NSAIDS INTOXICATION

MIRACLE Academy

سموم
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لجان الدفعات

قال تعالى (يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ)


صباح
صباح
النـدم
الياريتني
وانا ليه عملت في نفسي كده
على أغلى
المراكمين

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

Overview:

من الاثار الجانبيه الي يعملهم نزيف قرحه بالمعده يعارض ادويه الضغط ويرفع الضغط احتباس لسوائل وضرب الكلى ويعمل broncospasmeلناس الي معهم ازمه بس احنا رح نحكي اكثر عنهم بحاله التسمم وشو يعملو اكثر من الاعراض الجانبيه

هاي تتغير حسب ارتباطه بالبروتين

امتصاصهم يوخذ ساعه لساعتين ولكن اذا ماخذ وجبه كبيره تقلل حركه الأمعاء رح يتم امتصاصهم خلال 3 ل4 ساعات

Definition: NSAIDs are a chemically diverse class of drugs that have **anti-inflammatory, analgesic, and antipyretic, anti-aggregant properties**

KINETICS — Oral absorption of NSAIDs approaches 100 percent and peak serum levels usually occur **within one to two hours**. Large toxic ingestions or concomitant food consumption can delay peak levels up to three to four hours. NSAIDS are weak acids that are extensively (**up to 99 percent) protein bound**, with **a small volume of distribution** (0.1 to 0.2 L/kg**). Diseases** causing low protein levels or large NSAID ingestions can decrease plasma protein binding, resulting in an increased volume of distribution and greater penetration into body tissues, including the central nervous system.

ارتباطه مع البروتين عالي ولكن مش كثير كثير يخوف لانه عالي عنده TI ولكن اذا صار toxicبهتم فيه

