TOXICOLOGY - GENERAL APPROACH

INTRODUCTION

The combination of crawling, walking, fine pincer grasp, and oral exploration leads children to ingest substances that they find, particularly parents' and grandparents' medications and household products. Millions of young children are "exposed" to potentially toxic substances each year; the peak is at 2 – 3 years of age. Nonetheless, most children experience no or only mild symptoms. Poisoning morbidity is higher and fatalities are increased among suicidal or substance using adolescents.

TOXICITY IN TODDLERS IN A SMALL DOSE	
Antihistamines	Lindane
Benzocaine	Methanol
β-adrenergic antagonists	Methyl salicylates (oil of wintergreen
Calcium channel antagonists	Opioids (methadone, codeine, oxycodone)
Camphor	Phenothiazine
Clonidine	Quinine, chloroquine
Diphenoxylate-atropine	Sulfonylurea antidiabetic agents
Ethanol	Theophylline
Ethylene glycol	Tricyclic antidepressants

DIAGNOSIS

A careful history, physical examination and selected testing may help to identify the agent in an unknown ingestion and set initial management strategies. History should focus on the availability of specific agents in the home, potential amount taken, timing of ingestion, allergies or medical conditions and any first aid administered

Toxidromes are a constellation of signs and symptoms the may be use to identify a specific agent or class of agents. Individual signs and symptoms may also be used.

BLOOD PRESSURE	
HYPERTENSION	HYPOTENSION
Amphetamines	Beta blockers
Cocaine	Sedative-hypnotics
Sympathomimetics	Narcotics
Sedative/Narcotic withdrawal	Ca++ channel blockers
	Alpha blockers
	ACE Inhibitors

HYPERTHERMIA		
CLASS	EXAMPLE	MECHANISM
Alpha adrenergic	Amphetamines,cocaine	Vasoconstriction
Anticholinergics	Antihistamines	Impaired sweating
Cyclic Antidepressants	Imipramine	Anticholinergic
Neuroleptics	Haloperidol	Hypothalamic dysfunction
SSRI	Fluoxetine	Block serotonin uptake
MAOI	Pheneizine	↓ Serotonin catabolism
Salicylates	Aspirin	Uncouples phosphorylation

HYPERPYREXIA SYNDROMES*	
Neuroleptic malignant syndrome	Benzodiazepines
Serotonin syndrome	Benzodiazepines
Malignant Hyperthermia	Dantroline

* Altered mental status, neuromuscular changes and autonomic dysfunction

PUPILS (Normal = 4mm)			
MIOSIS		MYDRIASIS	
C	Cholinergics, Clonidine	A	Antihistamines
O	Opiates, Organophospate	A	Anticholinergics
P	Phenothiazines, Pilocarpine	A	Antidepressants
S	Sedative hypnotics	S	Sympathomimetics

SKIN CHANGES	
Diaphoresis	
	Sympathomimetics
	Organophosphates
	Salicylates
	PCP
Dry skin - Anticholinergic	
Red Skin – Cyanide	
Blue Skin – Methemoglobinemia	

SEIZURES	
P	Pesticides, propranolol
L	Lead
A	Alcohols, Amphetamines
S	Sugar (hypoglycemics), Salicyclates
T	Tricyclic antidepressants
I	Isoniazid, iron
C	Cocaine, Camphor

LABORATORY TESTING

Standard laboratory urine screening is generally not helpful in the initial management of the patients. Some hospital screens may for benzodiazepines, opiates/methadone, barbiturates, THC (cannabis) and PCP.

Basic laboratory parameters may also be helpful.

ANION GAP METABOLIC ACIDOSIS			
M	Methanol	P	Paraldehyde
U	Uremia	I	Iron, Isoniazid
D	DKA	L	Lactic acid
		E	Ethylene Glycol
		S	Salicylate

Anion gap = $((Na^+ - [Cl^- + HCO3^-])$, normal = 8-12)

OSMOLAR GAP	
Ethanol	Paraldehyde
Isopropanol	Ethyl ether
Methanol	Mannitol
Ethylene Gylcol	Renal Failure
Acetone	Lactic Acidosis
Trichloroethane	Alcoholic ketoacidosis

An osmolar gap (OG = measured osmols – calculated osmols).
Calculated osmols = {(2Na) + (GL/18) + (BUN/2.8)}

SERUM DRUG CONCENTRATIONS	
Acetaminophen	Methanol
Salicylates	Ethylene Glycol
Iron	Carbon Monoxide
Lithium	Methemoglobin

* Each of the agents listed above have specific antidotes and levels correspond to toxicity. Digoxin and Dilantin levels do not indicate need for treatment
Acetaminophen and salicylates should be screened for in most ingestions.

