Forensic & Toxicology Team

MED 433

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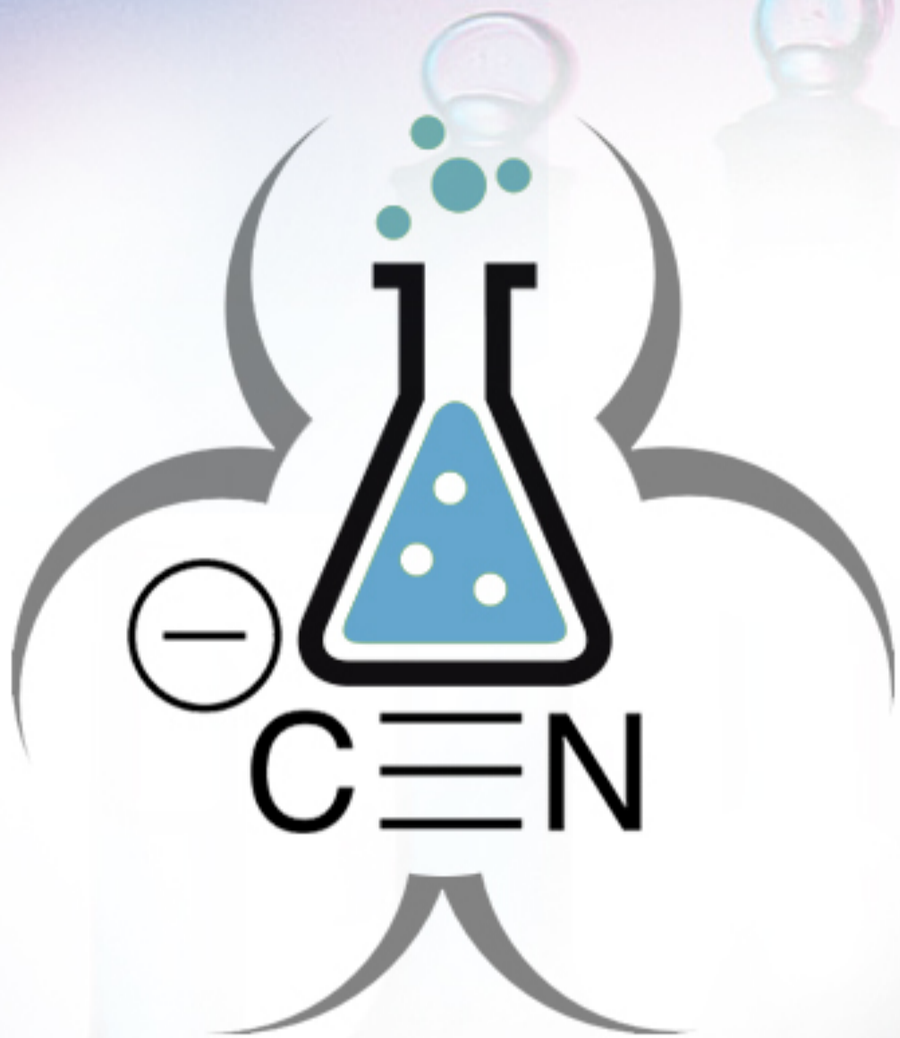

TOXICOLOGY SUMMARY

Introduction to toxicology

Sympathomimetics (Cocaine - Amphetamines -Ecstasy -Caffeine) :

FEATURES:

Tachycardia +/ - arrhythmias Mydriasis Diaphoresis Hypertension +/ - ICH Confusion with agitation Seizures Rhabdomyolysis

MANAGEMENT:

1-Supportive care

2-Benzodiazipines (to control and sedate the patient)

3-BP management if severe

4-Give BOTH alpha and beta blockers (labetalol).

Opiate (Morphine - codeine- Heroin - Methadone):

FEATURES:

Coma , Miosis (pin point pupil) ,Respiratory depression (slow shallow breathing).

MANAGEMENT:

- Competitive opioid antagonist: **Naloxone**

Anticholinergic (Atropine- Scopolamine- Amantadine) :

FEATURES:

1-**CNS muscarinic blockade:** Confusion Agitation Myoclonus Tremor Abnormal speech Hallucinations Coma

2- **Peripheral muscarinic blockade:** Mydriasis Anhidrosis* Tachycardia Urinary retention* Ileus

MANAGEMENT:

1-Supportive care IVF to replace insensible losses from agitation, hyperthermia

2-Benzodiazibines to stop agitation

3-Physostigmine (cholinomimetic) Induces cholinergic effects

Cholinergic (Organophosphate - carbamate insecticides – Physostigmine –Edrophonium) :

FEATURES: (SLUDGE syndrome)

Salivation ,Lacrimation Urination Diaphoresis GI upset: Diarrhea, vomiting ,Eye: Miosis

MANAGEMENT:

1- Supportive care

2- Antagonize muscarinic symptoms => Atropine

3- Stop aging of enzyme blockade => 2-PAM (Pralidoxime): regenerate AchE.

