr in children or 1-2 L/hr in adolescents) of a polyethylene glycol electrolyte solution
- assessment of the airway and abdominal exam before initiating WBI

# Intralipid emulsion (ILE) therapy

- sequesters fat-soluble drugs, decreasing their impact at target organs
- enhances cardiac function
- calcium channel blockers (verapamil, diltiazem), bupropion, and tricyclic antidepressants
- 20% Intralipid
  - a bolus dose of 1.5 mL/kg is given over 3 min, followed by an infusion of 0.25 mL/kg/min until recovery or until a total of 10 mL/kg

## **Enhanced Elimination**

- Urinary Alkalinization:
  - a continuous infusion of sodium bicarbonate
     containing IV fluids, with a goal urine pH of 7.5-8
  - useful in managing salicylate and methotrexate toxicity
- Complications

## Hemodialysis

- low volume of distribution (<1 L/kg) with a high degree of water solubility, low molecular weight, and low degree of protein binding
- methanol, ethylene glycol, salicylates, theophylline, bromide, lithium, and valproic acid
- severe electrolyte disturbances and acid-base derangements

## Multidose Activated Charcoal

- 0.5 g/kg every 4-6 hr (for 4 doses)
- significant ingestions of carbamazepine, dapsone,
   phenobarbital, quinine, and theophylline
- the airway and abdominal exam should be assessed before each dose



## Acetaminophen

- the most common cause of acute liver failure and is the leading cause of intentional poisoning death
- N -acetyl-p -benzoquinone imine (NAPQI)
  - >200 mg/kg in children and
  - >7.5-10 g in adolescents and adults



- Acetaminophen:
  - Tab 325-500
  - Syr 120mg/5cc
  - Supp 125-325
  - Drop 100mg/cc

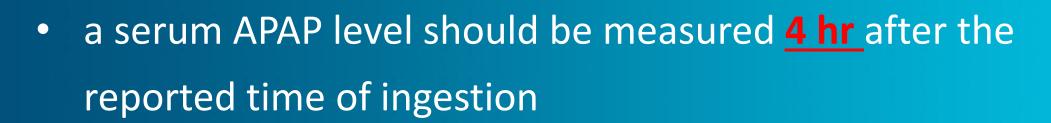
پس در کودکی با وزن ۱۰ کیلوگرم اگر حدودا یک شیشه ی ۶۰ میلی لیتری شربت آهن را کامل سر بکشد دوز توکسیک مصرف کرده است.

## Clinical and Laboratory Manifestations

The initial signs are nonspecific

#### Classic Stages in Clinical Course of Acetaminophen Toxicity

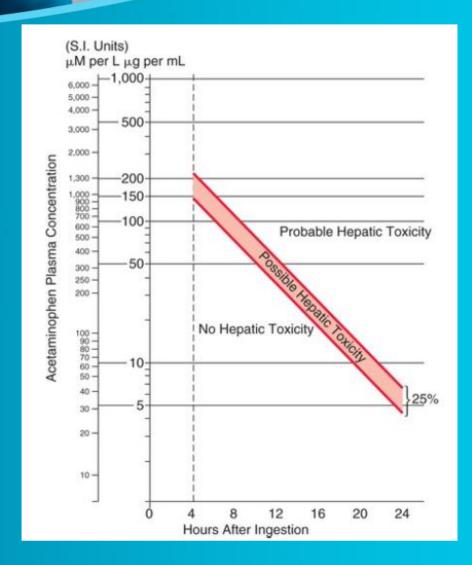
STAGE	TIME AFTER INGESTION	CHARACTERISTICS
I	0.5-24 hr	Anorexia, vomiting, malaise
		Lab tests typically normal, except for acetaminophen level
II	24-48 hr	Resolution of earlier symptoms; right upper quadrant abdominal pain and tenderness; elevated hepatic transaminases (aspartate > alanine), INR
III	3-5 days	Peak transaminase elevations; development of liver failure, multi organ-system failure, death <i>or</i> recovery begins
IV	4 days to 2 wk	Resolution of liver function abnormalities Clinical recovery precedes histologic recovery



