Biology 137  Name ____________________________
Fall 2001  Final Exam

Part I. Multiple choice (2 points each).

1. In the human body, toxicological processes ultimately take place at which level?
   A) cell  B) tissue  C) organ  D) organ system  E) the whole organism

2. The statement, "All substances are poisons; there is none which is not a poison. Only the dose determines that a thing is not a poison", is attributed to which of the following?
   A) Hippocrates  B) Theophrastus  C) Mithridates  D) Paracelsus  E) Catherine DiMedici

3. The appearance of lung cancer after a latency of 25-30 years from chronic exposure to cigarette smoke is an example of
   A) delayed toxicity.  B) acute toxicity.  C) systemic toxicity.  D) local toxicity.  E) synergistic effects.

4. The sigmoid (s) dose response curve is usually converted into a probit – probability presentation. Each probit unit of the transformed data represents
   A. 50% of the population  B) 99.7% of the population.  C) one standard deviation.  
D) two standard deviations.  E) the LD_{50} value obtained from the plot.

5. Snake venoms are mixtures of bioactive agents that are relatively independent of one another. One could say that their combined actions to produce toxic effects are
   A) additive  B) synergistic  C) potentiated  D) antagonistic  E) none of these

6. Dysregulation of gene expression can result from __________ by the toxicant.
   A) disruption of DNA transcription  B) interference with promoter regions of genes
   C) interference with phosphorylation networks involved in signal transduction  D) interference with signal production
   E) all of the above.

7. In general the process of biotransformation of xenobiotics produces molecules
   A) that have a longer biological half life  B) that have a shorter biological half life  
C) that can be distributed more uniformly in a single fluid compartment  D) that can be utilized as energy sources
   E) None of the above

8. A functional group that is added or exposed on xenobiotic molecules during Phase I biotransformation is
   A) glutathione  B) glucuronic acid  C) sulfhydryls (SH)  D) sulfates (SO_{4})  E) hydroxyl groups

9. The cofactor, __________, is necessary for sulfate conjugation.
   A) NADPH  B) NADH  C) Uridine diphospho-glucuronic acid (UDPGA)  
D) S-adenosylmethionine  E) 3'-phosphoadenosyl-5'-phosphosulfate (PAPS)

10. The deamination of adenine (A) to form hypoxanthine (H) results in hypoxanthine pairing with cytosine (C) during subsequent DNA replication. The end point mutation that can occur is
    A) A:T \rightarrow C:G transition  B) A:T \rightarrow C:G transition  
C) A:T \rightarrow G:C transition  D) H:C \rightarrow C:G transition  E) none of these are correct

11. During the predifferentiation (preimplantation) stage of embryogenesis the primary teratogenic effect observed is:
    A) malformations of the nervous system  B) mutation and development of neoplasms in the newborn individual
    C) death of the embryo  D) survival of a complete individual if at least one cell survives  
E) both (C) and (D) are possibilities
12. During embryogenesis many of the processes that control axial differentiation along the primitive streak such as the development of brachial arches and limb buds are under the control of:
   A) mesoderm  B) ectoderm  C) endoderm  D) homeobox genes  E) p53 genes

13. A toxicant that specifically targets the megakaryocytes in the bone marrow will result in:
   A) leukocytopenia  B) anemia  C) hemorrhaging  D) aplastic anemia  E) granulocytopenia

14. When toxic agents shift the oxygen dissociation curve of hemoglobin to the right, the hemoglobin has a ___________ affinity for oxygen and will release O₂ at ___________.
   A) greater, higher O₂ tensions than normal  B) lower, higher O₂ tensions than normal  C) greater, lower O₂ tensions than normal  D) lower, lower O₂ tensions than normal  E) greater, normal O₂ tensions

15. A hapten activates the immune system by:
   A) binding directly to the antibody receptors of B-lymphocytes  B) binding to receptors of mast cells  C) irreversibly binding to large molecules such as proteins  D) binding to DNA  E) stimulating macrophages

16. One of the postulated mechanisms for the induction of autoimmune reactions is:
   A) activation of CD 4 lymphocytes  B) interference with T-helper cells (CD4)  C) interference with the immunoregulation activity of CD8 T-suppressor cells  D) improper reactivity to hapten-protein complexes  E) mediated by the release of histamine from mast cells that possess reactive IgE on their surfaces

17. Acute cytotoxic liver damage can be detected clinically by the presence of _________ in blood plasma.
   A) transferrin  B) methemoglobin  C) aspartate aminotransferase  D) alanine aminotransferase  E) both C & D

18. The mushroom toxin, phalloidin, contributes to cholestasis by binding to cytoskeletal actin microfilaments and thereby impairing:
   A) paracellular tight junctions.  B) trans cytosis.  C) contraction of hepatocytes and slowing down of bile movement in the canaliculus.  D) transporters involved in bile formation.  E) both A & B.

