\*Toxins can be (inhaled / insufflated (snorted) / orally ingested / injected / absorbed dermally)

\*common targets of toxicity include ( central nervous system, lungs, kidney, heart, liver, blood, acid/base and electrolyte balance of the body)

\*lifethreatening toxic effect >>profound increases or decreases in ( blood pressure / heart rate / breathing /body temperature )or any dangerous dysrhythmias

\*EMERGENCY TREATMENT OF THE POISONED PATIENT

- Airway, breathing, and circulation(ABC) are assessed and addressed initially

-Acid/base and electrolyte disturbances, along with an *acetaminophen* and salicylate blood level >> assessed as laboratory results are obtained

-administering oxygen and obtaining intravenous access and placing the patient on a cardiac monitor >> if altered mental status >> “coma cocktail”

“coma cocktail” consists of; intravenous ((dextrose to treat hypoglycemia // *naloxone* to treat possible opioid or *clonidine* toxicity // *Thiamine* for ethanol-induced Wernicke encephalopathy))

-assessment for decontamination can occur >> once the patient is stabilized and this may includes :

1- flushing of the eyes with saline or tepid water to a neutral pH for ocular exposures

2- rinsing of the skin for dermal exposures

3- administration of gastrointestinal (GI) decontamination with gastric lavage, activated charcoal, or whole bowel irrigation (utilizing a polyethylene glycol electrolyte balanced solution)

- Several substances do not adsorb to activated charcoal (lead and other heavy metals, *iron, lithium, potassium*, and alcohols) >> limited to coingested products

\* Elimination enhancement by HUM-(Hemodialysis / Urinary alkalinization / Mutiple-dose activated charcoal)

1- Hemodialysis (if certain properties are met by the toxin and they include:( low protein binding/ small volume of distribution/ small molecular weight/ water solubility) // examples methanol, ethylene glycol, salicylates, *theophylline*, *phenobarbital*, and *lithium*.)

2- Urinary alkalinization (enhances the elimination of salicylates or *phenobarbital // Increasing the urine pH with intravenous sodium bicarbonate>>* *transforms the drug into an ionized form>>* *prevents reabsorption //* *goal urine pH is 7.5 to 8 and ensuring that the serum pH does not exceed 7.55 )*

*3- Multiple-dose activated charcoal (enhances the elimination of theophylline, phenobarbital, digoxin, carbamazepine, valproic acid // works by creating a gradient across the lumen of the gut >>* *Medications traverse from areas of high concentration to low concentration >>* *medication already absorbed to cross back into the gut to be adsorbed by the activated charcoal //* *blocks the reabsorption of medications that undergo enterohepatic recirculation(like phenytoin) //*

Bowel sounds must be present prior to each activated charcoal dose to ensure movement of the GI tract and prevent obstruction)

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\*\*\*Acetaminophen (toxic when metabolic pathways become saturated)

\* undergoes metabolism by sulfation, glucuronidation, and *N*-hydroxylation by the cytochromeP450 system

\* When a toxic amount of *acetaminophen* is ingested, the first two processes are overwhelmed and more *acetaminophen* is metabolized by the cytochrome P450 system to a hepatotoxic metabolite (*N*-acetyl-*p*-benzoquinoneimine, NAPQI).>> glutathione is depleted, leaving the metabolite to produce toxicity

\* in therapeutic *acetaminophen* ingestions, the liver generates glutathione, which detoxifies NAPQI

\* antidote for *acetaminophen* toxicity, *N-acetylcysteine* (*NAC*), initially works as a glutathione precursor and glutathione substitute and assists with sulfation.

Later on, *NAC* may function as an antioxidant to aid in recovery (*NAC* is the most effective when initiated 8 to 10 hours postingestion)

\* *acetaminophen* toxicity (4) phases (1-phase one (0-24)h – loss of spetite and malaise /2-phase two (24-72)h abdominal pain and increase liver enzymes

3-phase three (72-96)liver necrosis,jaundice,encephalopathy,renal falire and death / 4-phase four (>4 days to 2 weeks) organ failure and resolution of semptoms.

\*\*\* Alcohols

1- (Methanol-(in windshield washer fluid and model airplane fuel) and ethylene glycol-(in radiator antifreeze))

\*themselves relatively nontoxic and cause mainly CNS sedation

\* methanol and ethylene glycol are oxidized to toxic products (formic acid in the case of methanol/ glycolic, glyoxylic, oxalic acids in the case of ethylene glycol)

\* Fomepizole inhibits this oxidative pathway by blocking alcohol dehydrogenase. It prevents the formation of toxic metabolites and allows the parent alcohols to be excreted by the kidney.