4- Prevent and terminate seizures => Diazepam

sedative – hypnotics (Benzodiazepines - Diazepam) :

FEATURES :

CNS depression, lethargy Can induce respiratory depression Can produce bradycardia or hypotension

MANAGEMENT:

1Supportive care

2Use benzo antidote "Flumazinil"

It is an antagonist at the benzodiazepines receptor RARELY INDICATED

If seizures develop either because of benzo withdrawal, a co-ingestant or metabolic derangements, have to use 2nd line agents, barbiturates, for seizure control.

Psychiatric drugs

1- Monoamine Oxidase Inhibitors(MAOIs)

- Bind irreversibly to monoamine oxidase
- Aged cheese and wine have double effect with Monoamine oxidase inhibitors

because they **both contain**: Tyramine precursor ➔more release of NE ➔Hypertensive crisis.

2: Tricyclic Antidepressants (TCA)

other uses: (migraine, IBS etc.) e.g., amitriptyline

TCA's Major Pharmacodynamics Effects

Inhibition

1- Inhibition of reuptake of biogenic amines. (e.g., norepinephrine, serotonin).

2- Indirect GABAa antagonism caused by binding at picrotoxin receptor.

blockade

3- Alpha1-adrenoreceptor blockade ➔ hypotension.

4- Muscarinic Receptor blockade ➔(anticholinergic effects)

5- Histamine receptor blockade
6-Potassium efflux blockade.
} (widens QT) → Ventricular tachycardia (polymorphic) (torsades de pointes)

7-Sodium channel blockade →widens QRS ➔ Ventricular tachycardia (monomorphic)

Effects of TCA'S on ECG (important)

1. Sinus Tachycardia
2. Prolonged QT Interval
3. Widening of the QRS interval
4. RAD (Right axis deviation).
5. Prominent R in aVR (also called positive aVR) → Due to Sodium channel blockade

Specific Management → (NaHCO3) **for tow reasons**

A: Plasma Alkalization (NaHCO3/ Hyperventilation)

B: Sodium Load (NaHCO3 or 3% Saline)

3: Selective serotonin reuptake inhibitors; (SSRI)

SSRIs have a wide therapeutic index

SSRIs can cause
- **1- QT prolongation.**
- **2-Seizures** due to severe hyponatremia

- Hyponatremia
  - in Young patient think about SSRI
  - in Old patients think about Diuretic Especially Thiazides

Serotonin Syndrome:

Clonus associated with overdose in Hx ➔ think of serotonin Syndrome Immediately.

Cyproheptadine → (Antidote for serotonin Syndrome).

Acetaminophen overdose

- Therapeutic dose of acetaminophen is 10-15 mg/kg/dose for children. 325-1000 mg/dose every 4-6 hours for adults, with a maximum of 4g/day.
- Toxic dose of APAP is 150 mg/kg for children up to 12 years old and > 6g in adults.
- 90% of APAP metabolism is through hepatic (glucuronide/sulfate) conjugation, 5% excreted unchanged in the urine and 5-15% through oxidation by P450 cytochromes to NAPQI (Normally, NAPQI will be detoxified by glutathione).
- In case of APAP overdose, **over saturation** of glucuronidation and sulfation pathways causes p450 cytochromes to take over which will lead to accumulation of NAPQI (toxic metabolite).

There are 4 clinical stages for APAP toxicity:

- **I Preinjury**: 0.5-24h Nausea/Vomiting, anorexia or asymptomatic
- **II Liver Injury:** 24-48h Resolution of stage I + RUQ pain, High PTT, INR, bilirubin + enzymes (at the latest by 36h)
- **III Max. liver injury**: 48-96h Liver failure (encephalopathy, coagulopathy, hemorrhage, acidosis)
- **IV Resolution:** 4-14 days

- If the patient has a history of APAP overdose, a serum APAP level should be measured between 4 -24 hours after ingestion and evaluated according to **Rumack-Matthew nomogram** to determine the risk of hepatotoxicity and the need for NAC therapy.
- The Rumack-Matthew nomogram uses the serum acetaminophen level, correlated with time after ingestion, to assess hepatotoxicity risk for single acute ingestions of acetaminophen.
- 60% of patients whose APAP level falls above the upper line of the Rumack-Matthew nomogram will develop hepatotoxicity.

