Pathology 438 Final Examination due: 15 June 2015
Spring 2015
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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 OR to 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.

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

A. 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

Exposure: Organophosphates are found in common pesticides that are very effective and have a minimal environmental impact. However, it is a deadly neurotoxin to humans. It is more regulated in the United States than other parts of the word such as India, where it is common to find cases of death due to organophosphate poisoning. In the US, farmers make sure the small amounts that are on the crops do not surpass safe levels whereas in Indian, they do not and have the risk of poisoning when ingesting the crops.

Toxicokinetics: It is absorbed mainly through oral intake (usually on food), but can be transdermal and through inhalation as well. Time is usually less than 4 hours depending on the exact type of organophosphate. Since certain types are lipid soluble, this is how it can cause chronic effects by building up in the adipose tissue in the body. Total time for elimination depends on if it is lipid soluble, how quickly it acts on acetylecholinesterase, and whether or not it needs to be metabolized before it can be eliminated. Certain forms of organophosphates require cytochrome P450 to form the active oxon in order to be eliminated while other do not. In the end, most forms as metabolized as serum esterases and are eliminated by the kidneys.

Toxicodynamics: Organophosphates are highly toxic to humans as it is a nerve agent by inhibiting acetylcholinesterase. In acute toxicity, it causes acetylcholine to accumulate in the central and peripheral nervous system. Symptoms include weakness or paralysis, altered mental status, diarrhea, vomiting, sweating and could lead to respiratory arrest due to weakness/paralysis of muscles. Since it affects the nervous system, there is a long list of possible signs and symptoms that will present with toxicity. If acute poisoning occurs, one needs to get to the hospital in the intensive care unit to be observed for at least 12 hours. The drug, Pralidoxime, is used to treat nerve agent poisoning.

Chronic toxic effects will be similar to the acute symptoms, just in a delayed timeline if someone is consistently exposed to low level doses. Some symptoms will include memory loss and impaired cognitive function, delayed reaction times, insomnia, and death, just to name a few.

Works Cited:

Ker Than. "Organophosphates: A Common But Deadly Pesticide." *National Geographic*. National Geographic Society, 18 July 2013. Web. 14 June 2015.

"Nerve Agent and Organophosphate Pesticide Poisoning." *CDC*. Centers for Disease Control and Prevention, n.d. Web. 14 June 2015.

"Parathion". *Pesticide Information Profiles*. Extension Toxicology Network. Sep 1993. Web. 14 June 2015.

B. 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-Amino-3methylimidazo[4,5-*f*]quinoline, which is abbreviated at IQ, is a compound in this class. It is formed in cooking when foods are smoked or burned at high temperatures of 125 – 300°C. When the creatine, amino acids and monosaccharaides heated together, IQ is formed within minutes. Factors that determine how much IQ is formed depends on temperature, what is cooked, degree of browning, and length of cooking time. Most common source of exposure if ground beef as it is common at all fast food chains. Other common sources include chicken and fish which have higher concentration of HCAs compared to pork. Interestingly, one studied by Knize and Kelton showed that by flipping beef patties every minute reduced the formations of HCA since each side is exposed for a shorter time, reducing the amount of charring that occurs.

There is not enough evidence that indicate that chronic toxicity of specifically IQ causes carcinogenic effects because most studies link fried foods. However, in animal studies, there is sufficient evidence that IQ causes both benign and malignant tumor formation in rats after long term exposure to IQ. Specifically, colon and mammillary glands were affected in rats after long term exposure. The rats' offspring also had a higher change of development adenocarcinomas as it is transferred in the milk. Even though there are no specific studies of the long term effects of IQ on humans, what happens in rats may also apply to humans as well.

Bibliography

"2-Amino-3-Methylimidazo(4,5-f)Quinoline 76180-96-6." *Sax's Dangerous Properties of Industrial Materials* (2004): n. pag. *U.S. Department of Health and Human Services Public Health Service. National* Toxicology Program. Web. 14 June 2015.

Augustsson, Katarina, Jennifer Lindblad, Eva Overvik, and Gunnar Steineck. "A Population-based Dietary Inventory of Cooked Meat and Assessment of the Daily Intake of Food Mutagens." *Food Additives and Contaminants* 16.5 (1999): 215-25. Web. 14 June 2015.

