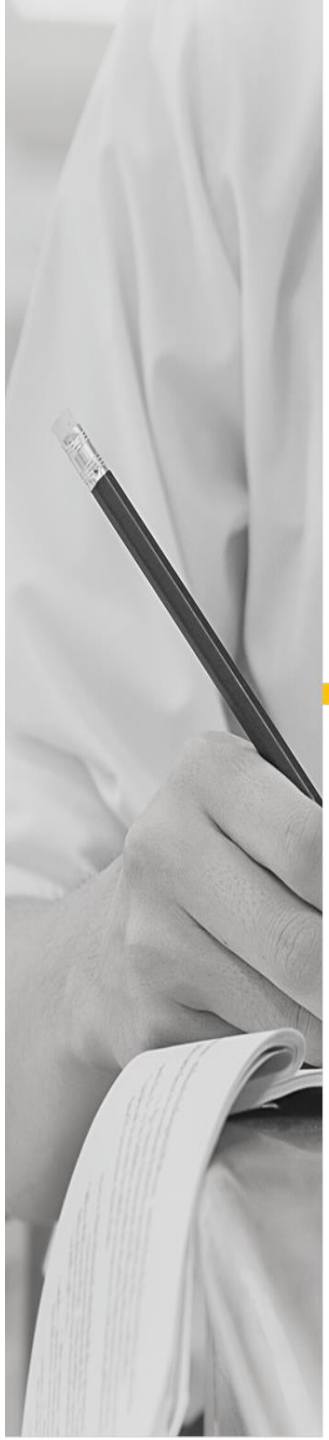

Tikrit University
College of Veterinary Medicine

Subject name:DRUG EVALUATION

Subject year: MSc - PHARMA

Lecturer name: MICRO. ASSAY

Academic Email:Sbc.s4@tu.edu.iq

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Subject name: DRUG EVALUATION

Subject year: MSc - PHARMA

LECTURER : Prof Dr Husamuldeen Alnajar

Lecture name: POISON ELIMIN.