  AST is the most sensitive lab test for early detection of hepatotoxicity.
- **A, B, C, D**econtamination (charcoal) **F**ind antidote (NAC) are the management guidelines for APAP OD.
- NAC (N-acetylcysteine) works as glutathione precursor, therefore as detoxifier for NAPQI.
- NAC optimally should be given between 8-10 hrs. but if it has been more than 10 hrs you still should give NAC.

❖ Indications for NAC:

- APAP level above the treatment line on Rumack-Matthew nomogram.
- Hx of significant APAP ingestion presenting close to 8h (give while waiting for level).
- All APAP ingestions who present late >24h with either detectable APAP or elevated transaminases.
- Chronic ingestions (>4g/day in adult, >120mg/d in child) with elevated transaminases.
- Hx of exposure and fulminant hepatic failure (FHF).

Cardiovascular drugs

Med:	Mechanism of action:	Diagnosis:	Management:
β-Blockers:	They inhibit endogenous catecholamines such as epinephrine at the beta-receptors. **Onset of toxicity is early, so the absence of symptoms 4 hours after ingestion indicates a low risk .**	- Diagnosis of β-blockers overdose depends on the clinical picture of the patient. - In children with β-blockers overdose, Hypoglycemia is common.	1- IV fluids ,Oxygen , and monitoring of card for rhythm and respirations. 2-Atropine, Glucagon, Sodium bicarbonate, Crystalloid fluids ,(HIDE),Calcium. 3-External or trans-venous pacemaker. 4-Cardioversion and defibrillation.
Calcium channel blockers:	Blocking the slow calcium channels in the myocardium and vascular smooth muscle leading to : ○ coronary and peripheral vasodilation. ○ Reduction in cardiac contractility ○ Depression of SA nodal activity ○ slow AV conduction	**Serum levels of calcium antagonists are not available.** Serum glucose and Electrolytes . ECG is necessary, A prolonged QRS or QT interval suggests **Bepridil** ingestion or a co-ingested Tricyclic antidepressant (TCA).	✓ IV fluids ✓ Oxygen supplement ✓ Cardiac monitoring ✓ Vomiting Atropine ✓ Intravenous calcium Epinephrine, norepinephrine, and dobutamine. ✓ Glucagon ✓ Insulin

Nitrates and Nitrites:	At lower doses nitrates primarily dilate veins At higher doses they also dilate arteries.	When methemoglobin levels exceed 15%, a venous blood sample appears chocolate brown, and the skin appears blue even while patients look remarkably comfortable.	IV methylene blue, but this antidote is usually not needed unless methemoglobinemia approaches 30%.
Digitalis:	Increasing the force of myocardial contraction . Decreasing atrio-ventricular(AV) conduction It inhibits membrane sodium-potassium adenosine triphosphatase (ATPase). ○ Digitalis indirectly increases vagal activity and decreases sympathetic activity.	Serum digoxin levels .	hemodialysis, hemoperfusion, and exchange transfusion are ineffective. ✓ Electrolyte Correction ✓ K (Potassium can be administered orally (which is safer) or intravenously I.V.) severe hyperkalemia treated with IV glucose, insulin, and sodium bicarbonate. (-ve Ab). ✓ magnesium sulfate. ✓ Atropine. ✓ external or trans-venous pacemaker. ✓ Cardioversion and defibrillation .

Heavy metals

- ✓ **Iron toxicity cause <u>gastrointestinal mucosal injury.</u>**
- ✓ **If patient swallow iron tablets and he came with no symptoms at all then no need to anything to him because he didn't reach the toxic dose.**
- ✓ **60 mg\kg is the toxic dose of iron toxicity.**
- ✓ **Sometime phase 4 toxicity have low iron level because it's distributed in the whole body .**
- ✓ **Carbonyl iron is the highest compound with 100 elemental concentration of iron**
- ✓ **Iron toxicity inhibit energy production "shut down mitochondria "**
- ✓ **No need for x-ray in a child who ingested tablets "it's not an investigation tool in toxicology except in special cases"**
- ✓ **Whole bowel irrigation contraindicated in <u>bowel obstruction and perforation</u>.**
- ✓ **Pregnancy is not contraindicated in Deferoxamine.**
- ✓ **Deferoxamine binds to iron to form the water-soluble compound ferrioxamine which is excreted in urine or dialyzed, it's administrated by infusion at a dose of 15 mg/kg/hr. for up to 24 hours.**