MANAGEMENT

The management of the poisoned patient should focus on supportive care. ("treat the patient not the toxin). In specific situations enhancement of elimination and/or specific antidotes may be indicated.
**Poison Control should be notified ASAP

GENERAL APPROACH TO MANAGEMENT OF ACUTE POISONINGS	
1	Resuscitation A. Secure airway. Intubate as needed B. Maintain oxygenation and ventilation, Naloxone for respiratory depression C. Fluid resuscitation for shock, ongoing cardiopulmonary monitoring D. Disability - Altered mental status, Seizures – check for hypoglycemia Decontamination – removed and plastic bag clothing for dermal exposures E. Environment - Assess for possible child abuse, suicidal intent, substance abuse
2	Clinical Evaluation (Hx/PE) to determine likely agent/agent class
4.	Testing Screen for Acetaminophen, Salicylates, pregnancy in all ingestions CBC, electrolytes, bedside glucose. Specific drug levels as indicated EKG - signs of drug toxicity - prolonged QRS, dysrhythmias CXR – for respiratory depression (aspiration pneumonitis, pulmonary edema) AXR - Fe, enteric coated, heavy metals
4	Administer specific antidotes - remember 0_2 and dextrose (see appendix)
5	Consider agent indicated elimination techniques
6	Supportive Care

ENHANCING TOXIN ELIMINATION

PREVENTION OR REDUCTION OF ABSORPTION

The majority of toxins are not toxic to the gastrointestinal tract (except caustics). Prevention of absorption can be accomplished by expelling the toxin from above or below are via neutralization. Efforts at gastrointestinal decontamination despite widespread use have not been demonstrated to be beneficial and are generally now indicated only in specific circumstances.

SYRUP OF IPECAC	
Mechanism	Plant extract that causes vomiting May be abused by bulemic patients
Indications	No longer recommended
Contraindication	Acids, alkalis, hydrocarbons, unprotected airway, depressed level of consciousness, seizure, cardio-pulmonary instability
Complications	Protracted vomiting, aspiration, esophageal rupture,

ORO-GASTRIC LAVAGE	
Mechanism	Use of a large bore tube - gastric irrigation, remove pill fragments
Indications	Should not be used routinely. It has limited utility in preventing toxicity; best within 1 hour with life threatening agents or agents not absorbed by activated charcoal
Contraindication	Acids, alkalis, hydrocarbons, unprotected airway
Complications	Aspiration (airway can be protected with endotracheal intubation) Gastric/esophageal rupture

ACTIVATED CHARCOAL	
Mechanism	Adsorption by charcoal prevents absorption GI dialysis – absorption of drug already in the blood stream
Indications	Ingestion of potential dangerous amount of a substance absorbed by charcoal within 1 hr of ingestion May be considered after 1 hr for substance that delays gastric emptying 2 times more effective than emesis or lavage
Contraindication	Absence of intact or protected airway, bowel obstruction, perforation Not absorbed by activated charcoal – acids/alkali, hydrocarbon, metals (Fe, Lithium), cyanide, pesticides, solvents, alcohols
Complications	Aspiration
Dose	1gm/kg PO/NG (child), 50-100 grams (adol/adult)

MULTIDOSE ACTIVATED CHARCOAL	
Mechanism	Uses GI tract as a dialysis membrane
Indications	Agents with enterohepatic or enteroenteric circulation – phenobarbitol, carbamazipine, theophylline, dilantin, digoxin, salicylates

ENHANCEMENT OF EXCRETION

CATHARTICS (SORBITOL)	
Mechanism	Hyperosmolar agent that increase stool output
Indications	Little evidence to support it use May be given with the first dose of activated charcoal
Contraindication	Children < 6 years
Complications	Electrolyte abnormalities

WHOLE BOWEL IRRIGATION	
Mechanism	Large volumes of polyethylene glycol are used to flush GI tract; no fluid/electrolyte abnormalities
Indications	Useful for small molecules such as Fe or Li, and sustained release or enteric coated preparations.
Contraindication	Ileus, GI obstruction/perforation
Dose	500 ml/hr (child), 1-1½ liters/hr (adol/adult)

