# Pathology 438 Final Examination due: 15 June 2015

Spring 2015

## NAME ZhiXuan Lawrence Jiang\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

The electronic responses to this examination are due on Monday, 15 June 2015 at end of day (5:00 pm). Submit them to [shalloran@lifewest.edu](mailto:shalloran@lifewest.edu) OR to [smhbizness@gmail.com](mailto:smhbizness@gmail.com). You will be sent an acknowledgement receipt.

You are not allowed to consult with classmates or any individuals *other than* the instructor as you research, prepare and compose your responses to the questions posed in this examination. Lecture content (slides) and your oral presentations are on MOODLE for you to use in preparing answers, in addition to access to the LCCW library, reference books and course text books, and on-line resources. Please proofread and organize your work and assemble the exam before submitting it.

Some answers require you to include a citation of the sources you consult to formulate your response. Format your citation according to MLA or APA standards. (If you wish, you can use the built-in Word feature that formats your references: under the References tab, use Insert Citation and fill in the fields as much as possible. Later you will use Bibliography->Insert Bibliography at the point of the cursor. You might learn how to use Section Break too in order to insert bibliographies under separate answers. I have put in section breaks in this document between questions.)

By working the examination and submitting it for grading you are agreeing to work independently of all other individuals and you are certifying that all the responses and answers to the examination questions are your own work.

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Within group A through C, choose ONE of any of the choices answer.  
Choose between D or E, and within D, choose ONE of any of the choices

* 1. Environmental Toxicants. Pick one from the three class of substances below and discuss exposure (places where it might be encountered), its toxicokinetics (ADME) and toxicodynamics (acute, chronic toxicity, effects on physiology and eliciting pathologies. You are allowed to focus on one compound in the class or discuss the toxicology of the class generally
     1. Polyaromatic hydrocarbons (PAHs)
     2. Pesticides—Insecticides: organophosphates
     3. Polychlorinated Biphenyls (PCBs)

* 1. Food Toxicants.

1. Heterocyclic amines (HCAs) can form when meat is cooked often at charring temperatures. Find one compound in this class, discuss how it is formed in cooking and sources of exposure, and discuss effects of chronic toxicity, either in humans or animal studies
2. Sulfur dioxide (SO2) is added to wine during its production. Discuss what is known about acute and chronic toxicity and other toxicodynamic features. Can wine be produced without using it? Are there are alternatives
3. Food Coloring Dyes. FD&C Blue No. 1, Red No. 40, Yellow No. 5, and Yellow No. 6 are common additives to food. Pick TWO of these and discuss what is known about the effect on health and name one alternative to using the dye, comparing financial costs and effect on health.

* 1. Drug-Nutrient Interactions. Select any of the drugs or drug classes below and explain how it affects diet (nutrient absorption). Either suggest an alternative drug and/or explain how an individual can compensate for any effect on nutrition

1. Laxatives
2. Antacids
3. Anticonvulsants

**You can do either D or E below**

* 1. Personal Care Products . Select one of the product types and the named compound usually contained in it. Discuss any facts on acute and chronic toxicity through dermal exposure, and discuss alternatives to
     1. Lipstick: lead acetate
     2. Antiperspirants: aluminum chlorohydrate
     3. Shaving Lotion: find a toxicant in the shaving lotion and discuss it
  2. Sexual dysfunction therapy. A medication for hypoactive sexual arousal disorder recently was in the news. This medication, flibanserin, is being called a “female Viagra.”  
     (a) Discuss the effect of the drug both at clinical and molecular level  
     (b) Discuss alternative therapies, including those in chiropractic medicine

Answer

A) PAHs

PAHs have two or more fused aromatic rings. The have a relatively low solubility in water, but are hightly lipophilic. Most of PAHs with low vapor pressure in the air are adsorbed on particles. When dissolved in water or adsorbed on particulate matter, PAHs can undergo photodecomposition when exposed to ultraviolet light from solar radiation.

PAHs are formed mainly as a result of pyrolytic processes, especially the incomplete combustion or organic material during industrial and other human activity, such as processing of coal and crude oil, combustion of natural gas, including for heating, combustion of refuse, vehicle traffic, cooking and tobacco smoking, as well as in natural processes such as carbonization.

Toxicokinetic

Absorption: In humans, the major routes of uptake of PAH are thought to be trough the lungs and the respiratory tract after inhalation, the gastro-intestinal tract after ingestion of contaminated food or water, and the skin as a result of contact with PAH-bearing materals.

Distribution: PAH occurs in almost all internal organs, organs rich in adipose tissue can serve as storage depots from which the hydrocarbons are gradually release.

Metabolism: Polycyclic aromatic hydrocarbons require multistep metabolic activation by specific enzymes. The enzyme system primarily responsible for PAH metabolism is the mixed-function oxidase system, which requires NADH or NADPH and molecular oxygen to convert the nonpolar PAHs into the polar hydroxyl derivatives and arene oxides.

Elimination: Most metabolites of PAH are excreted in feces and urine.