<u>Phases of iron toxicity:</u>

1) **Phase 1 is characterized by GI upset and + abdominal pain.**
2) **Phase 2 is the recovery phase after phase 1 but it is a dangerous phase.**
3) **Phase 3 is the shock face "dehydration – hypotension and acidosis, etc..**
4) **Phase 4 is called Fulminant hepatic failure.**

Opioids and sedatives

Opioids	
Examples	• **Opiate:** natural opioids causes histamine release > vasodilation > hypotension (e.g., Morphine and codeine) • **Opioid:** synthetic derivative has a cardiovascular stable effect, no hypotension (e.g, Fentanyl and Meperidine) • **Narcotic:** referred to any compounds with sleep induction effects
Clinical effects	• Pain killer – Diarrhea – Euphoria producing
Toxicity effects	• CNS depression • Respiratory depression • Miosis • Other: Sensorineural loss – Hypotension – Nausea and vomiting – Urinary retention – Pruritus
Antidote	• Naloxone: Action duration of opioids are longer than Naloxone. So, patients have to be observed for the recurrence of opioid toxicity
Withdrawal	• Symptoms: Sweating – Mydriasis – Tachycardia – Goosebumps – Abdominal pain – Vomiting – Diarrhea • Methadone is the treatment

Benzodiazepine	
Examples	Alprazolam – Clonazepam – Diazepam – Lorazepam – Midazolam etc ..
Clinical effects	Sedatives – Hypnotic – Anxiolytics - Anticonvulsant
Toxicity effects	CNS depression – Resp. depression – Hypotension – High anion gap metabolic acidosis (WHY? Due to propylene glycol)
Antidote	• Flumazenil: ✓ It is for Acute overdose , not chronic users ✓ Contraindicated in seizures
Withdrawal	• Nonspecific: Anxiety – Depression – Insomnia – Tremor – Tachycardia - Sweating • Severe: Visual hallucinations – Delirium - Seizures

Cocaine and sympathomimetics

- Cocaine, amphetamines, and derivatives of amphetamines are called sympathomimetics.

Metabolism:

- Cocaine metabolism occurs **in the liver and the plasma.**
- In the liver, primarily to the active metabolite norcocaine, which potentiates the parent drug.
- In the plasma, to ecgonine methyl ester via pseudocholinesterase (plasma cholinesterase). ***If psedocholinesterase is dificient, cocaine intake will cause sudden cardiac arrest.***
- **Benzoyl ecgonine is a metabolite found in the plasma and is the metabolite identified by urine toxicology screens.**

Clinical features: (Excitation of the sympathetic nervous system)

- Patients with moderate toxicity are alert and awake but may have , **diaphoresis, tachycardia, mydriasis, and hypertension without organ damage.**
- A more severely intoxicated patient may present agitated, combative, and **hyperthermic.**
- Signs and symptoms of **end-organ damage may be present, including acute hypertensive emergencies.**
- Patients may present with focal**, acute pain syndromes; circulatory abnormalities; delirium; or seizures.**
- Patients who are “speed balling,” using IV heroin **(morphine)** and cocaine together, may be **initially sedated**, and administration of naloxone may reveal the underlying cocaine intoxication.
- Mortality is high with temperatures greater than 41.1°C.

Diagnosis criteria

1-Urine test:

- Concain is metabolsed to benzoyl ecgonine and excreted in the urine (present for 3 days after last use).

2-ECG:

- Torsades de pointes or wide-complex tachycarida

Complications:

Arrhythmia:

- **Sinus tachycardia** is the most common but other forms of arrhythmia (AF & supraventricular tachycardia) could happen
- Happens due to sodium channel blockage.
- **ECG:** Torsades de pointes or wide-complex tachycarida
- **Treatment**: sodium bicarbonate (first line of treatment) & lidocaine

Hyperthermia:

- Increased motor tone can release intramuscular (CK) with rhabdomyolysis and renal and electrolyte complications.
- Best route to assess the temperature is rectal.
- **Treatment**: for severe active cooling

Hypertension crisis:

- **Complication of hypertension:** Aortic dissection, pulmonary edema, myocardial ischemia and infarction, intracranial hemorrhage, strokes, infarction of the anterior spinal artery.
- **Treatment: phentolamine** (Alpha blockers) (DO NOT GIVE BETA BLOCKERS)

Rhymbdomylosis :

- Due to Hyperthermia or myocardia infarction
- Investigation: high Creatinine kinase (CK), hyperkalemia
- Complications: Acute kidney injury
- **Treatment:** Fluids

Seizure:

Treatment: Benzodizepan (diazepam lorazepam midazolam)

Other complications:

- Crack dancing: a transient choreoathetoid movement disorder
- Endocarditis:
- Pneumothorax & pneumomediastanum

Organophospates

❖ **Pesticides :** all pest-killing agents.