NSAIDs

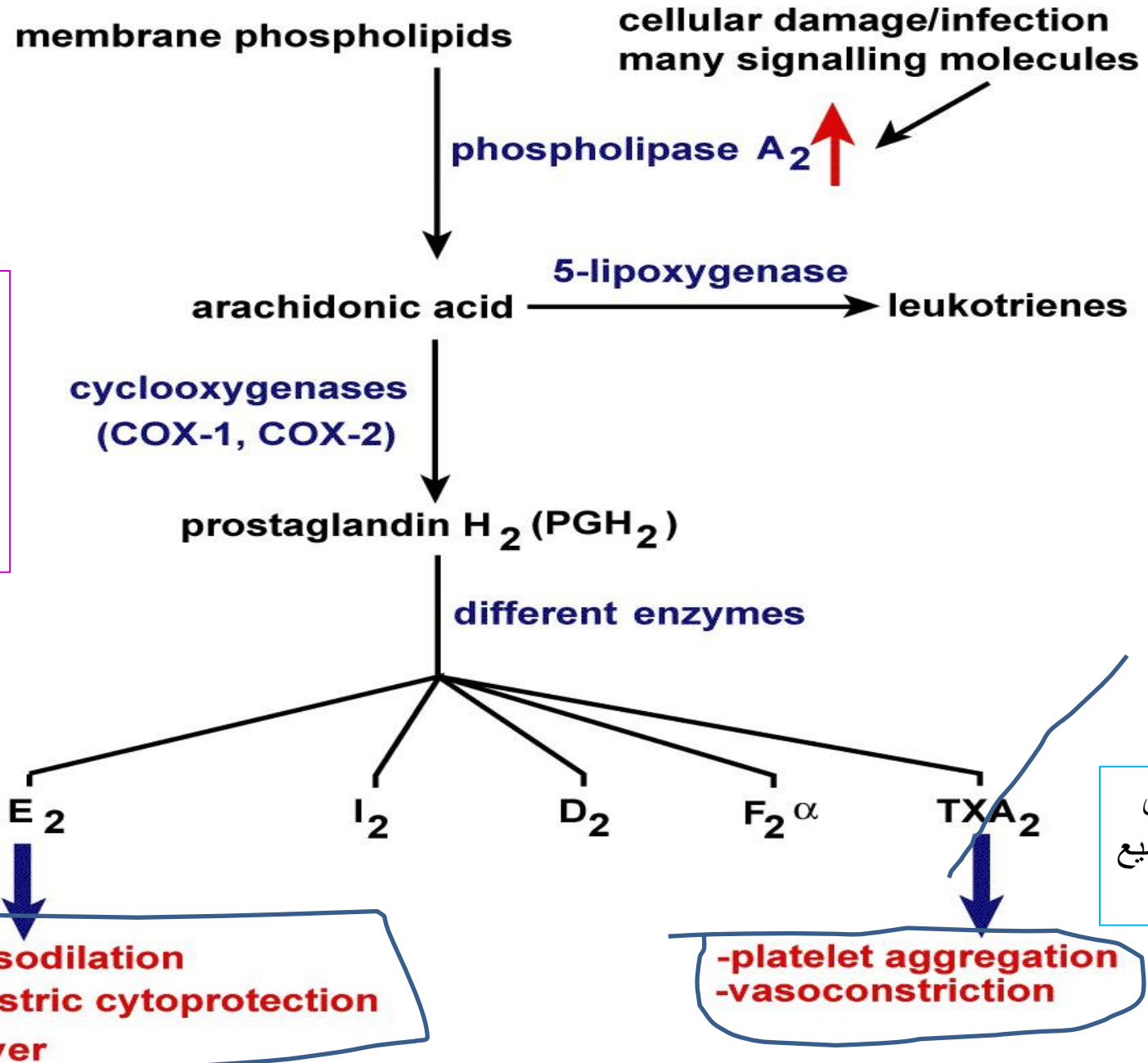
الأرقام مش حفظ

- Among the most frequently prescribed drugs worldwide:
- 70 million people/day prescribed NSAIDs
- 230 million people/day take OTC NSAIDs
- USA: 80 billion aspirin tablets consumed/year

USES

1. **Anti-inflammation**
2. **Analgesic**
3. **Anti-pyretic**
4. **Treatment of gout, arthritis**
5. **Prophylaxis of heart disease (myocardial infarction and stroke)**
6. **Prophylaxis of colorectal cancer**

Properties of Prostaglandins



NADSلما تكون non
selectiveتكون اكثر امان
للقلب لانها تشتغل
vasoconstriction and
vasodilation at the same
time

هاد اذا ثبطته بيعكس
التاثير يعني يعمل تميع
vasodilation

NSAID Mechanism

هاد الغير محترم يشتغل على
cox1
Cox2 selective

هاد دايما موجود هاد اهون بحاله في مرض للقلب
هاد بحاله الالتهابات

a) NSAIDs inhibit cyclooxygenase (COX)

b) Three types of cyclooxygenase:

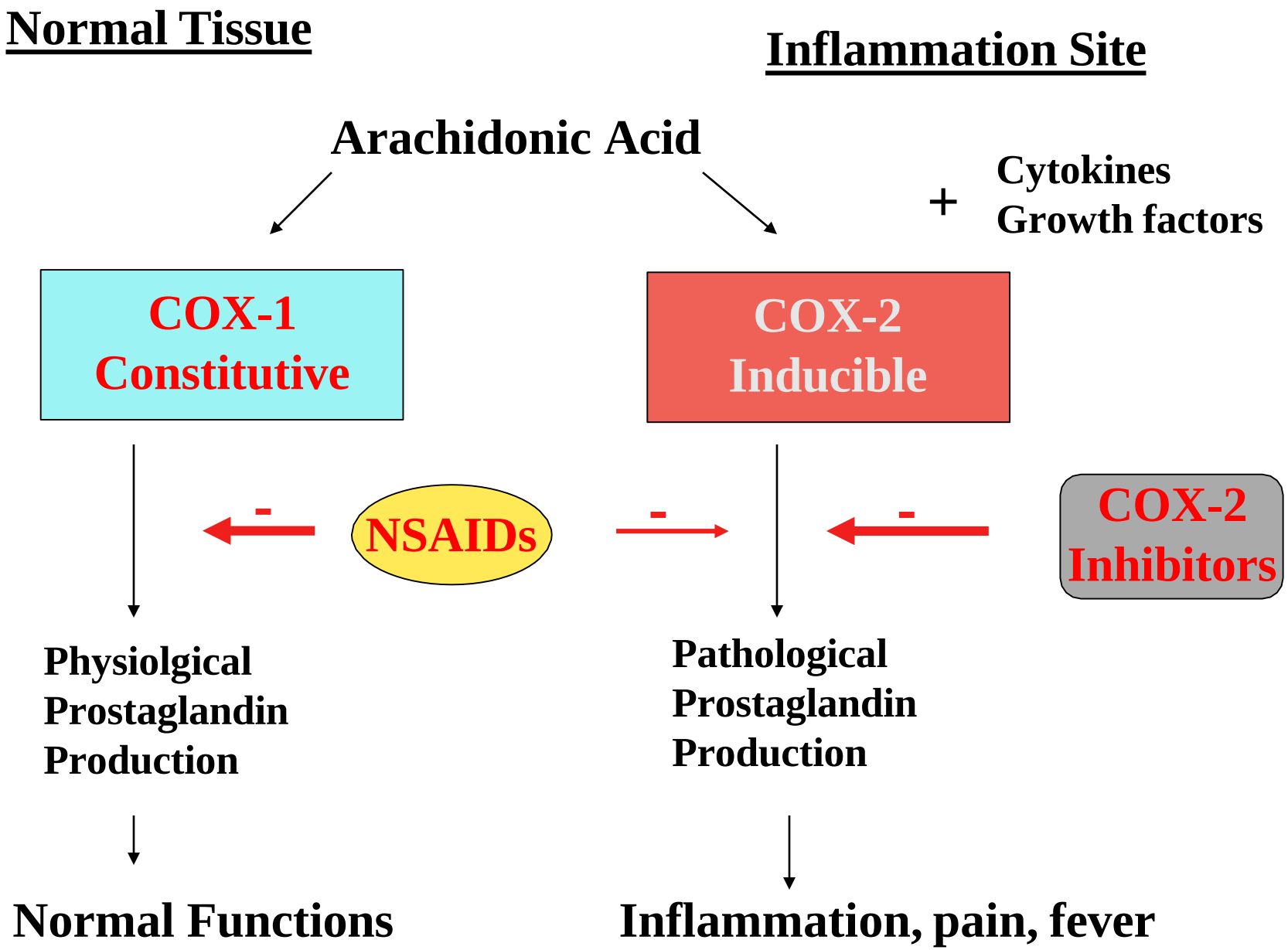
- COX-1 is constitutively expressed

- COX-2 is induced at sites of inflammation by inflammatory mediators

- COX-3 recently identified

هاد يشتغل ب normal
physiological
Without stress

COX-2 Hypothesis (1990s)



Side Effects of NSAIDs

- GI: N, V, abdominal pain, GI hemorrhage from local irritation
- Hematologic: hemorrhage resulted from impaired platelet aggregation
- Renal: Na and water retention. Nephrotoxicity is due, in part, to interference with the autoregulation of renal blood flow
- Cardiac: worsening of congestive heart failure due to water and sodium retention
- Obstetric: delay in the onset of labor, prolonged labor, increased risk of hemorrhage and may close ductus arteriosum by inhibition of PG
- Neurologic: minor CNS disturbances….drowsiness, blurred vision
- Hypersensitivity reactions

ياثرو على البروستاغلاندين الي يوسعو الارتري الي بغذو الكليه

بيعطوه لياجلو الولاده

هسا لما يعطوهم NSAIDsرح يصير في خطر انو الشريان الي يغذي البيبي بيسكر فيعمل فشل بالقلب عند البيبي والفكره انو البروستاغلاندين بيخليه فاتح (وهاد البيبي بالواقع ما يتنفس انما يوخذ الاكسجين من الام)