Knize, Mark G., and James S. Felton. "Formation and Human Risk of Carcinogenic Heterocyclic Amines Formed from Natural Precursors in Meat." *Nutrition Reviews* 63.5 (2005): 158-65. Web. 14 June 2015.

Skog, K.I, M.A.E Johansson, and M.I Jägerstad. "Carcinogenic Heterocyclic Amines in Model Systems and Cooked Foods: A Review on Formation, Occurrence and Intake." *Food and Chemical Toxicology* 36.9-10 (1998): 879-96. Web. 14 June 2015.

C. 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

The exact mechanism of laxatives are unknown. There are 4 common types which include bulk forming laxatives, saline and osmotic laxatives, stimulant laxatives and stool softeners. They work by changing osmotic effects and the release of extracellular regulators of the GI tract membrane. Some laxatives increase NO synthase and platelet-activating factor (PAF) in the gut. Laxatives affect diet absorption by accelerating the rate of which nutrients travel though the gastrointestinal tract which may impair absorption of all nutrients including lipids, carbohydrates and protein. However, in one study, the laxative, polyethylene glycol (PEG), showed that lipid absorption in the intestines were not impaired in rats. The laxative itself is minimally absorbed so it is considered safe to use during pregnancy.

An alternative to using laxatives can be to eat more insoluble and soluble fiber foods to help GI motility, keep your body hydrated and to increase movement such as going for walks. All these can help the GI tract function better and help intestinal motility in healthy individuals without the use of laxatives.

Those who use laxatives should compensate for the effect by consuming for electrolytes as the increased GI motility may cause an electrolyte imbalance. Another factor to consider is hydration levels while consuming laxative as both solid and liquids move faster through the system which may result in dehydration.

Bibliography

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University of Nebraska Medical Center. "Physiology of GI motility and secretion". June 2006. PowerPoint Presentation. Retrieved from http://webmedia.unmc.edu/medicine/scholar/GIdrugs.ppt

Wulp, Mariëtte Y.m. Van Der, Frans J.c. Cuperus, Frans Stellaard, Theo H. Van Dijk, Jan Dekker, Edmond H.h.m. Rings, Albert K. Groen, and Henkjan J. Verkade. "Laxative Treatment With Polyethylene Glycol Does Not Affect Lipid Absorption in Rats." *Journal of Pediatric Gastroenterology and Nutrition* 55.4 (2012): 457-62. Web. 14 June 2015.

2. Antacids

3. Anticonvulsants

You can do either D or E below

D. 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

Aluminum chlorohydrate is the most common active ingredient in antiperspirants. The aluminum acts as a plug on the sweat ducts to temporarily prevent sweat to come to the surface of the skin. However, there are many risks associated with that.

Acute toxicity: Most people can use antiperspirants with this compound without any harmful effects on the skin. However for some, it may cause irritation to the skin, eyes and respiratory system. It also may be harmful if swallowed. The oral toxicity is low to moderate with LD50 range of 162 – 750 mg of Al/kg body weight. There are very few studies that explore the effect of aluminum chlorohydrate so the effects are largely unknown.

Chronic toxicity: In long term exposure to the skin, it may be harm to people with kidney disorders as they are not able to eliminate it from their system as efficiently. There are a few questions that show a link below the use of underarm, antiperspirants and breast cancer. One study (Mannello et al., 2009) suggested that breast cysts could form is enough aluminum is absorbed through the skin into the breast tissue over the long-term. At this point, there is not enough information to suggest there is a causal relationship, only a correlation.

Alternatives: There are many alternatives to antiperspirants with aluminum in it. Look for ones that are aluminum free or choose use deodorant instead so that your sweat ducts can be free, but you can still control the body odor. Some options include large crystals made from potassium aluminum sulfate that is wetted and applied to the underarm, corn starch and baking soda, and lemon juice. The large crystal, even though it as aluminum, the molecules are too large to be absorbed which is why it is a safer option.

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Altivia. "Aluminum Chlorohydrate." *Material Safety Data Sheet* (n.d.): n. pag. *Altivia*. 31 Jan. 2014. Web. 14 June 2015.

Mannello, Ferdinando, Gaetana A. Tonti, Virginia Medda, Patrizia Simone, and Philippa D. Darbre. "Analysis of Aluminium Content and Iron Homeostasis in Nipple Aspirate Fluids from Healthy Women and Breast Cancer-affected Patients." *Journal of Applied Toxicology*. 31.3 (2011): 262-69. Web. 14 June 2015.

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