❖ **Principle of disease:**

- Organophosphorus insecticides are **highly lipid soluble**
- organophosphorus compounds are less potent than their result in **delayed onset of clinical toxicity.**
- Because of the global penetration of organophosphorus compounds, inhibition occurs at tissue sites (true acetylcholinesterase represented by erythrocyte cholinesterase) and in plasma (circulating pseudocholinesterase).

❖ **Clinical feature sign and symptom:**

- The clinical syndrome of muscarinic acetyl cholinesterase inhibition is commonly called the SLUDGE syndrome or DUMBELS.

❖ **Complications:**

- Muscle hyperactivity eventually gives way to muscle paralysis (including respiratory muscles and diaphragm).Respiratory insufficiency results in death if not anticipated and corrected.

❖ **Diagnostic strategy:**

- Known or suspected exposure to cholinesterase inhibitors should be confirmed by ordering plasma and erythrocyte (RBC)cholinesterase levels.
- In acute exposures, the plasma cholinesterase levels decrease first, followed by decreases in RBC cholinesterase levels.
- The RBC cholinesterase level is more indicative of what is occurring at the nerve terminal.

❖ **Management:**

- Standard treatment is resuscitation, supportive care, decontamination, and use of atropine.

Chemical and Radiation Exposure

- **determinants of the degree of injury** (Concentration, Duration of exposure, Anatomically weaker body parts)
- **Aciditic injury:** Cause protein denaturation & coagulative necrosis, and then **Eschar formation.**
- **Alkalitic injury:** Saponification and liquefactive necrosis of body fat. **(MORE DANGEROUS)**

❖ Hydrofluoric Acid:

- Liquefactive necrosis (similar to alkalis).
- Free fluoride ion is responsible for the injury
- Dermal injury is the most common

Management:

- ✓ Irrigation for 15 to 30 minutes and Blister removal.
- ✓ Detoxification Locally, Infiltration or Intra-arterial infusion of Ca. Gluconate

❖ Hydrocarbon:

- Lungs (aspirations) are the most common organ affected
- Perioral or perinasal dermatitis with pyoderma. This so-called "huffer's rash"
- Substances with high volatility, low viscosity, and low surface tension are **the most toxic.**

Management:

- ✓ Remove offending agent, Irrigation, Airway management.
- ✓ Bronchodilators, Observation for minimum of 6 h after ingestion

❖ Nerve agent:

- Primary clinical toxic effects are **respiratory .**
- Effects of **Muscarinic Rceptors:**
  - ✓ **DUMBELS** (diarrhea, urination, miosis, bronchoconstriction or bronchorrhea, emesis, lacrimation, and salivation).
  - ✓ **SLUDGE** (salivation, lacrimation, urination, defecation, and gastrointestinal emesis)
- Effects of **Nicotinic Receptors**:
  - ✓ Muscle fasciculations and weakness

Management:

- ✓ Decontamination , Maintaining an airway and restoring adequate oxygenation and ventilation.
- ✓ Anti-muscarinic (Atropine), pralidoxime.
- ✓ Benzodiazepines for seizures.

❖ Cyanide:

- It's a Cellular toxin that Inhibits oxidative phosphorylation and cause Cellular hypoxia and death.
- Sudden cardiovascular collapse, Coma, metabolic acidosis , characteristic odour of **bitter almonds.**

Management:

- ✓ Decontamination, Personal Protective Equipment, ABCD
- ✓ Antiarryhthmics
- ✓ Antidotes :
  1. Cyanide antidote kit (Amyl nitrite, sodium nitrite, and sodium thiosulfate)
  2. Hydroxocobalamin.

❖ Radiation exposure

Acute Radiation Syndrome:

- The early indicator for a significant radiation exposure is the absolute decreased lymphocyte count.
- median lethal whole-body dose estimated to be approximately 4.5 Gy.

Management:

- ✓ Reduce Exposure.(time, distance, and shielding)
- ✓ Decontamination
- ✓ ABCD's & Supportive measures.
- ✓ Chelating agents for Internal contamination.