Academic Email:Sbc.s4@tu.edu.iq

بسم الله وبه نستعين

جامعة تكريت – كلية الطب البيطري
ماجستير علم الادوية - فارماكولوجي

Poison Elimination

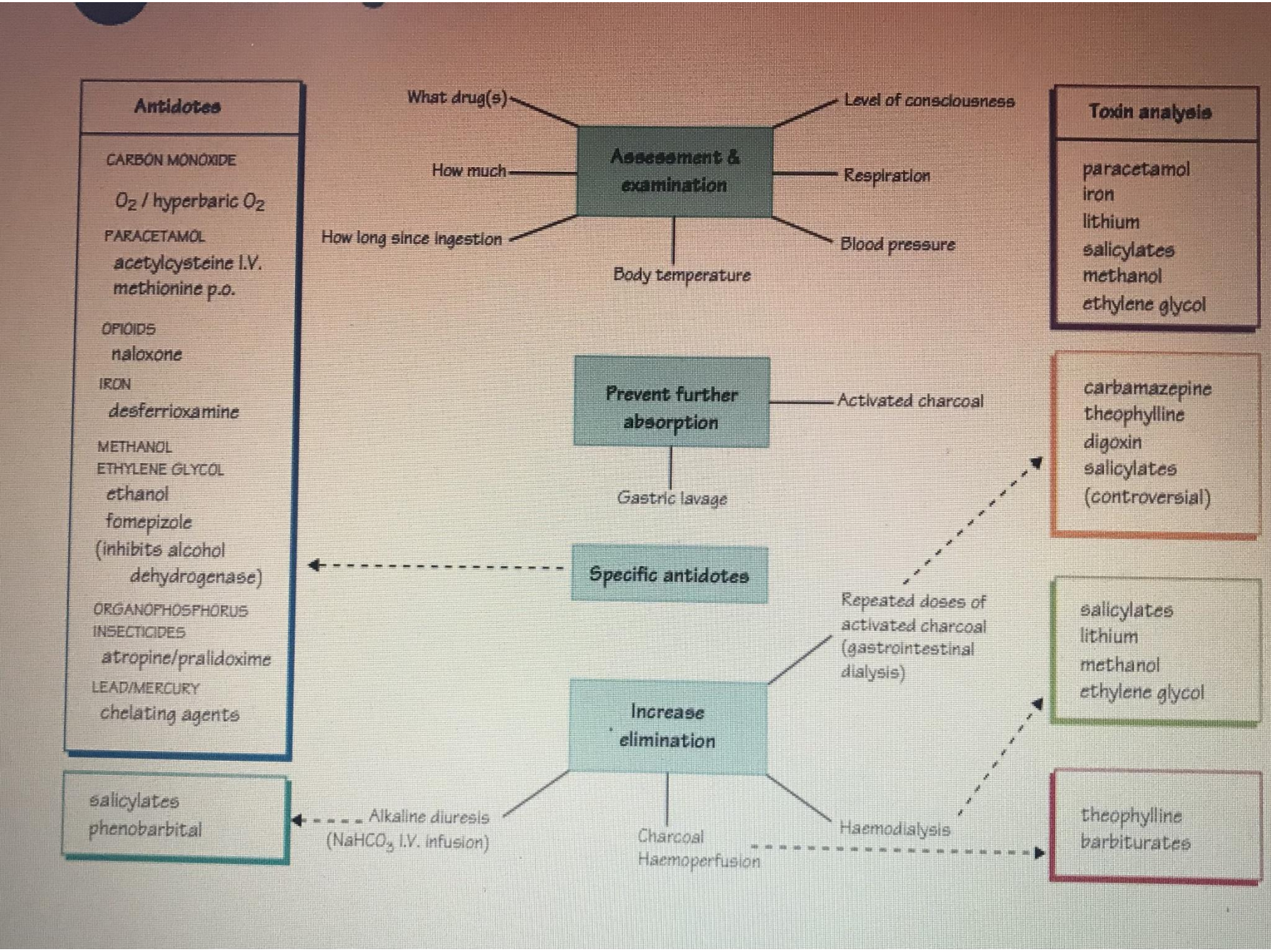
2023-2024

DRUG EVALUATION

أ د حسام الدين النجار

- The most common drugs causing death by self-poisoning are **Coproxamol, paracetamol alone and tricyclic antidepressants.**
- However, the **most common cause of fatal self-poisoning, especially in men, is carbon monoxide originating from a car exhaust.**
- Selfpoisoning with two or more drugs is not uncommon and alcohol is also taken in about 50% of incidents.
- Most cases of **intentional selfpoisoning are cries for help (parasuicide): any nonfatal, self-injurious behavior with a clear intent to cause bodily harm or death** . Thus parasuicide includes both lethal suicide attempts and more habitual or low-lethality behaviors such as cutting or other self-mutilation but more than 3000 people a year successfully kill themselves by poisoning.

- **Once in hospital the mortality of self-poisoners is less than 1%.**
- **Accidental self-poisoning occurs mainly in young children (under 5 years) and usually involves medicines or household chemicals (e.g. bleach) left within reach.**
- Patients presenting with poisoning must be given an initial assessment (top), including a rapid but careful clinical examination. **It is important to exclude other causes of coma and abnormal behaviour (e.g. head injury, epilepsy, diabetes).**
- Most patients admitted for self-poisoning require only general supportive measures.
- **Drug screens are rarely needed as an emergency, but with some drugs (top right) the clinical state of the patient may not reflect the severity of the overdose, and measurement of the plasma concentration can indicate the use of lifesaving techniques (centre bottom) or specific antidotes.**


Antidotes
CARBON MONOXIDE
O_2 / hyperbaric O_2
PARACETAMOL
acetylcysteine I.V.
methionine p.o.
OPIOIDS
naloxone
IRON
desferrioxamine
METHANOL
ETHYLENE GLYCOL
ethanol
fomepizole
(inhibits alcohol dehydrogenase)
ORGANOPHOSPHORUS INSECTICIDES
atropine/pralidoxime
LEAD/MERCURY
chelating agents
What drug(s)
How much
How long since ingestion
Level of consciousness
Respiration
Blood pressure
Body temperature
Assessment & examination
Toxin analysis
paracetamol
iron
lithium
salicylates
methanol
ethylene glycol
Prevent further absorption
Activated charcoal
Gastric lavage
carbamazepine
theophylline
digoxin
salicylates
(controversial)
Specific antidotes
Repeated doses of activated charcoal (gastrointestinal dialysis)
salicylates
lithium
methanol
ethylene glycol
Increase elimination
salicylates
phenobarbital
Alkaline diuresis
($NaHCO_3$ I.V. infusion)
Charcoal Haemoperfusion
Haemodialysis
theophylline
barbiturates

Traditionally, routine attempts were made to reduce further absorption of the drug.

