



CLINICAL TOXICOLOGY LAB.

5<sup>TH</sup> STAGE / 1<sup>ST</sup> SEMESTER

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# CLINICAL TOXICITY OF ACETYLSALICYLIC ACID (ASPIRIN)

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## **BACKGROUND:**

- Aspirin & other salicylates are among the oldest medications remaining in clinical practice
- the use of aspirin as analgesic has declined because of
  - Association with Reyes syndrome in children
  - The development of other types of NSAIDs
- Aspirin remains the most widely used analgesic (locally; available as methyl salicylate in gel preparations for sore muscle), and as keratolytic in skin ointments
- Aspirin remains the most widely prescribed antiplatelet therapy for patients with cardiovascular & cerebrovascular diseases, and thus aspirin toxicity remains an important clinical problem

## **MECHANISM OF PHARMACOLOGICAL ACTION:**

- Aspirin non-selectively inhibits both (COX1 & COX2) isoforms
- It forms irreversible binding with the cyclo-oxygenase enzymes
- Causing inhibition of all types of prostaglandin and thromboxane synthesis, and producing (analgesic, antipyretic, anti-inflammatory and antiplatelet effects)

## MECHANISM OF TOXICITY:

- Rapidly absorbed after oral ingestion over the small intestine, with peak C<sub>plasma</sub> of one hour
- Stimulation of the CRTZ in the medulla >>> nausea and vomiting
- Activation in the respiratory center in the medulla >>> hyperventilation, and respiratory alkalosis
- Interferes with cellular metabolism (Krebs cycle and oxidative phosphorylation) >>> metabolic acidosis
- By inhibiting the cyclo-oxygenase enzymes >>> inhibiting PG & TXa<sub>2</sub> synthesis >>> platelet dysfunction, and gastric mucosal injury
- Increase fatty acid metabolism >>> ketosis, lactic acidosis and hypoglycemia.

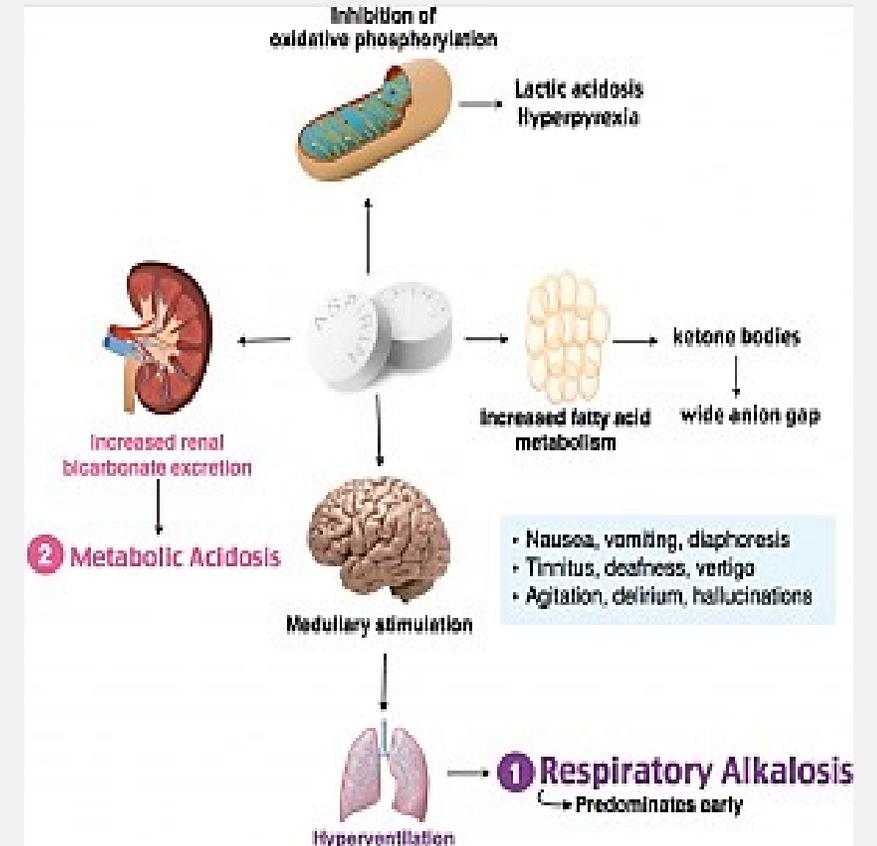
# CLASSICAL TOXIC EFFECTS OF ASPIRIN:

## • In overdose with aspirin:

- Peak levels are frequently delayed (up to six hours)
- Degree of protein binding is decreased and hepatic detoxification becomes saturated
- Slow renal elimination and half life increases up to 30 hours

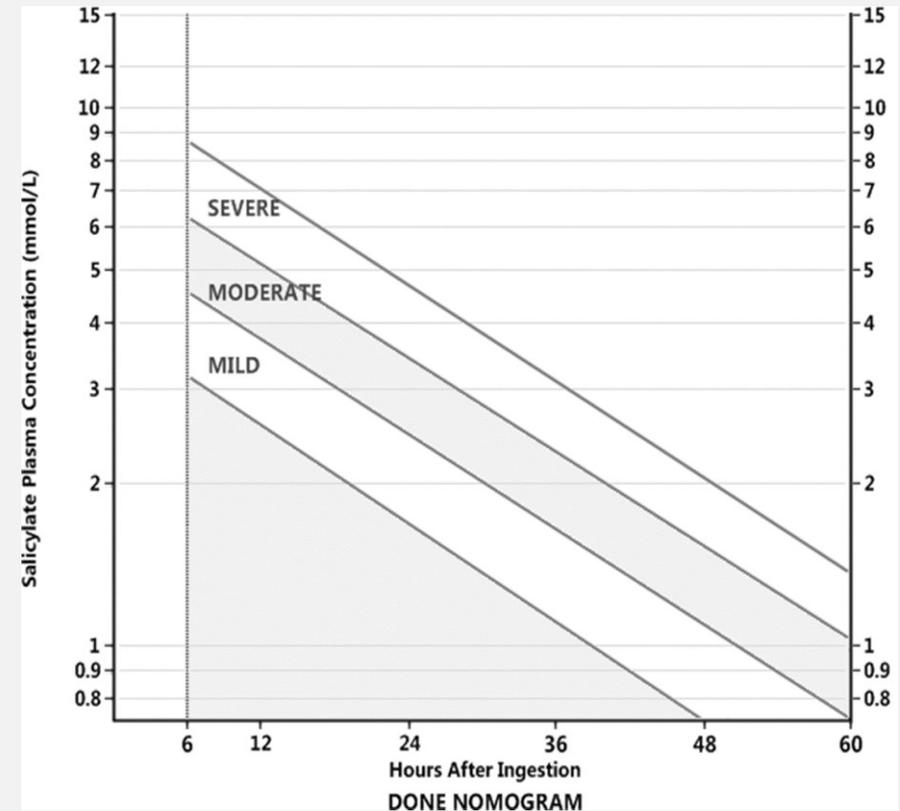
## • General toxic effects:

- Reye s Syndrome
- Non-cardiogenic pulmonary edema (NCPE).
- Hypoprothrombinemia and platelet dysfunction
- Nausea, vomiting , slow GI motility , hemorrhagic gastritis
- Rhabdomyolysis from hypermetabolism, seizure activity, and increased heat production.
- Tinnitus preceding deafness



# DIAGNOSIS:

- Confirm ASA by FeCl<sub>3</sub> test; A few drops of FeCl<sub>3</sub> and 1ml urine turns purple for a positive test
- Obtain serum ASA:
  - therapeutics 15-30 mg/dl,
  - toxic level above 40 mg/dl,
  - potentially lethal 100mg/dl.
- Confirm positive urine ketones secondary to anaerobic fatty acid metabolism
- Respiratory alkalosis and metabolic acidosis (serum bicarbonate, potassium, and chloride)
- Coagulation changes



## IMPORTANT NOTES:

- If the patient present with unexplained pulmonary edema, always this of ASA toxicity
- If the patient present with mixed acid-base disturbance, always think of ASA toxicity
- Serum salicylate value above 40mg/dl is associated with toxicity, while serum levels above 100mg/dl are associated with high morbidity and mortality, and an indication for hemodialysis
- Serum salicylate level should be measured every 2 hours after starting the management
- Toxic dose = 200 – 300 mg/kg, while lethal dose = 500mg/kg

## MANAGEMENT OF TOXICITY:

- Support ventilation (specially if there is pulmonary or cerebral edema)
- Gastric lavage followed by AC (within 1 hour of ingestion)
- Fluid replacement and correction of K depletion
- Glucose supplement to correct hypoglycemia and ketosis (specially when there is cerebral edema)
- IV NaHCO<sub>3</sub> to counteract metabolic acidosis in blood and alkalization of urine for enhancement excretion
- Vitamin K to avoid coagulation defects
- diazepam for seizure if present
- Hemodialysis is indicated in severe poisoning, renal failure, and seizures with coma



Thank you  
for your  
attention