\* Hemodialysis is often utilized to remove the already-produced toxic acids

\* cofactors are administered to encourage metabolism to nontoxic metabolites (*folate* for methanol, *thiamine* and *pyridoxine* for ethylene glycol)

\* If untreated (methanol causes blindness,metabolic acidosis,seizures,coma /Ethylene glycol causes renal failure, hypocalcemia, metabolic acidosis,heart failure

2- Isopropanol (rubbing alcohol, isopropyl alcohol):

\* metabolized to acetone via alcohol dehydrogenase / cannot be further oxidized to carboxylic acids, and therefore, acidemia does not occur

\* Isopropanol is a known CNS depressant and GI irritant. ((No antidote is necessary))

\*\*\* Carbon monoxide ( مصادره حرق و هيك معروفة)

\* after inhalation binds to hemoglobin to produce carboxyhemoglobin. >> reducing oxygen delivery >> may produce “cherry red” skin.( presence of this highly oxygenated blood) >>

\* binding affinity of carbon monoxide to hemoglobin is 230-270 greater than O2

\* can occur also after inhalation or ingestion of methylene chloride found in paint strippers >> metabolized to carbon monoxide through the cytochrome P450

\*Symptoms like hypoxia //\* brain and heart showing the greatest sensitivity //\* high exposure >> seizures, coma, and death

\*management of a carbon monoxide–poisoned patient(removal from source of carbon monoxide and institution of 100% oxygen by nonrebreathing face mask or endotracheal tube. // if severe intoxication >> oxygenation in a hyperbaric chamber

\*\*\* Cyanide

\* products of combustion ,cyanide salts used in electroplating, and hydrogen cyanide may be produced during photographic developing and petroleum refining

\* cyanide quickly binds to many metalloenzymes, thereby rendering them inactive

\* toxicity occurs as a result of the inactivation of the enzyme cytochrome oxidase (cytochrome a3), leading to the inhibition of cellular respiration.

\* even in the presence of oxygen, tissues such as the brain and heart, which require a high oxygen demand, are adversely affected

\* Death can occur quickly due to respiratory arrest of oxidative phosphorylation and production of adenosine triphosphate

\* new antidote, *hydroxocobalamin* (vitamin B12a) –(IV)- bind the cyanide and produce *cyanocobalamin* (vitamin B12) without the worry of hypotension or methemoglobin production

\* older cyanide antidote kit comprises *sodium nitrite* to form cyanomethemoglobin and *sodium thiosulfate* to accelerate the production of thiocyanate, which is much less toxic than cyanide and is also quickly excreted in urine.

\* In patients with smoke inhalation and cyanide toxicity, the induction of methemoglobin with *sodium nitrite* should be avoided unless the carboxyhemoglobin

 concentration is less than 10%. Otherwise, the oxygen-carrying capacity of blood becomes too low.

\*\*\* Iron

\* may show up on an abdominal radiograph

\* Toxic effects can be expected with as little as 20 mg/kg--// 60 mg/kg may be lethal.

\* quantity ingested and patient’s weight, and the elemental iron concentration >> assessment of potential toxicity can be made

\* A serum iron level should be obtained, since levels between 500 and 1000 μg/dL have been associated with shock and levels higher than 1000 μg/dL with morbidity and mortality

\* latent period or may progress quickly to hypovolemia, metabolic acidosis, hypotension, and coagulopathy.> hepatic failure , multisystem failure, coma, death

\*Deferoxamine*,* an iron-specific chelator >> binds free iron, creating ferrioxamine to be excreted in the urine

\* intravenous route for *deferoxamine* is preferred, but hypotension may occur if rapid boluses are administered instead of a continuous infusion

\*\*\*lead

\* From old paint, drinking water, industrial pollution, food, and contaminated dust((inorganic lead salts - most chronic))

\* Adults absorb about 10% of an ingested dose / children absorb about 40%. يعني الطفل يحتاج كمية اقل للتسمم (ربع الكمية)

\* Inorganic forms of lead are initially distributed to the soft tissues and more slowly redistribute to bone, teeth, and hair

\* it impairs new bone formation and causes increased calcium deposition in long bones visible on x-ray

\* appear on an abdominal radiograph if present in the GI tract (radiopaque)

\* Lead has an apparent blood half-life of about 1 to 2 months // half-life in the bone is 20 to 30 years // Chronic exposure > serious effects on several tissues

\* chelators can be utilized in the treatment of lead toxicity //

\* levels are( > 45 μg/dL, but < 70 μg/dL in children, *succimer (dimercaptosuccinic acid, DMSA),* an oral chelator

\* levels > 70 μg/dL or if encephalopathy is present, dual parenteral therapy ( *dimercaprol* given IM and *calcium disodium edetate* given IV)

\* *Dimercaprol* is suspended in peanut oil and should not be given to those with a peanut allergy



\*\*\* Organophosphate and carbamate insecticides

\* toxicity through inhibition of acetylcholinesterase, with subsequent accumulation of excess acetylcholine producing nicotinic(mydriasis, fasciculations, muscle weakness, hypertension) and muscarinic(diarrhea, urination, miosis, bradycardia, bronchorrhea, emesis, lacrimation, salivation) effects

\* Carbamates reversibly bind to acetylcholinesterase, whereas organophosphates undergo an aging process to ultimately irreversibly inactivate the enzyme.

\* Organophosphate nerve agents, such as sarin, soman, tabun, have same mechanism of action, but the aging process is more rapid compared to insecticides

\* *Atropine*, a muscarinic receptor antagonist >> treat muscarinic effects(IV or IM)

\* *pralidoxime an oxime to reactivate cholinesterase>> treat nicotinic effects(IV or IM)*