The oral administration of activated charcoal is used to reduce drug absorption.

In volunteer studies, **charcoal has been shown to reduce the absorption of many drugs, especially in the first hour after administration.** Unfortunately, clinical studies have failed to show that charcoal affects the outcome of poisoning. Nevertheless, charcoal is often given to patients who have ingested a potentially toxic amount of poison within the last hour.

Techniques used to increase drug elimination (bottom) have a limited role, but are important in a small number of severely poisoned patients.

Reduction of absorption

- Emesis Syrup of ipecacuanha induces emesis in more than 90% of patients. It can only be used in conscious patients. There is no evidence that ipecacuanha reduces the severity of poisoning and its use has been abandoned.
- Gastric aspiration and lavage An orogastric tube is passed into the stomach, which is then washed out with 300–600mL of water (three or four times or until the effluent is clear). **If the patient is unconscious, the airway must be protected with a cuffed endotracheal tube.**

- After an hour from the time of ingestion, lavage removes only a tiny proportion of the poison and there is no evidence that the procedure is beneficial.
- **Early lavage (within 60min of ingestion) may benefit patients who have taken a potentially life-threatening amount of poison.**
- **Gastric lavage is contraindicated in poisoning with corrosives or petroleum compounds.**

- Activated charcoal

Activated charcoal is a very fine porous black powder with an enormous surface area in relation to weight (1000m2 g−1).

It binds many drugs and 10 g of charcoal will absorb about 1 g of drug.

Charcoal does not absorb iron, lithium, corrosive agents or organic solvents.

Charcoal is contraindicated in patients with an unprotected airway (e.g. drowsy or comatose patients) because there is a risk of pulmonary aspiration.

How to Make Activated Charcoal Coconut and What are the Benefits of Them

Activated Charcoal Coconut is now getting much popular due to its industrial applications and numerous benefits. In here we are a plan to discuss how to make this activated charcoals and what is the benefit of them.

What is Coconut Shell

Coconut shell is originally made of the hard part which consists of cellulose and lignin. Due to the high quality of coconut shell, it is got much durable. The ability to absorb the toxic, harmful chemicals and odors are the most useful benefits of this coconut based active carbons.

What is activated charcoal coconut

Coconut shell is much famous to create active carbon because it creates the highest quality active carbon.

Most of the application which uses this active carbon is in purification industry. In so many industries purifications is essential and for that purpose active carbons are widely used. Example for these industries which purification essential are

sugar industry

drugs

industrial gases

water purification

air purification

Due to the demand of these industries, there is huge demand for coconut shell based active carbons.

Coconut shells are used as main raw material to make this active carbon.

In most of the hospitals treated activated charcoals are use for treat patient who swallows harmful chemicals like poison. This work more efficient and easier to use with a lot of benefitted results.

- **Enhancement of elimination**

Enhancement of elimination can reduce the time of recovery, but there is little evidence that it changes morbidity, except in severely comatose patients (grade IV coma).

Repeated oral doses of activated charcoal may increase elimination by gastrointestinal dialysis; it has the merit of being relatively safe (unless aspirated).

- **Alkaline diuresis.**

The urine is made alkaline (pH 7.5–8.5) by the administration of $NaHCO_3$ (intravenous infusion). This ionizes weak acids, e.g. aspirin, in the renal tubules and reduces reabsorption.

Similarly, acid diuresis may be useful in cases of poisoning with basic drugs such as amfetamine and 'ecstasy' MDMA. Forced alkaline diuresis using large intravenous volumes of water containing $NaHCO_3$ is hazardous and is no longer used.

- Haemodialysis and haemoperfusion are invasive techniques requiring cannulation of an artery and vein (usually in the arm) to establish a temporary extracorporeal circulation.
- In haemodialysis, the drug passes down its concentration gradient through the dialysis membrane and is removed in the dialysis fluid.
- In haemoperfusion, the blood is passed through a column of activated charcoal or resin on to which the drug is absorbed.
- These techniques have significant risks (haemorrhage, air embolism, infection, loss of a peripheral artery) and the shortened elimination half-life does not necessarily correlate with improved clinical state (i.e. reduced morbidity or mortality).
- In some cases, e.g. carbamazepine and phenobarbital poisoning, multiple doses of activated charcoal are as effective as haemoperfusion.