19. Agents that damage and/or disrupt axonal microtubule polymerization and depolymerization cause peripheral sensorimotor and autonomic neuropathy by:

20. A chemical that induces a Parkinson-like condition in humans and in experimental laboratory mice.
   A) methyl mercury  B) MPTP  C) doxorubicin  D) catecholamines  E) trimethyltin

21. The highest concentration of cytochrome P450 enzymes in the kidney occur in the:
   A) S1 portion of the proximal convoluted tubule.  B) S2 portion of the proximal convoluted tubule.  C) S3 portion of the proximal convoluted tubule.  D) distal convoluted tubule.  E) collecting duct.

22. Which of the following results in a reflexive vasoconstriction when exposure to it stops? This occurs in workers who are exposed in their occupations.
   A) ergot alkaloids  B) arsenic  C) pure O₂  D) nitroglycerine  E) doxorubicin

23. Atherosclerosis is a proliferative vascular wall response of _________ cells to injury by toxicants.
   A) endothelial  B) smooth muscle  C) fibroblast  D) macrophages  E) lymphocytes
24. Which of the following is a mechanism that contributes to the intracellular transport of mercury, Hg, in kidney proximal tubule epithelial cells?  
A) endocytosis of Hg bound to proteins  
B) transport of Hg-glutathione complexes via the action of brush border associated \( \gamma \)-glutamyltranspeptidase and amino acid transporters  
C) transport via a basolateral anion transporter of Hg-SH-protein conjugates  
D) transport of Hg-glutatione complexes via the action of brush border dipeptidases and amino acid transporters  
E) All of the above.

25. Myocardial infarcts (heart attacks) result from a loss of blood supply to portions of the myocardium. When the blood supply is restored (reperfusion) which of the following will result.  
A) the O\(_2\) combined with chemicals released by damaged cells generate ROS  
B) lipid peroxidation  
C) altered calcium homeostasis  
D) membrane damage  
E) all of the above.

26. A mechanism that prevents toxic substances from reaching the spermatogonia and the developing spermatids is  
A) secretion of testosterone by Leydig cells  
B) the production of FSH by the pituitary  
C) the blood-testis barrier  
D) cytochrome P450  
E) both (C) and (D)

27. The chemical diethylhexyl phthalate, an industrial plasticizer, and its metabolites induce membrane alterations and interfere with FSH receptors in Sertoli cells. These effects will result in  
A) reduced production of testosterone  
B) suppressed production of estradiol  
C) premature separation of developing spermatids resulting in their death and destruction  
D) reduced sperm motility  
E) interference with meiosis and production of chromosomal aberrations.

28. The heavy metal, lead (Pb), has been known for a long time to cause sterility. The female gametes are more sensitive than the male gametes.  
A) True  
B) False

29. Unlike other tissues the reproductive cells have a limited capacity for repair of genotoxic injury (DNA damage). Spermatogenic cells have been found to exhibit limited _________ repair and the female gamete unlike the spermatogonia possesses ___________ repair capacity.  
A) excision, unscheduled DNA synthesis  
B) unscheduled DNA synthesis, excision  
C) recombination, excision  
D) unscheduled DNA synthesis, recombination  
E) Both types of reproductive cells do not have any repair capacity.

30. Ecotoxicology is a rapidly developing discipline in which one needs to know chemical effects on:  
A) individual organisms  
B) populations  
C) communities  
D) ecosystems  
E) all of the above

31. Chemicals are dispersed in the air mainly by the process of __________ and transported from the air to water by the process of __________.  
A) laminar flow, advection  
B) turbulent flow, advection  
C) advection, diffusion  
D) diffusion, bulk flow  
E) adsorption, diffusion

32. The rate of movement of chemicals and metals through soils is similar to the chromatographic process involving partitioning between fluid and solid phases and the pore water velocity.  
A) True  
B) False

33. In aquatic environments the bioavailability of a metal depends primarily on  
A) the concentration in sediments  
B) its water solubility  
C) its persistence in sediments  
D) forming inorganic complexes  
E) none of the above
34. In a soil sample the acid volatile sulfides (AVS) and simultaneously extracted metal (SEM), cadmium was measured and the ratio of SEM:AVS was found to be 1.65. From this measurement one could predict that:
   A) divalent cadmium is more bioavailable  B) cadmium would be toxic to sensitive species living in the soil  C) little or no cadmium toxicity would be observed  D) both (A) and (B) are true  E) Both (A) and (C) are true

35. Insecticides, such as DDT, that affect mainly axonal membranes and their ion regulatory processes are classified as
   A) organochlorine insecticides  B) organophosphorus insecticides  C) carbamate insecticides  D) viruses  E) nicotinic insecticides

36. Which of the following is a neuronal target of insecticides
   A) acetylcholinesterase  B) calmodulin  C) Ca-Mg ATPase  D) neurotransmitter receptors  E) all of the above.