INHALED TOXINS

FIRST : SIMPLE ASPHYXIANTS : (e.g carbon dioxide)

#If the FiO2 fall to be from 21% to 15% patients will develop: 1- Autonomic stimulation 2- Cerebral hypoxia

#If FiO2 falls below 10% : patient will have Cerebral Edema and Lethargy.

#If FiO2 falls below 6%: It is **Fatal.**

#asphyxiation is the most fatal type of inhaled toxins.

Management :

- Removal from exposure and supportive care.
- this will terminate the hypoxia and results in clinical improvement.
- Failure to improve suggests complications of ischemia (e.g., seizures, coma, and cardiac arrest) That is poor prognosis.

SECOND: PULMONARY IRRITANTS :

- These gases when they go to the lung and dissolve because they are water soluble.
- **In Massive or prolonged exposure:** *laryngeal edema *Laryngospasm *bronchospasm *Acute Lung Injury.

Management :

1. Signs of upper airway dysfunction (hoarseness and stridor) ⇛Visualization of the larynx and immediate airway stabilization .
2. Bronchospasm ⇛ Inhaled beta2-adrenergic agonists (Salbutamol) or Ipratropium bromide (Atrovent).
3. Chlorine or hydrogen chloride gas ⇛ Nebulized 2% sodium bicarbonate solution symptomatic relief .
4. Diagnosis of ALI (ARDS) ⇛ Advanced ventilation modes in ICU.+ Exogenous surfactant + Nitric Oxide (NO) ventilation

THIRD: SMOKE INHALATION:

- 1)Irritant injury: heated particulate matter and adsorbed toxins injure normal mucosa, similar to other irritant gases.
- Carbon monoxide and Cyanide are systemic toxins.

Clinical Features :

- respiratory tract damage, Thermal and irritant induced laryngeal injury
- Cough, Stridor, Bronchospasm
- Early death result from : (asphyxia - airway compromise - .metabolic poisoning "e.g., CO ")

❖ **Cyanide** ⟶ Metabolic acidosis! (with serum lactate level greater than 10 mmol/L)

Management :

Supportive : Bronchoscopy with bronchoalveolar lavage

Management of victims of smoke inhalation and irritant inhalational injuries : similar.

- Rapid assessment of the airway and early intubation is critical!
- Inhaled beta-adrenergic agonists
- Optimal supportive care
- maintenance of adequate oxygenation (e.g., suctioning and pulmonary toilet) "most important aspects of care"

Toxic Alcohols

 # Methanol, Ethylene Glycol and Isopropanol are the Toxic Alcohols but not Ethanol which is not toxic.

1)Methanol:

#you can find it in the antifreeze fluid, paints thinner and inks.
#it is rapidly absorbed (≤ 1 hour) and that limited the decontamination use in the management.
#half-life is 24-36 hour.
#only 4ml could be lethal.
#Methanol is not toxic as it is, but its metabolic products (Formaldehyde and Formic Acid) which produce in the liver by Aldehyde Dehydrogenase enzyme are causing the problem.
#they cause: CNS depression (putamen and basal ganglia hemorrhage), Optic neuropathy (blindness), high anionic gap metabolic acidosis (because of formic acid and lactic acid accumulation)→(cause tachypnea to compensate the acidosis) and cause high osmolar gap(≥10 moles).

#patients present late(24-72 hour) because it takes time for the toxic metabolites to accumulate.

2)Ethylene Glycol:

#you can find it in the antifreeze fluid.
#it is rapidly absorbed like Methanol.
#30% execrated throw the kidneys and 70% get metabolized in the liver.
#the harmful metabolites of Ethylene Glycol metabolism are: Glycolic Acid and Glycoxylic Acid that produce by the liver and they cause: high anionic gap metabolic acidosis, high osmolar gap, CNS depression, renal problems (because of Calcium Oxalate accumulate in the renal tubules and case the present of Oxalate Crystals in the urine) and hypotension.

Management (for both Methanol and Ethylene Glycol):

#1-ABCs …. 2-Saudium Bicarbonate $NaHCO_3$ (for the acidosis) …. 3-Fomepizole (to block the enzyme Aldehyde Dehydrogenase) …. 4-Hemodialysis (to get rid of the toxic substance) …. 5-Calcium some times in Ethylene Glycol toxicity.

3)Isopropyl Alcohol:

#do not cause high anionic gap metabolic acidosis but cause high osmolar gap.
#the end result in Isopropyl Alcohol metabolism is acetone and that cause acitosis.
#Cause CNS depression and hypotension but it is not toxic as Methanol and Ethylene Glycol and the management is supportive.

