



THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 14 March 2006

TOXICOLOGY

First Paper

Answer FOUR questions ONLY
Time allowed – THREE HOURS

1. Write short notes on any FOUR of the topics a) to f) below (suggested length half-page per answer).
 - a) Organophosphorus-induced delayed type neurotoxicity
 - b) The comet assay
 - c) α -2u globulin nephropathy
 - d) The respiratory toxicity of asbestos
 - e) Minamata disease
 - f) Balkan nephropathy
2. Explain why the toxicity of a metabolically-activated chemical, as assessed in an *in vitro* hepatocyte system, may differ from that shown observed in the liver during an *in vivo* oral gavage study in the rat.
3. Describe the effects of administration of a PPAR α agonist to a rat. Describe the downstream sequence of changes following interaction of the agonist with its respective receptor and how you might monitor these using current molecular biology methodologies.

Please turn over for Questions 4, 5 and 6

4. Describe and discuss the approaches available for the identification, characterisation and assessment of skin and respiratory chemical allergens.
5. Describe and discuss the mechanisms by which chemical exposure can lead to thyroid gland hypertrophy, hyperplasia and cancer. Use specific chemical examples to illustrate your answer.
6. A chemical accident has occurred in which 20,000 litres of benzene has been spilled onto the motorway.
 - a) What biological samples would you take from individuals exposed to the spillage?
 - b) What biomarkers would you measure to assess any acute organ toxicity and why?
 - c) What follow up medical investigations would you recommend?
 - d) What information would you need to manage the risks associated with the incident?



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Part 1 Examination

Tuesday 15 March 2005

TOXICOLOGY

First Paper (General Toxicology)

Candidates must answer FOUR questions ONLY

Time allowed - three hours

1. “The skin is an important organ in determining the toxicity of topically applied chemicals”. Describe the structure of the skin and discuss this statement.
2. Write short notes (maximum half a page) on **four** of the following:
 - (a) In relation to chemical exposures define the terms ‘hazard’ and ‘risk’ and explain the differences between the two terms.
 - (b) Explain the principles of ‘dose-response’ and its importance for toxicology
 - (c) Define ‘enterohepatic’ circulation and its importance in toxicology illustrating your answer with some specific chemical examples
 - (d) Define the importance of the formation of acyl glucuronides in toxicology and illustrate your answer with specific chemical/drug examples
 - (e) Loss of contraceptive protection in epileptic women

Please turn over for questions 3, 4 and 5

3. Define the concept of the '3Rs'. Describe the considerations that need to be accounted for in using results from an *in vitro* human hepatocyte system and where, and with what reservations, results from this study might this be used to predict subsequent studies in man.
4. 'Initiation and promotion' are important concepts in the theory of chemical carcinogenesis. Differentiate initiation from promotion and illustrate how this hypothesis has been explored using a defined *in vivo* model system. What are the limitations of the two-stage hypothesis in explaining the carcinogenic process?
5. Metabolism studies on a novel chemical have shown that no parent compound could be detected in the blood at any time following oral administration. Discuss what could have happened to the chemical, the organs and the metabolic and kinetic processes that might have caused this.