

Exam TOKS3001
Medical (human) toxicology

Wednesday May 23rd 2012, 9.00 am - 1.00 pm

ECTS credits: 7.5

Number of pages (included front-page and semi logarithmic paper): 5

Examination support: Calculator and English/Norwegian or
Norwegian/English dictionary.

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Exam results:

Examination results are announced on <http://studweb.ntnu.no/>

Problem 1

- a) In toxicokinetics, what do we mean by “absorption”?
- b) What is “Volume of distribution”?

An afternoon at the hospital, two men, Alf and Ole, come in with symptoms that look like a poisoning of some kind. Blood samples are immediately taken, and also collected for 8 hours. The laboratory identifies a chemical entity from a pesticide responsible for the symptoms. The chemical is extensively metabolized by CYP3A4. The plasma concentration of the chemical is given in table 1.

Table 1.

Time [hrs]	Concentration [ng/ml]	
	Alf	Ole
1	11	4
2	8	2.9
3	6	2.1
4	4.2	1.6
6	2.3	0.85
8	1.2	0.46

- c) Make semi logarithmic plots of the plasma concentration versus time curves of the toxic compound for both Alf and Ole (in the same diagram).
- d) Calculate the biological elimination half-life ($t_{1/2}$) and the total elimination rate constant (k_e) for the toxic compound as accurate as possible, for both Alf and Ole.

The two men live together, and during the examination, they inform the doctor that they have eaten the same amount of bananas that day, as a part of a special diet. The two men weigh about 70kg and spend much time together:

- e) Discuss possible factors that contribute to the fact that Alf seems to achieve higher plasma concentrations of the toxic compound than Ole.

In the literature, we find that the compound’s NOAEL (from rats) is 0.1mg/kg/day and the volume of distribution is 25 litres.

- f) Calculate the ADI.
- g) Calculate the dose Alf and Ole has ingested. Are the symptoms of poisoning legit?
- h) Is ADI a reasonable value to compare with? Why / why not?

Problem 2

Metal toxicology:

- a) For three essential metals the daily required dose is above 1 mg. Please name them
- b) For each of these metals please indicate medical use:
 - Bismuth
 - Gallium
 - Gold
 - Lithium
 - Platinum
- c) Name three effects of Zn deficiency.
- d) Lead exposure may cause anemia. What is the mechanism behind this symptom?
- e) Given three reasons why children are the primary population when we consider safe levels for lead exposure.
- f) The critical organ in cadmium toxicity is:
 - Heart?
 - Peripheral nervous system?
 - Kidney?
- g) The body half-life of cadmium is:
 - 15-30 years?
 - 5-10 years?
 - More than 35 years?
- h) Which of these chemical forms of mercury are nephrotoxic as a primary target organ:
 - Methylmercury
 - Hg^+
 - Mercury vapor
 - Hg^{2+}
 - Phenylmercury
- i) Is Cr^{3+} or Cr^{6+} an essential element?
- j) Name two compounds that can be used as antidotes in cases of metal intoxication.
- k) Name four metals where we have adequate knowledge for using biological monitoring in non-occupationally exposed population.

Problem 3

Describe elaborately the toxic effects on humans of organophosphate and carbamate insecticides, including effect mechanisms, acute effects and the phenomena “aging” and “dying back” neuropathies. What is the difference between organophosphates that have a sulphur atom bound with a double bond to the central phosphor atom and those who have an oxygen atom instead of the sulphur atom in the same position? What is the difference between the organophosphates and the carbamate insecticides? Describe shortly general principles for treatment of poisoning with these substances.

Problem 4

Which type of allergy may be caused by nickel? List also other substances that may cause the same type of allergy. Describe the immunologic mechanisms for this reaction, that is, what happens in the sensitization phase, what happens in the effector phase, down regulation of the reaction and in which organ does the major part of the reaction takes place.