الي عندهم تفول ما بقدرو يوخذوهم وكمان الازمه ما بقدرو

COX-2 Specific Inhibitors

- **The newest generation of NSAIDs**, (rofecoxib [Vioxx], celecoxib [Celebrex], valdecoxib [Bextra]), selectively inhibits the COX-2 isoform at therapeutic doses
- The likelihood **of GI bleeding is less with these drugs** than with conventional NSAIDs
- There is limited information regarding overdoses of COX-2 inhibitors……**hypertension**, **acute renal failure**, **respiratory depression**, and **coma** may occur in overdose
- Rofecoxib and valdecoxib have been removed from the market because **increased risk for CV events** (including MI & stroke)

هدول انسحبو من السوق بسبب سميتهم

NSAIDs Classification

NSAIDs are subdivided into six groups based on their chemical structure

1. Salicylates
2. Pyrazolones: phenylbutazone
3. Indoleacetic acid (pyroles): diclofenac, indomethacin
4. Phenylpropionic acids: ibuprofen, ketoprofen, naproxen
5. Anthranilic acids: mefenamic acid
6. Oxicam: piroxicam

هدول نستخدمهم بس للحيوانات

هدول اقل الادويه selective
لذلك هم اخطر اشي للقلب

اكثر واحد
امن للقلب

اكثر اشي امنين
الجسم بخلص منهم

مش امن لا على
الكلى ولا على القلب
مش من المفضلين
اكثر واحد امن للكلى
هو الاسبرين

هدول اعطل اشي
للمعده لانهم بطولو
بالجسم لاتخلص منهم

Salicylate poisoning

- Adverse effects of aspirin & some NSAIDs related to alteration of COX include gastrointestinal (GI) ulcerations & bleeding, interference with platelet adherence, & a variety of metabolic & organ-specific effects.

- Salicylate is rapidly absorbed from aspirin tablets in the stomach. The pK a of aspirin is 3.5, & the majority of salicylate is nonionized in the acidic stomach.

لما امتصه لازم يكون nonionized ولما اتخلص منه احوله لionized

- Ingesting high doses of salicylate results in switching salicylate metabolism from first-order to zero-order kinetics.

اذا اخذته بجرعه كبيره رح يتحول من

- Toxic doses — An adult ingesting 10 to 30 g aspirin or a child ingesting as little as 3 g is potentially lethal. The ingested dose, to some extent, determines the clinical manifestations of salicylate toxicity. In general, the aspirin dose ingested produces the following severity of toxicity:

- <150 mg/kg: No symptoms or minimal symptoms
- 150 to 300 mg/kg: Mild to moderate toxicity
- 301 to 500 mg/kg: Severe toxicity
- >500 mg/kg: Potentially lethal

الي عليهم هايلايت ازرق حسيت الدكتوره ركزت عليهم الي تحت قرأتهم قراءه وحكت رح يتكررو لقدام

Aid–base disturbance caused by salicylate poisoning:

- Salicylate stimulates the respiratory center in the brainstem, leading to hyperventilation & respiratory alkalosis.

ويصير كمان نتيجه اله metabolic acidosis
فتبلش الرئه تخسر البيكروبونات والصوديوم
والبوتاسيوم حتى يصير acidosis وبنفس الوقت
يتحكم في carbohydrate metabolism

- Salicylates in toxic concentrations titrate approximately 2 to 3 mEq/L of plasma bicarbonate.

- Salicylate interferes with the Krebs cycle, which limits production of adenosine triphosphate (ATP).

- It also uncouples oxidative phosphorylation, causing accumulation of pyruvic & lactic acids .

ويعملو زياده بالاكتيك اسيد بالعضلات
ويعمل metabolic acidosis

- Salicylate-induced increased fatty acid metabolism generates ketone bodies, including β-hydroxybutyric acid, acetoacetic acid, & acetone.

يصير معهم اسيدوسزز
بسبب الكيتون والاسيتون

- A marked elevation in temperature resulting from the uncoupling of oxidative phosphorylation caused by salicylate poisoning is one indication of severe toxicity.

