Kafrelsheikh University
Faculty of Veterinary Medicine
Department of Forensic Medicine,
Toxicology and Vet. Regulations

Toxicology Exam
Time allowed: ٢ hours
Date: ٢٣/٠٥/٢٠١٦
No. of pages: two
٤th level students (حديث)

Please answer the following questions:

[I] Two days ago, a veterinarian received three suspected toxicity cases in a toxicology lab. The first one was suspected **plumbism**, the second was suspected **ergotism** and the third was suspected **paraquat** toxicity. During their registration a veterinarian mess up the related articles of the three cases

A- How can you help the veterinarian to reorganize these respective cases to their histories, signs, submitted samples and first aid treatments? **(٦ marks)**

	Plumbism	**Ergotism**	**Paraquat toxicity**
Histories	٣	١	٢
Signs	١	٣	٢
Submitted samples	١	٣	٢
First aid treatment	١	٣	٢

I- **Histories:**

١) Cattle farm fed on concentrates containing wheat imported from Argentine. **(Ergotism)**

٢) Sheep fed on weeds after harvest in preparing land for planting. **(Paraquat toxicity)**

٣) Cattle farm fed on silage stored beside battery factory. **(Plumbism)**

II- Signs:

١) Colic, constipation, head pressing behavior, anemia, ataxia and convulsion. **(Plumbism)**

٢) Hematemesis, diarrhea, cough, dyspnea and anemia. **(Paraquat toxicity)**

٣) Reduced milk production in the dairy animals with sloughing of the hooves, tails and ears. **(Ergotism)**

III- Submitted samples:

١) Whole blood, urine and kidney. **(Plumbism)**

٢) Whole blood and urine. **(Paraquat toxicity)**

٣) Feed. **(Ergotism)**

IV- First aid treatment:

١) Administration of calcium, charcoal and diazepam. **(Plumbism)**

٢) Administration of charcoal and mannitol. **(Paraquat toxicity)**

٣) Sodium nitroprusside, as potent, direct-acting vasodilator. **(Ergotism)**

B- <u>Discuss fully the specific antidotes which can be used in the treatment of first case</u>

١- BAL (British anti-lewisite - ٢,٣ dimercaptol)

- The first choice for cases with lead encephalopathy due to it cross the blood-brain barrier
- May be administered to cases with renal failure.
- BAL action starts within ٣٠ minutes.
- Chelates intracellular and extracellular lead forming BAL-Pb complex which excreted in bile and urine.
  Dose: ٣-٥ mg/ kg body weight deep I/M every ٤ hours in the first two days then every ٦ hours in the third day.

٢- CaNa٢-EDTA

- Second-line for lead toxicity
- Should never be used as the sole agent in cases with lead encephalopathy, because it does not cross the blood-brain barrier
- Not recommended with renal failure and only given IV
- Chelates only extracellular lead
- CaNa٢-EDTA does not enter host cells but depends on excretion of lead from bone into blood resulting in a transient increase in blood lead levels with appearance of clinical signs, so that EDTA should be used together with BAL (٤ hours post the first dose of BAL)
- It form a stable EDTA-Pb complex which excreted in urine.
- It increases renal excretion of lead ٢٠–٥٠ times.

Administration of EDTA instead of mono calcium, disodium EDTA may leads to hypocalcaemia due to the high affinity of EDTA to calcium.

٣- Dimercaptosuccinic acid, Succimer (DMSA)

- ✓ Dose: ١٠mg/kg orally ٣times ٥days
- ✓ More effective than BAL
- ✓ Wider therapeutic index than BAL
- ✓ Does not re-distribute Pb to brain
- ✓ Can be used to chelate Hg, As, and Pb

(٢ marks)

[II] Write fully on: (٦ Marks)

١. <u>Bio-magnification of methyl mercury.</u>

- In water, elemental mercury is bio-transformed by aquatic organisms and vegetation into methyl mercury
- Zoo-plankton picked up methyl mercury from the water
- An anchovy eats many of zoo-plankton throughout its lifespan
- A tuna eats many of these anchovies throughout its lifespan
- Large fish eats many of tuna throughout its lifespan
- Birds→ animals → human
- The end result is the methyl mercury content is biomagnified.
- Methyl mercury is poorly eliminated so it concentrates up the food chain
- Methyl mercury becomes biomagnified in the fish as fish protein binds about ٩٠٪ of the consumed methyl mercury
- Biggest and oldest predators at the top of the ecosystem have the highest concentrations
- Methyl mercury is not changed by cooking

٢. **Line of treatment of SMFA toxicity case.**

- Emetics are contraindicated if clinical signs are present.
- Gastric lavage and adsorbents (activated charcoal, ٠.٥ g/kg) are recommended.
- Barbiturates are preferred for controlling seizures.
- Calcium gluconate for controlling seizures.
- Glyceryl monoacetate (monacetin) as a competitive antagonist of fluoroacetate. The recommended dose is ٠.٥٥ ml/kg, IM, or IV in sterile saline solution, every ٣٠ min for several hours.