Aspirin Toxicity

Introduction

- Aspirin is highly absorbed by intestine (2/3 of ingested dose within 1 hour) and reach peak levels within 2-4 hours after ingestion. It's metabolized by hydrolysis in intestinal wall, liver and RBCS, it's then transferred by albumin to kidney to be excreted as free salicylate.
(Before that, some is conjugated by glucourination in the liver to be inactive).
- The metabolic pathways become saturated when plasma levels ≥ 30mg/dl, at which toxicity can occure.

Manifestations

1/Acid base disturbance, the acidic nature of salicylate lowers plasma PH, this will stimulate hyperventilation to compensate. However, compensatory hyperventilation doesn't exist for a long time.
- Persistent toxicity suppresses the mitochondrial oxidative phosphorylation, where lactic acidosis and ketoacidosis develop and worsen the metabolic acidosis.
- Urinary bicarbonate excretion is an additive factor to the acidosis as well.

All these play a role in the development in hypoglycemia and hyperthermia eventually.

2/Fluid and Electrolytes abnormalities, Mainly K loss due to vomiting, renal excretion, inhibition of active transport system in the body "which has a big role in K preservation"

3/Pulmonary and cerebral edema, due to unknown mechanism. Patients require immediate dialysis.

- Salicylate toxicity due to chronic ingestion, common in elderly secondary to impaired metabolic activity. They can be more ill than patients with acute toxicity due to the high levels of unbound (active) salicylate molecules.

- Acute salicylate toxicity: require a single dose of (200-300mg/kg), (500mg/kg) is lethal. Initial symptoms are tinnitus, deafness, vomiting, hyperventilation and hyperthermia.
It can lead to severe dehydration.
Non-cardiac pulmonary edema present as severe shortness of breath.

Diagnosis

1/Serum levels after 6 hours, (a 2nd sample should be obtained 2 hours later ± serial measurements).
2/ABGs (decreased PH, decreased HCo3 and CO2) Hemodialysis is required.

Management

- Initially, examine the patient including vital signs, chest auscultation and O2 saturation.
- Aim is to correct acid/base abnormalities as well as fluid and electrolytes disturbance.

1/ IV fluid: (monitor urine output, it shouldn't exceed 2-3ml/kg/h, since increased amount may worsen brain and pulmonary edema), fluid is of dextrose type.
2/Urine alkalization: Sodium bicarbonate (1–2 mEq/kg) over 1 to 2 hs (until urine PH=7.5-8) can potentially enhances salicylate excretion.
3/Hemodialysis.
4/Exchange transfusion (can be indicated in congenital salicylism)

Note: Gastric emptying and activated charcoal is of no value in salicylate poisoning.

Caustic injury

Summary

	Acid	Alkali
Type of necrosis	Coagulation necrosis	liquefactive necrosis
Effect	eschar formation & systemic acidosis	fat saponification, and protein disruption
Features	strong odor and cause immediate pain on contact	odorless and colorless and does not cause immediate pain
Esophagus injury	less likely to cause esophageal and pharyngeal injury	typically affects the oropharynx, hypopharynx, and esophagus.
Clinical features	oral pain, abdominal pain, vomiting, drooling, wheezing, coughing and chest pain .	
Diagnosis	chest radiograph, abdominal CT or US, ABG, endoscope and bronchosope	
Management	**ABCD, NG tube, Surgical exploration,** Corticosteroids	
Special cases	1. **Ocular alkali:** Lavage with at least 2 L of normal saline per eye 2. **Dermal caustic exposures:** Clothing removal, copious irrigation, and local wound debridement 3. **Hydrofluoric acid:** hypocalcemia and dysrhythmias 4. **Povidone-iodine (Betadine):** GIT injury → starch or milk 5. **Phenol or Formaldehyde:** GIT injury 6. **Concentrated hydrogen peroxide (H2O2):** GIT injury → Hyperbaric oxygen 7. **Button batteries**	

Calculation of Anion Gap and Osmolar Gap

- The normal blood pH range is 7.35 to 7.45. In order for normal metabolism to take place, the body must maintain this narrow range at all times.
- The PH is inversely proportional to the number of hydrogen ions (H+) in the blood.
- **When the PH is acidic**: Negative inotropic effect + decrease in vascular response to catecholamines.
- **When the PH is alkalotic**: this interferes with tissue oxygenation and normal neurological and muscular functioning.
- Significant changes in the blood pH >7.8 or <6.8 will interfere with cellular function, and if uncorrected, will lead to death .