بالاصل هو خافض حراره ولكن اذا
وصلت لدوز توكسيك رح يرفع الحراره

وبسبب هاد تبع الفوسفوريليشن
يصير ارتفاع بالحراره

- An acute respiratory acidosis is rare in the early stages but may develop in the later stages of profound toxicity.

صار هيك لانه الرئه تعبت

- The net result of all of these metabolic processes is an anion gap metabolic acidosis.

نعيد
ونزيد
نفسهم

Clinical manifestations of salicylate poisoning:

Acute salicylate toxicity:

- The earliest signs & symptoms of salicylate toxicity, which include nausea, vomiting, diaphoresis, & tinnitus, typically develop within 1 to 2 hours of acute exposure.

- Other early CNS effects may include vertigo & hyperventilation manifested as hyperpnea or tachypnea, hyperactivity, agitation, delirium, hallucinations, convulsions, lethargy, & stupor.

- Coma is rare & generally occurs only with severe acute poisoning.

اول اشي يعمله وبعدين بالتسلسل

Clinical manifestations results of salicylate toxicity:

- Acid–Base disturbances caused by salicylate poisoning
- Central nervous system effects
- Coagulation abnormalities
- Gastrointestinal effects
- Hepatic effects
- Metabolic effects
- Pulmonary effects
- Renal effects

ارقامهم

باثر على الكبد لانه وبضرب هدول 5-6-7-10 ويكون نسبه حدوث نزرف عاليه

رح يصير metabolic acidosis استجابه لل respairatory alkalosis الي موجود وبعدين تتعب الكرئه ويصير respairatory acidosis ويصير protein urie وترتفع الحراره

يعمل انخفاض بالسكر بالجسم

اولها بكون تنفسه قوي hyperventilation وبعديب يبلش يضرب القلب ويضعف ويصير تجمع سوائل بالرئه وبعدين hypoventilation

Acid–Base disturbances caused by salicylate poisoning:

- Respiratory alkalosis (predominates early)
- Metabolic acidosis.
- Respiratory acidosis.
- Hypokalemia

حفظ
انا
حكيتهم
قبل
واندكر
و كثير
معنا

Metabolic:

- Diaphoresis
- Hyperthermia
- Hypoglycemia

Central nervous system:

- Tinnitus
- Diminished auditory acuity
- Vertigo
- Hallucinations
- Agitation
- Coma
- Lethargy
- Convulsions

Coagulation Abnormalities:

- Hypoprothrombinemia
- Inhibition of factors V, VII, and X
- Platelet dysfunction

Gastrointestinal

- Nausea
- Vomiting
- Hemorrhagic gastritis
-

Hepatic

- Abnormal liver enzymes
- Altered glucose metabolism

Pulmonary:

- Tachypnea
- Respiratory alkalosis
- Respiratory acidosis- in profound toxicity

Renal:

- Tubular damage
- Proteinuria
- NaCl & water retention

ما بعرف اذا حفظ او لا بس قرأتهم الدكتوره

Range of toxicity	S &S	Blood level range (mg/dl)	Single oral dose ingested (mg/kg)	Approximate n. of tab	
				Baby aspirin	Adult aspirin
Asymptomatic		<45			
mild	N,V,mild hyperpnea, tinnitus	45-65	150-200	Up to 37	Up to 9
Moderate	Hyperpnea, hyperthermia, sweating, dehydration	65-90	200-300	37-74	9-18
Sever	Sever Hyperpnea, coma, convulsion, pulmonary edema, cyanotic, CV collapse	90-120	300-500	74-123	18-30
lethal	Coma, death	120	>500	>123	>30

NB: daily therapeutic dose is 40–60 mg/kg/d

Chronic salicylate toxicity:

- Chronic salicylate poisoning most typically occurs in elderly individuals as a result of unintentional overdosing on salicylates used to treat chronic conditions such as rheumatoid arthritis & osteoarthritis.