ION TRAPPING (URINARY ALKALINIZATION)	
Mechanism	Alkalinization of the urine may enhance the excretion of acids
Indications	Significant salicylate or phenobarbitol ingestions Dose 1-2 meq/kg $NaHCO_3$ Q3-4 hours (Goal urine PH 7.0-8.0)
Complications	Must maintain normokalemia. Hypokalemia will decrease K+/acid exchange in the kidneys

HEMODIALYSIS	
Mechanism	Direct removal of agents from the blood Corrects metabolic abnormalities
Indications	Failure of supportive care and antidotes Toxins that are small, little protein binding and in blood (low volume of distribution Methanol, Ethylene glycol, phenobarbitol, salicylates, Theophylline and lithium

TOXIDROMES - A constellation of signs and symptoms which aids in identifying a class of agents						
		Sympathomimetic	Anticholinergics	Opiates	Sedative-Hypnotics	Cholinergics
Examples		Cocaine Amphetamines	Antihistamines TCA Antipsychotics	Heroin Morphine Clonidine	Benzodiazepines Barbiturates Ethanol	Organophosphates Nerve Agents Mushrooms
Status*		UP (increased)	UP (increased)	Down(decreased)	Down (decreased)	Down (decreased)
Mental Status		Restless Agitated, anxious Paranoia Insomnia, Mania Hallucinations Seizure	Pyschosis (Mad as a Hatter) Delerium Coma Seizure Chorea	Sedation Confusion Coma	Sedation Confusion Delerium Ataxia Coma	Confusion Drowsiness Coma Seizure
Pupils		Mydriasis	Mydriasis (Blind as a bat)	Miosis	Mydriasis or miosis Blurred vision Nystagmus	Miosis
Vital Signs	HR BP RR T	Tachycardia Hypertension Hyperthermia	Tachycardia Hypertension Hyperthermia	Hypotension Bradypnea. Apnea Hypothermia	Hypotension Bradypnea, Apnea Hypothermis	Bradycardia Tachypnea Hypothermia
Physical Exam		Tremor Diaphoresis Warm Skin Hyperactive bowel sounds Hyperreflexia	Dry, flushed Skin (Dry as a bone Red as a beet) Urinary retention Hypoactive bowel sounds		Hypoactive bowel sounds Hyporeflexia	Salivation Lacrimation Urination Defecation Emesis Bronchorhea Musc fasciculation Diaphoresis
Treatment		Benzodiazepine	Physostigmine	Naloxone	Supportive	Atropine Pralidoxime

* Status – overall increase or decrease in mental status, vital signs and pupils

ANTIDOTES	
AGENT/CLASS	ANTIDOTE
Acetaminophen	N-Acetyl Cysteine
Anticholinergics - eg Benadryl	Physostigmine*
Beta Blockers - eg Propranolol	Glucagon, Insulin, Dextrose
Benzodiazepines	Flumazenil
Calcium Channel Blockers	Calcium, Insulin, Dextrose
Carbon Monoxide	O_2, Hyperbaric O_2
Crotalid Envenomation	Crotalinae Polyvalent Immune Fab Antivenom
Cyanide	Amyl nitrate, Sodium nitrate Sodium thiosulfate, Hydroxocobalamine
Digoxin	Digoxin specific Antibody
Ethylene Glycol	Ethyl alcohol, 4 Methylpyrazol, Pyridoxine
Heparin	Protamine*
Iron	Deferoxamine
Isoniazid	Pyridoxime* (Vitamin B6)
Lead	BAL, $CaNa_2EDTA$ (encephalopathy) Dimercaptosuccinic acid (DMSA)
Malignant Hyperthermia	Dantrolene
Methanol	Ethyl alcohol, 4 Methylpyrazol
Methemoglobin inducers eg. Nitrates	Methylene blue
Neuroleptic Dystonia	Diphenhyrdramine
Neuroleptic Malignant Syndrome	Bromocriptine
Opiods	Naloxone
Organophosphates	Atropine, Pralidoxime* (2-PAM)
Sulfonylurea Hypoglycemic Agents	Dextrose, Octreatide
Tricyclic Antidepressants	$NaHCO_3$ (dysrhythmias) Benzodiazepines (seizures)
Warfarins	Vitamin K_1

BEWARE The 4 P's

Phystostigmine - Anticholinergics
Pralidoxime - Organophosphates
Pyridoxime – Isoniazid
Protamine - Heparin