



The Royal College of **Pathologists**

Pathology: the science behind the cure

Part 1 examination

Toxicology: Second paper (Toxicologic Pathology Subspecialty)

Tuesday 23 March 2010

Candidates must answer FOUR questions ONLY

Time allowed: 3 hours

1. Describe the expected histopathology, biochemistry and clinical chemistry changes that would be seen in a rodent chronically administered a mixed PPAR α/γ agonist by gavage for periods of up to two years.
2. Describe the histology of the different regions of the rat nasal passages including the precise methodology used to prepare it for histological assessment following inhalation exposure of xenobiotics. Survey the toxicological lesions that might be encountered in the nasal cavities of rats with examples of chemicals known to be toxic to the nose.
3. Define the terms “hyperplasia”, “metaplasia”, and “neoplasia” and, using a single example of a chemical or physical situation that induces these changes, illustrate how they help explain the multi-stage theory of carcinogenesis.

Please turn over for Questions 4, 5 & 6

4. A fungicide given chronically to rats for two-years in the diet induced a small, but statistically significant, increase in the incidence of combined “mixed uterine tumours” in the mid dose but not in the top or bottom dose level. Describe how you would address whether or not this was a true, treatment-related, effect.

5. Describe the clinical chemistry assessment of kidney function and how knowledge of the anatomy/physiology, biochemistry and molecular biology has been used in the development of the newer biomarkers being introduced for assessing kidney damage.

6. Describe the potential non-chemically related pathologies associated with the oral gavage route of exposure versus the intravenous route in rodents.



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Tuesday 24 March 2009

Candidates must answer FOUR questions ONLY

Time allowed: 3 hours

1. Describe the common spontaneous pathology in specific rodent strains used on lifetime carcinogenicity studies and discuss how these could impact the interpretation of a potential drug-induced effect?
2. Describe and differentiate the morphological features of a carcinoma and a sarcoma and the special techniques that could be used to help distinguish an undifferentiated neoplasm into its tissue of origin?
3. A novel pesticide produces clinical symptoms of “seizure” at the end of a standard 28 day rat study. Describe the methodology that you would use to specifically investigate the possible pathology underlying the effect?

Please turn over for Questions 4, 5 & 6

4. Discuss the possible predictive role of a 28-day rodent toxicity study in assessing likely non-genotoxic carcinogens. How can existing protocols for such tests be improved for this purpose?

5. Describe the anatomical, physiological and biochemical basis of pathology of the testes with specific chemical examples of testicular toxicants?

6. Compare and contrast the non-compound specific pathologies expected from the different routes of administration of compounds to laboratory animals?



The Royal College of Pathologists

Part 1 examination

**Toxicology: Second Paper
(Toxicologic Pathology Subspecialty)**

Tuesday 18 March 2008

Candidates must attempt to answer FOUR questions ONLY

Time allowed – three hours

7. A novel pesticide has been shown to induce a small, but significantly increased, incidence of uterine sarcomas, of mixed morphology, in mice at the top dose level only. No increased incidence was observed in rats. Describe the questions that you would pose and how you would approach evaluating the relevance of this finding to man and the risk assessment process required?
8. Describe how transgenic mouse models can be used to identify genotoxic and non-genotoxic carcinogens, explaining how the genetic changes accelerate the carcinogenic process and the factors that are important in design of such studies?
9. Describe the cardinal pathological features of “light hydrocarbon nephropathy”, explain the underlying mechanism for the induction of the nephropathy and describe how you would prove that a small, but statistically increased, incidence of kidney tumours in a rat study was due to this proposed mechanism?

Please turn over for Questions 4 & 5

10. Describe the features and tissues/organs affected by an immunosuppressive agent and describe what biomarkers of immunosuppression and the methodology that might be used, to evaluate such an agent?

11. Discuss the causes and significance of drug-induced hepatomegaly in a 1 month rodent study, the mechanisms involved and describe how you would address the possible significance of the effect to man illustrating your answer with selected chemical examples?