- as compared with acute toxicity, symptoms in chronic toxicity can be milder, often go unrecognized or attributed to another condition, and occur at lower serum salicylate concentrations. Some patients with chronic toxicity may even have a salicylate concentration within the therapeutic range.

تراكيز التسمم ما تكون عاليه(يعني ما وصلت لل(acute ورغم هذا هو خطير لانه أصلا بيكون عنده الكلى مضروبه والمعده لانه يستعملهم باستمرار

Diagnostic testing:

- Careful observation of the patient,
- correlation of the serum salicylate concentrations with blood pH
- repeat determinations of serum salicylate concentrations every 2 to 4 hours are essential until the patient is clinically improving and has a low serum salicylate concentration in the presence of a normal or high blood pH.

Management of poisoning:

- Salicylate poisoning from acute oral ingestions of large quantities requires prompt medical attention.

هدول الي لازم انتبه الهم في حاله التسمم بحطه
على جهاز لتنفس حتى أحاول اسيطر عليه

- For a salicylate-poisoned patient who presents severely ill & requires mechanical ventilation for airway stabilization, maintenance of hyperventilation requires an extremely careful approach if death is to be avoided.

- Gastric decontamination: The general sequence for managing salicylate toxicity should begin with gastric decontamination through gastric lavage & activated charcoal.

- The use of Multiple dose activated charcoal (MDAC) to decrease GI absorption of salicylate overdoses is warranted, particularly if an extended-release preparation is suspected.

- Theoretical support may be found for the use of whole-bowel irrigation (WBI) consisting of polyethylene glycol electrolyte lavage solution (PEG-ELS) in addition to AC to reduce systemic absorption.

- Fluid replacement: the patient's volume status must be adequately assessed & corrected if necessary, along with any glucose & electrolyte abnormalities.

لانه حكينا يصير معه جفاف
لانه رح ترتفه حرارته
واحتمال يستفرغ ولكن لازم
نكون حذرين

- Alkalinization of the serum through intravenously administered sodium bicarbonate reduces the fraction of salicylate in the nonionized form (Figure 1).

- Urine pH should be maintained at 7.5 to 8.0.

السالساليت حمض ضعيف واحنا صار عنا acidosis بقدر اشيلهم من urein اذا كان alkaline وبخليه قاعدي من خلال sodium bicarbonate

- Enhanced salicylate elimination by urine alkalization: salicylic acid is a weak acid (pK a 3.5),& alkalinization of the urine (defined as pH ≥7.5) with sodium bicarbonate results in enhanced excretion of the ionized salicylate ion.