❑ The buffer response has two components:

1- **RESPIRATORY**: The blood pH will change according to the level of carbonic acid present. This triggers the lungs to either increase or decrease the rate and depth of ventilation until the appropriate amount of CO2 has been re-established.
Activation of the lungs to compensate for an imbalance starts to occur **within 1-3 minutes.**
2- **RENAL**: As the blood pH decreases, the kidneys will compensate by retaining HCO3- and as the pH rises, the kidneys excrete HCO3- through the urine. (**It takes hours to days.)**

❑ Components of blood gas are:

- PH: based on the H+ ions present.
- PaCO2: Amount of CO2 dissolved in blood (35-45)
- PO2: pressure of O2 in arterial blood (80-100 mm Hg).
- SaO2: O2 saturation (95% - 100%)
- HCO3: the amount of HCO3 in the bloodstream (22-26 mEq/liter)
- B.E: base excess indicates the amount of excess level of HCO3 in the system (–2 to +2 mEq/liter).

Special thanks for those who contributed to this work:

- Abdullah Alatar
- Omar Aldhasee
- Naif Alhefdhi
- Ahmed Alhussein
- Maan Alherbish
- Hisham ghabbani
- Noha almndeel
- Nawal Asiri
- Fatimah Alqarni
- Malak Almutairi

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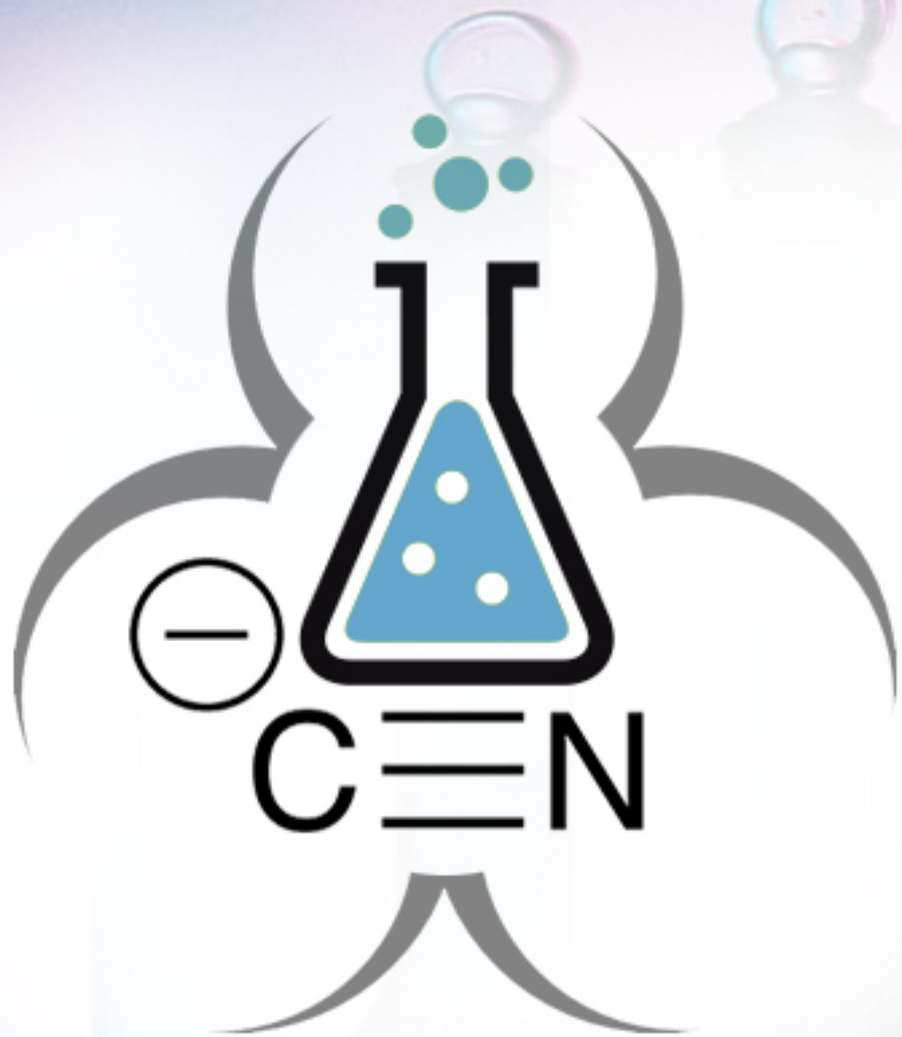

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