٣. **Bio-activation of aflatoxins.**

- AFB1 oxidized by Cytochrome P450 enzymes to several hydroxylated metabolites including the reactive 8,9-epoxide form, which is capable of binding to DNA, RNA
- AFB1-DNA adduct concentrations is the main cause of liver cancer in animals and humans. Reactive Aflatoxin epoxide binds to the N7 position of guanines, thereby reducing its biosynthesis. (Inducing guanine into thymine)

- 8,9-epoxide form is capable of **binding** to cellular **proteins** and inhibit polymerases responsible for DNA and RNA synthesis, as well as degranulation of endoplasmic reticulum.
- This resulted in **impairment of protein synthesis** (immunosuppressive effect) and **fat metabolism** which appear in the liver of affected animals in the form of hepatic necrosis and fatty changes
- Aflatoxin results in **oxidative stress** that cause damage of critical cellular macromolecules, including DNA, lipids and proteins in addition to decreasing in the activity of several enzymes
- Aflatoxin **increase mitochondrial permeability** and interrupt electron transport with a decline in respiration
- Aflatoxin **increase lysosomal membranes permeability** resulting in acid hydrolases leak out, in addition to activation of lysosomal enzymes and their effects on cellular structures
- Aflatoxin **inhibits the synthesis of blood clotting factors I, II, V, VII, VIII, IX and X**., glucose metabolism via the 6-phosphate pathway and the synthesis of fatty acids and phospholipids.

٤. **Contraindicated cases for emetics.**

a) In ingestion of corrosives, volatile hydrocarbons and petroleum distillates
b) In unconscious or semi-comatose or animals without an active cough reflex
c) In addition to convulsing poisons

[III] Tabulate the differences between the following: (٦ Marks)

١. **Mechanism of action of ANTU and warfarin.**

ANTU	Warfarin
• Increase the permeability of the lung capillaries leading to their damage. Causing pulmonary edema. • It is also antagonize the thyroid gland secretion and carbohydrate metabolism.	• It inhibits epoxoid reductase enzyme which is responsible for activation of vit K

٢. Neurotoxic and cardiotoxic effects of snake venom.

Neurotoxic snake venom	Cardiotoxic snake venom
• A curare like action on neuromuscular junction causing non depolarizing blockage. • Action on respiratory center in the brain producing convulsion crisis and paralysis of the respiratory center.	• It causes sharp drop in blood pressure. • The main pharmacological action of purified cardio toxin is depolarization of all membranes affecting skeletal muscles, cardiac and smooth muscles. • Also causing sudden general collapse from circulatory failure and systolic arrest. • It's lethal potency is ١/٢٠ of neurotoxin.

٣. Fulminant and gastroenteric types of arsenic toxicity.

Fluminant type	Gastroenteric type
• Massive doses of arsenic (٣-٥g) when rapidly absorbed cause death in one to three hours due to shock and peripheral vascular failure. • All the capillaries are markedly dilated, especially in the splanchnic area with a marked fall of blood pressure.	• This is the common form of acute poisoning and resembles bacterial food poisoning. • Symptoms usually appear half to one hour after ingestion, but may be delayed many hours especially when arsenic is taken with food. • Burning and colicky pain in the esophagus, stomach and bowel occur. • Intense thirst, diarrhea and severe vomiting are the common symptoms.

[IV] Give reason for the following: (٥ Marks)

١. Infestations with Ascaris and Ancylostoma favor CCL_4 toxicity.

In these cases CCL_4 not kill the ascaris worms but irritate them leading to their accumulation and intestinal obstruction occurs or the worms may even block the common bile duct opening in the duodenum or they may even travel through stomach to oesophagus to pharynx and larynx causing suffocation. Furthermore, ascaris in the presence of CCL_4 secret chemical toxin which has selective action on liver.Hypocalcemia increase its toxicity, beside CCL_4 cause decrease in Ca blood level as it increase bilirubin level which combines with and fix blood Ca.

٢. **Stage II of iron toxicity sometimes called the latent period.**

Due to transient resolution of GI signs as the iron passes deeper into the body and damages internal organs

٣. **Acetylcholine level varied in case of OP and methyl mercury toxicity case**

-In case of OP, acetylcholine level is increased while in methyl mercury decreased.

٤. **Analgesics should be given while morphine should be avoided in the treatment of scorpion bite.**

Generally Analgesics should be given due to presence of intense pain at the site of the sting except morphine which has a synergistic action with scorpion venom.

٥. **Repeated oral doses of activated charcoal may be useful in the treatment of organochlorine and thalium toxicity even after they pass to circulation.**

These toxicants excreted in the bile so repeated doses of activated charcoal decrease their reabsorption (cut the enterohepatic circulation)

Good luck

Prof. Dr. Hanaa Hegazy