لما يكون urein ph 8
بيكون unionize فيصير
كميه ionizeقليله فيبلش
يسحب من البلازما

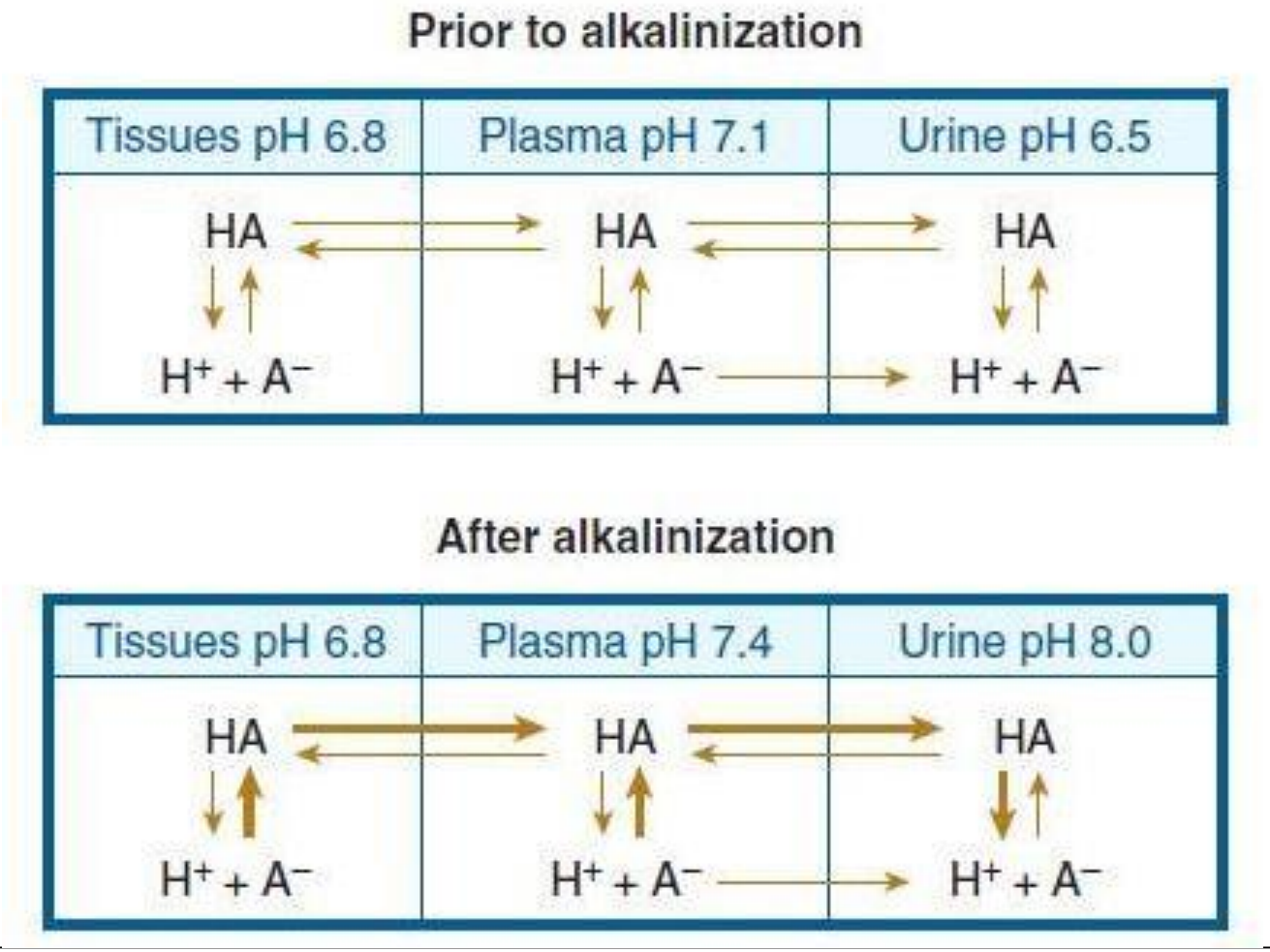


Figure 1. Rationale for alkalinization. Alkalinization of the plasma with respect to the tissues and alkalinization of the urine with respect to plasma shifts the equilibrium to the plasma and urine and away from the tissues, including the brain.


خذني يا سوبرمان
من الفايننلز للأمان

- Extracorporeal removal: Extracorporeal measures are indicated if the patient has severe signs or symptoms, a very high serum salicylate concentration regardless of clinical findings, severe fluid or electrolyte disturbances, or is unable to eliminate the salicylates.

  In most In most instances of severe salicylate poisoning, HD is the extracorporeal technique of choice

Pyrazolones

الدكتوره قال هدول
مسحوبين من السوق
بستخدمهم للحيوانات بس

- **Phenylbutazone; oxyphenbutazone**: available for **veterinary use**, may present in some herbal preparation (withdrawn from the market)

- **Aplastic anemia** and **agranulocytosis** have been associated with the use of **phenylbutazone**

Indoleacetic acid (pyroles)
diclofenac, indomethacin

من اسوأهم على القلب
non لانهم اقل اشي
selective يعني كثير
selective

- **Management:**

1. **Gastric lavage** should be performed in cases of serious overdose
2. **Activated charcoal** should be given and repeated every 4 hrs
3. **Supportive and symptomatic treatment**