- more than 4 hr after ingestion, a stat APAP level should be obtained
- hepatic transaminases, renal function tests, and coagulation parameters



- 1 Prophylactic:
  - Rumak-matthew





- 2 Hepatic Injury
  - Any patient in this category requires therapy with NAC (IV or oral)
- 3 Acute Liver Failure
  - acidemia(serum pH <7.3) after adequate fluid resuscitation, coagulopathy (INR >6), renal dysfunction (creatinine >3.4 mg/dL), and grade III or IV hepatic encephalopathy

#### **NAC**

- IV form is used in patients with intractable vomiting, those with evidence of hepatic failure, and pregnant patients
- Administration
- complications

### Nonsteroidal Antiinflammatory Drugs(NSAIDs)

- GI irritation, reduced renal blood flow, and platelet dysfunction
- Ibuprofen:
  - ingestions of >400 mg/kg
- Symptoms
- Treatment

## **Prescription Opioids**

- Methadone
  - cause QTc interval prolongation
- Buprenorphine
- Naloxone
  - 1-2 mg
  - -0.04-0.4 mg

## β-Adrenergic Receptor Blockers

- propranolol is considered to be the most toxic member
- Clinical and Laboratory Manifestations
- Glucagon

### Calcium Channel Blockers

- diltiazem and verapamil are the most dangerous in overdose because of their higher lipophilicity and direct cardiac suppressant effects
- profound hypotension with preserved consciousness
- IV <u>Calcium-High-dose insulin euglycemia therapy</u>

### Iron

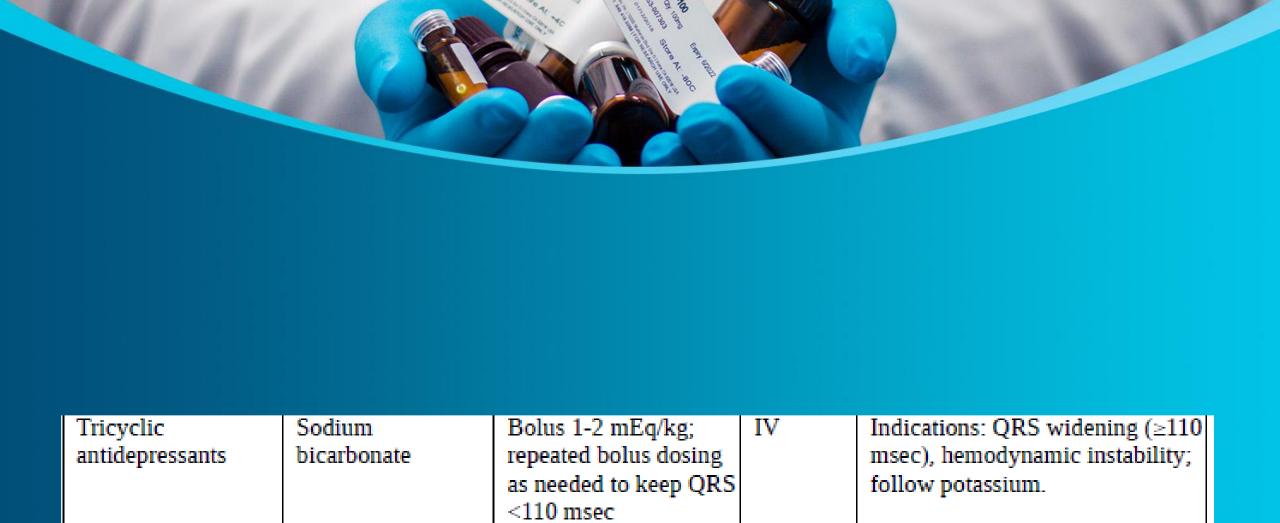
- Ferrous sulfate contains 20% elemental iron, ferrous gluconate 12%, and ferrous fumarate 33%
- corrosive to the GI mucosa
- >40 mg/kg of elemental iron
- 5 stages
- Deferoxamine