Aspirin

The symptoms of salicylate poisoning include tinnitus, hyperventilation and sweating.

Coma is uncommon and indicates very severe poisoning.

Acid–base disturbances are complicated because aspirin stimulates the respiratory centre, causing a respiratory alkalosis, but also uncouples oxidative phosphorylation, which may cause a metabolic acidosis.

Immediate management includes measurement of plasma salicylate concentration (at 4–6h post ingestion), electrolytes and blood gases. Gastric lavage (up to 1 h after ingestion) is followed by activated charcoal administration.

Severe poisoning (plasma concentration above 500mgL−1) requires urinary alkalinization.

In very severe poisoning, haemodialysis is the treatment of choice.

Paracetamol Patients may be asymptomatic or complain only of nausea and vomiting. But, after a delay of 48–72 h, relatively small amounts (more than10g, 20–30 tablets) may cause fatal hepatocellular necrosis.

Normally, paracetamol is metabolized, mainly by conjugation reactions in the liver, but high doses saturate these pathways and the drug is then oxidized to a reactive (toxic) quinone intermediate (N-acetylbenzoquinoneimine).

The quinone can be inactivated by combination with glutathione, but high doses of paracetamol deplete the hepatic glutathione stores and the reactive quinone then covalently binds to thiol groups on the cell proteins and kills the cell.

- Acetylcysteine (intravenous or oral) and methionine (oral) are potentially life-saving antidotes in cases of paracetamol poisoning because they increase the synthesis of liver glutathione.
- **Patients who have taken an overdose of paracetamol should have a blood sample taken at 4h (or later) after ingestion to determine quickly the plasma concentration of drug so that the antidote can be given.**
- If less than 1h has elapsed since ingestion, a dose of activated charcoal should be given.

- The most effective antidote is acetylcysteine given intravenously within 8 h of paracetamol ingestion. Adverse effects, including anaphylactoid reactions, occur in about 5% of patients.

- **Opioids**

Opioids cause coma, pinpoint pupils and respiratory depression.

They are specifically antagonized by naloxone, which is given intravenously in repeated doses until ventilation is adequate.

Naloxone has a shorter half-life than most opioids and toxicity may recur, necessitating further doses.

Naloxone may cause an acute withdrawal syndrome in opioid addicts.

- **Tricyclic antidepressants**

- **Toxicity following overdosage arises mainly from central anticholinergic effects (respiratory depression, hallucinations, convulsions) and cardiotoxicity.**

- Most patients require only observation or simple supportive measures, such as oxygen to correct hypoxia and activated charcoal (within 1h).

- The most common arrhythmia is sinus tachycardia as a result of an atropine-like effect. Lengthening of the QRS complex (a quinidine-like effect) is an ominous sign and may presage convulsions, which may be controlled by intravenous diazepam or chlomethiazole.
- **The use of gastric lavage in tricyclic poisoning is controversial because the gastric contents may be pushed beyond the pylorus and increase the amount of drug absorbed.**

question?

- 47-year-old man with a history of a seizure disorder, maintained on phenytoin, presented to the emergency department with salicylate toxicity. The salicylate level was 50 mg/dL (15 to 35 mg/dL therapeutic range) and the phenytoin level was 15 mg/L (10 to 20 mg/L therapeutic range). What therapy can be considered to enhance the elimination of salicylate without impacting the phenytoin?
- A. Multiple doses of activated charcoal
- B. Urinary alkalinization
- C. Whole bowel irrigation
- D. Urinary acidification

Correct answer

B. Urinary alkalinization enhances the elimination of the salicylate but does not affect the therapeutic phenytoin level.

Multiple doses of activated charcoal would lower the concentration of both medications, rendering the phenytoin subtherapeutic.

Whole bowel irrigation is another GI decontamination modality involving administration of large quantities (up to 2 L/h in adults) of a polyethylene glycol–balanced electrolyte solution via a nasogastric tube until the patient generates clear rectal effluent.