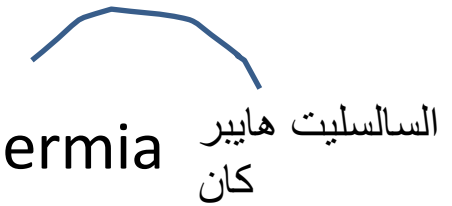
Phenylpropionic acids

- **Ibuprofen, fenoprofen, flurboprofen, ketoprofen, naproxen**
- **In general**, **overdose** with “propionic acids” **do not result in significant morbidity or mortality**, although death after overdoses of ibuprofen & fenoprofen have occurred
- **Ibuprofen**: the most widely used and rapidly absorbed from GI

والتخلص
منه جدا
سريع

Ibuprofen

- Therapeutic range: adult 400-2400 mg/day
  children 20-50 mg/kg/day
- **Poisoning is usually manifested by** mild GI symptoms: N, V, abdominal pain, anorexia, GI hemorrhage (rare)
- CNS depression
- Nystagmus, tinnitus
- Respiratory depression
- Metabolic acidosis
- Headache, seizures
- Hypotension, bradycardia, hypothermia



Ibuprofen

Treatment…..GI decontamination

1. **Ingestion less than 100mg/kg**: dilute with water to reduce gastric irritation

2. **More than 100mg/kg**:

- **Gastric lavage**
- After gastric emptying, **activated charcoal and a saline cathartics should be administered**

زيه زي
الاسبرين

Ibuprofen

4. **Hypotension:** treated with i.v. fluids , if it persist dopamine or NE may be required
5. **Seizures:** treated with diazepam
6. **Bradycardia** may respond to atropine
7. **Metabolic acidosis** (PH < 7.1) may require administration of sodium bicarbonate
8. Ibuprofen weak acid….**urine alkalinization**?

بالغالب ما بحتاجه لانه
½ life كثير قصير

Anthranilic acids

بالسالسليت كانت ليسته أطول منا والايبوبروفين يبلشو ب cns depression

Mefenamic acid & maclofenamate

- Is well absorbed, more than 50% excreted unchanged in urine, the reminder as conjugate

Toxicity:

اغلب سميته تأثر على CNS

1. **May produce no symptoms**
2. Muscle twitching either focal or generalized has been reported
3. Seizures are common following overdose
4. Diarrhea, rash, elevated BUN and coma

Management of Toxicity

- Supportive management.
- Administer activated charcoal. Gastric emptying is not necessary for most ingestions if activated charcoal can be given promptly. Perform gastric lavage for massive overdoses.
- Antacids may be used for mild GI upset.

لحمايه
المعده

الدكتوره قراتهم للأسف فبالغالب مطالبين فيه

Clinical aspects of NSAIDs poisoning

Organ	Manifestation	Management
Gastrointestinal	Anorexia, nausea, vomiting abdominal pain, gastric mucosalirritation	**Nonabsorbable antacids e.g. aluminium and magnesium antacids H_2-receptor antagonists, proton pump inhibitors, misoprostol**
Hepatobiliary	Hepatic dysfunction	
Respiratory	Hyperventilation Respiratory depression	**Mechanical ventilation**
Cardiovascular	Sinus tachycardia Hypotension Cardiovascular collapse Cardiac arrest	**IV fluids, vasopressors, haemodynamic monitoring**
Renal	Haematuria, proteinuria Acute renal failure	**Haemodialysis**
Haematological	Hypoprothrombinaemia agranulocytosis, leucopenia, thrombocytopenia	**Vitamin K**
Metabolic	Hyper-and hypothermia Electrolyte abnormalities	**Correct imbalance**
Neuromuscular	**Confusion, disorientation, drowsiness, headache, tinnitus, dizziness, blurred vision, nystagmus,diplopia, ataxia, hypertonia, hyper-reflexia, muscle twitching, convulsions, coma**	**Anticonvulsants(e.g. diazepam) for convulsions**

وهيك يا جماعه انا خلصت التفاريغ الي علي ان شاء الله تجيبو علامات عاليه وربنا يرزقكم الرمز الي ببالكم