# Oral Hypoglycemics

- Hypoglycemia and symptoms associated with hypoglycemia
- ingestion of a single sulfonylurea tablet can lead to significant toxicity
- bolus of IV dextrose
- octreotide

# Tricyclic Antidepressants

- even with ingestion of 1 or 2 pills (10-20 mg/kg)
- Cardiovascular and CNS symptoms
- activated charcoal-vasopressor
- Indications for sodium bicarbonate



### Selective Serotonin Reuptake Inhibitors

- sedation and tachycardia, Cardiac conduction abnormalities
- serotonin syndrome
- Cyproheptadine

## **Atypical Antidepressants**

- Cardiac conduction defects, including QRS and QTc prolongation, and seizures
- Benzodiazepines-Intralipid emulsion
- vasopressors

## Antipsychotics

- extrapyramidal symptoms, tardive dyskinesia, and development of the neuroleptic malignant syndrome (NMS)
- sedation, tachycardia, and QTc prolongation
- supportive care, IV fluids, cooling, benzodiazepines, and bromocriptine or dantrolene
- diphenhydramine and benztropine

#### Household Products:

- Pesticides
  - Cholinesterase-Inhibiting Insecticides
    - organophosphates and carbamates
- <u>DUMBBELS</u>: diarrhea/defecation, urination, miosis, bronchorrhea/bronchospasm, bradycardia, emesis, lacrimation, and salivation
- Basic decontamination
- Atropine
- Pralidoxime

#### Pyrethrins and Pyrethroids

- allergic reactions ranging from dermatitis to urticaria to anaphylaxis
- acute lung injury
- Decontamination
- antihistamines and corticosteroids
- benzodiazepines for tremors and seizures

#### Hydrocarbons:

- The most important manifestation of hydrocarbon toxicity is aspiration pneumonitis through inactivation of the type II pneumocytes and resulting in surfactant deficiency
- Compounds with low viscosity and high volatility produce significant injury
- unique toxicities

#### Clinical and Laboratory Manifestations

- Transient, mild CNS depression
- Chest radiographs may initially be normal, but they often show abnormalities within 6 hr of exposure in patients who have aspirated
- Fever and leukocytosis
- Pneumatoceles
- ventricular dysrhythmias-type IV renal tubular acidosis
- Emesis and lavage are contraindicated given the risk of aspiration
- charcoal is not useful.
- treatment is supportive

#### Toxic Alcohols

- Drowsiness, mild inebriation, nausea, and vomiting
- metabolic acidosis and visual disturbances
  - feeling of being in a snowstorm
- osmolar gap
- Electrolytes (including calcium), acid-base status, kidney function, and ECG
- Ethanol/Fomepizole
  - Classic indications for fomepizole
- Indications for dialysis

#### Carbon Monoxide:

- CO binds to hemoglobin with an affinity >200 times that of oxygen, forming carboxyhemoglobin (HbCO)
- headache, malaise, nausea, and vomiting
- arterial or venous blood gas analysis with HbCO determined by COoximetry, CK level in severely poisoned patients, pregnancy test, and ECG in any patient with cardiac symptoms
- 100% oxygen

#### Hydrogen Cyanide

- headache, agitation/confusion, sudden loss of consciousness, tachycardia,
   cardiac dysrhythmias, and metabolic acidosis
- severe lactic acidosis (lactate >10 mmol/L) in fire victims
- Treatment:
  - high concentrations of oxygen
  - The cyanide antidote kit
  - Hydroxocobalamin
    - the preferred antidote for cyanide poisoning

#### Miscellaneous Toxic Agents Found in the Home

- Nicotine-Containing Products
- Single-Use Detergent Sacs
- Electric Dishwasher Detergent