37. Herbicides that are directly toxic to exposed animals and humans
   A) chlorophenoxy compounds (2,4-D & 2,4,5-T)  B) pyrethrums  C) rotenone  D) bipyridyl compounds (paraquat)  E) mercury compounds

38. Match the effect in the left-hand column with the pesticide in the right-hand column.

39. carcinogenic  A) pyrethrum
40. teratogenicity  B) DDT
41. lung toxicity  C) ethyl dibromide fumigant
42. hypersensitivity reactions  D) paraquat
43. hepatotoxic  E) carbamate insecticides

44. If it is suspected that a person has been chronically exposed to arsenic over a period of time, a good indicator of the history of exposure is
   A) to make repeated measurements of blood levels  B) make repeated measurements of excretion in the urine  C) make measurements of arsenic at different lengths of hair  D) measure arsenic levels in soft tissue biopsies  E) measure arsenic levels in bone biopsies

45. An important factor that affects the dose of a heavy metal at the target site is
   A) induction of hypersensitivity  B) environmental concentration  C) duration of exposure  D) its biological half-life  E) all affect the dose except (A)

46. A mechanism that has been proposed for the carcinogenicity of metals is their
   A) ability to induce double strand breaks in DNA  B) binding to enzymes  C) substitution for Zn in zinc-finger loops of transcription factors  D) concentration in lysosomes  E) chemical form

47. Methyl mercury is a common pollutant in bodies of water as a result of contamination from mining and manufacturing processes.
   A) True  B) False

48. For the general population the most common source of mercury exposure is
   A) consuming fish that are at the top of the food chain  B) drinking contaminated drinking water  C) eating grains that have been preserved with mercury based fumigants  D) elemental mercury from mirrors and thermometers  E) none of the above
49. Which of the forms of mercury is most likely to cause proximal tubule damage in the kidney
   A) mercury metal   B) mercury vapor   C) inorganic monovalent mercury   D) inorganic divalent mercury   E) methyl mercury

50. Common source(s) of lead exposure to the general population
   A) leaded gasoline   B) paint   C) batteries   D) lead pipes carrying drinking water   E) All of these

Match the item in the left column with the item in the right column for items 51 to 55.

51. methyl mercury    A) the lack of this metal will result in hypochromic microcytic anemia
52. cadmium           B) peripheral endarteritis resulting in gangrene of lower extremities
53. arsenic           C) a cofactor of the enzyme glutathione peroxidase
54. selenium          D) toxicity manifested by presence of small molecular weight proteins in the urine (proteinuria)
55. copper            E) fetal brain damage

56. Which of the following components would not be found in snake venoms
   A) peptides   B) proteolytic enzymes   C) derma necrosis factor 33 & 37   D) thrombin like enzyme   E) hyaluronidase

57. The venom of the brown recluse spider is primarily
   A) a neurotoxin   B) a hemolytic agent   C) a mixture of enzymes that produce tissue necrosis at the site of the bite   D) an anticoagulant   E) a myoneural active agent that results in muscle excitability and rigidity

58. A plant toxin that causes a block in the formation of microtubules and subsequently interfering with cell division processes is
   A) the alkaloid colchicine   B) the lectin Ricin I   C) the lectin Ricin II   D) calcium oxalate   E) a resorcinol

59. The resorcinol, 5-n-heptadecatrienyl, from poison ivy and poison oak induces skin dermatitis by
   A) direct caustic skin irritation   B) physical means involving penetration of the skin by calcium oxalate crystals   C) induction of a type IV delayed hypersensitivity   D) inhibition of keratinocyte mitosis   E) all of the above

60. For ionizing radiations the unit of dose is
   A) the Roentgen   B) the sievert   C) the gray   D) the RBE   E) the LET

61. Of the natural background radiation dose that we receive the greatest contribution comes from
   A) radioactivity in food   B) radioactivity in the ground   C) radon gas in the air   D) fallout from nuclear weapons detonations   E) nuclear power plants

62. Almost all of the energy deposited in biological material from ionizing radiation occurs from
   A) X-rays   B) γ-rays   C) secondary high kinetic energy electrons   D) neutrons   E) α-rays

63. Which of the following would be expected to modify radiation cell survival?
   A) phase in the cell cycle   B) repair processes   C) the presence or absence of O₂   D) the presence of radical scavengers   E) All of the above.
64. The figure above depicts the mean radiation survival time as a function of dose in mammals. One can conclude from this response that the basis for the differential sensitivity to ionizing radiation is A) tissues that receive more O₂ are less sensitive. B) the more differentiated a tissue the more sensitive it is. C) tissues that are actively dividing are more sensitive. D) the more sensitive tissues have less repair capability. E) Both (C) and (D) are true.

Part I. Short answer.

65. What are directly ionizing and indirectly ionizing radiations? What is the distinction? (2 points)

66. What is meant by direct effect and indirect effects of ionizing radiations? (2 points)

67. Repair is an important process that may ultimately determine whether or not a chemical or radiation will manifest toxicity. Describe briefly the three levels of repair and give an example of each. (6 points)
68. What is oxidative stress? List three mechanisms that cells have that protect them from ROS. (5 points)

69. The heavy metal lead (Pb) is found throughout our environment and exposure to it is primarily due to human activities (industrial and domestic uses). List five (5) different effects that can result from acute and chronic exposures. (5 points)