B)

2-Amino-3-methylimidazo[4,5-f] quinoline, IQ, is reasonably anticipated to be a human carcinogen based on sufficient evidence of benign and malignant tumor formation at multiple tissue sites in multiple species of experimental animals.

IQ is one of many heterocyclic amines formed when various meats and fish are cooked. Originally, it was isolated from broiled fish, fried ground beef, and beef extracts. No uses have been identified that would be expected to lead to the release of IQ into the environment. Environment occurrence of IQ may arise from food waste and disposal in landfills.

IQ was found when certain compounds were mixed and heated, such as in meat extracts. Meat extracts typically are formed by heating a source of amino acids, reduce sugars, fats, and other ingredients at temperature greater than 100 degree for times sufficient to develop flavor. IQ also was found in mixtures of creatinine and phenylalanine or creatinine, phenylalanine, and glucose, heated to 200 degree and in a dry mixture of serine and creatinine heated to 200 degree.

A substantial body of literature suggests that risk of several cancers may be related to consumption of meat, particularly red meat, and to methods of food preparation, particularly grilling and frying. Then mechanism underlying this risk it as yet unclear. One possibility is that HCAs formed when meat is cooked are involved.

IARC reviewed studies of IQ carcinogenicity in experimental animals (IARC 1993). In one of these studies, groups of 40 male and 40 female CDF mice, seven weeks of age, were fed either basal diet or diet containing IQ (> 99.6% pure) at a concentration of 300 ppm for 675 days. Survival of animals administered IQ was similar to that of controls. Body weights of females receiving IQ were slightly less than those of controls. Administration of IQ caused significant increases in the incidence of hepatocellular adenomas and carcinomas(combined), adenoma and adenocarcinomas (combined) of the lung, and papilloma and squamous cell carcinomas (combined) of the forestomach in both sexes.

C)Laxative

Laxative promote and facilitate bowel evacuation by acting locallyto stimulate intestinal peristalsis, to soften bowel contents, or both.

Bulk laxitives. Distention of the intestinal wall by bowel contents stimulates propulsive movements of the gut musculature. Activation of intramural mechanoreceptors induces a neutrally mediated ascending reflex contraction and descending relaxation whereby the intraluminal bolus is moved in the anal direction.

Osmotically active laxatives are soluble but nonabsorbable particles that retain water in the bowel by virtue of their osmotic action. The osmotic pressure of bowel contents always corresponds to that of the extracellular space. The intestinal mucosa is unable to maintain a higher or lower osmotic pressure of the luminal contents. Therefore, absorption of molecules occurs isoomotically, i.e., solute molecules are followed by a corresponding amount of water.

Castor oil comes from Ricinus communis; it is obtained from the first coldpressing of the seed. Oral administration of 10-30 mL of castor oil is followed within 0.5 to 3 h by discharge of a watery stool. Ricinoleic acid, but not the oil itself, is active. It arises as a result of the regular processes involved in fat digestion: the duodenal mucosa releases the enterohormone cholecystokinin/pancreozymin into the blood. The hormone elicits contraction of the gallbladder and discharge of bile acids via the bile duct, as well as release of lipase from the pancreas. Because of its massive effect, castor oil is hardly suitable for the treatment of ordinary constipation. It can be employed after oral ingestion of toxin in order to hasten elimination and to reduce absorption of toxin from the gut. Castor oil is not indicated after ingestion of lipolhilic toxins likely to depend on bile acids for their absorption.

Anthraquinone derivatives are of plant origin. They occur in the leaves or fruits of the senna plant, the bark of Rhammus frangulae and Rh purshiana, the root of rhubarb, or the leaf extract from Aloe species. The structural features of anthraquinone derivatives are illustrated by the prototype structure. Among other substituents, the anthraquinone nucleus contains hydroxyl groups, one of which is bound to a sugar. Following ingestion of galenical preparation or of the anthraquinone glycosides, discharge of soft stool after a latency of 6 to 8 h. the anthraquinone glycosides themselves are inactive but are converted by colon bacteria to the active free aglycones.

D) Lipstick: lead acetate

Acute toxicity: No study is found in acute toxicity through dermal exposure.

Chronic toxicity: Lowered RBC count, decreased MCH and MCV are other concordant hematological change were found in the group which lead acetate was administrated. Anemia was in the form of microcytic and hypochromic. This might be due to effects of lead in cell metabolism, alteration of the enzyme activity, and interaction with reactions in which calcium is their secondary mediator. Lead induced inhibitory effects on the erythrocyte enzymes GA3PD and G6PD have already been proved. Interaction of lead with heme biosynthesis has been related to the inhibition of cytoplasmic and mitochondrial enzymes, and a decrease in the activity of the main enzymes in heme biosynthesis due to defects in iron metabolism has also been reported.

The use of lead acetate in the erythroid tissue culture medium has shown that lead nearly inhibits the proliferation of erythroid lineage, and perturbs cell development and hemoglobin synthesis. In the present study, total leukocyte count had increased mainly due to an increase in neutrophil and monocyte count.