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
3. **Polychlorinated Biphenyls (PCBs)**

Answer A3-

Polychlorinated Biphenyls (PCBs) are a group of manmade chemicals first manufactured in the U.S. in the late 1920's. PCBs are used in various products, including but not limited to: electrical equipment, surface coatings, inks, adhesives, flame-retardants and paints.[1] Since developing an understanding of the dangers PCBs have on the environment and to humans and animals, they have largely been banned around the globe. However, about 10% of all PCBs manufactured since 1929 still remain in the environment today. Humans are largely exposed to

PCBs through consumption of foods and liquids in plastic containers that are heated and subsequently released and consumed.

The toxicokinetics of PCBs are vast and well researched. Toxicokinetics includes Absorption, Distribution, Metabolism and Excretion.

PCBs are absorbed through various routes, but most commonly through oral, inhalation, and transdermal. Inhalation exposure is largely responsible for occupational exposures to PCBs. Oral exposure is predominately the route, this occurs when plastic containers are heated and the PCBs are released from the plastic. Transdermal exposure is not of huge concern, but does tend to occur in the adipose tissue of manufacturer workers.

Studies pertaining to the distribution of PCBs in humans largely come from exposure to humans through occupational and manufacturers workshops. Initially PCBs are taken up by the liver and muscle due to the high blood perfusion rates. Highly chlorinated congeners are metabolized very slowly and thus stored in adipose tissue. PCBs have also been found in high concentrations of glandular tissues, including ovaries and breast milk. This is thought to be largely due to the increased fat content of these body parts.

The metabolized half-life of PCBs depends largely on the ability of the body to break it down. This is because the metabolism of PCBs is the rate limiting step in the elimination of toxic compounds. As a rule of thumb, PCBs with more than five chlorines are less susceptible to hydroxylation and therefore show the longest half-lives.

The absorbed PCBs can either be excreted or retained in adipose tissue, skin, specific tissue (organs such as the liver, kidney, muscle, adrenal, lungs, or spleen) on a lipid basis, or in body fluids. PCBs are broken down into polar compounds that can then be excreted from the tissues. Elimination is achieved via biphasic elimination commonly. The initial half life is short, but the subsequent half-life is long and structure dependent.

The toxicodynamics of PCBs are a bit more straight-forward, I believe. They seem to be much less potent when compared with dioxins and furans, often times by a factor of 10,000 or 100,000.[2] As mentioned previously, the higher chlorine content, the higher the toxicity to animals. "Coplanar" PCBs are associated with higher "TCDD-like" toxicity (hence the comparison to the furans and dioxins). Studies including animal models showed various forms of toxicity, including: hepatotoxicity, neuropathy, reproductive abnormalities, decreased antibody response, certain cancers, xenoestrogen effects. Studies including human and primate models include the following toxicities: hepatotoxicity, otitis media, reproductive harms, neuro-developmental disorders.

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. Sulfur dioxide (SO_2) 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.

Answer B1-

Heterocyclic Amines (HCAs) are chemicals formed when muscle meat, including beef, port, fish, or poultry, is cooked using high-temperature methods, including pan frying or grilling over an open flame. These chemicals include at least one heterocyclic ring. Pyrrolidine seems to be the most common and therefor more researched HCA.

HCAs form when amino acids and creatine react at high cooking temperatures. Sources of HCAs are the various meat products listed above cooked at a high charbroiling temperature.

Researchers have identified 17 different HCAs that are thought to likely be carcinogenic. The long term exposure toxicity to HCAs appears to be largely cancer, though undescribed neurologic disorders also occur with chronic toxicity.[3]

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

2. Antacids

3. Anticonvulsants

Answer C2-

Millions of Americans currently take antacids to compensate for the indigestion and associated acid reflux involved with unhealthy digestive systems.

Antacids are a type of drug known as Proton Pump Inhibitors (PPIs).[4] These drugs work by stopping the acid production from cell within the stomach, which can often aid in the acid reflux disease symptoms. Unfortunately, these cells that PPIs target are also responsible for producing Intrinsic Factor, which is necessary to absorb B12. Therefore, chronic use of PPIs can result in Vit B12 deficiencies. Vit B12 deficiencies result in neurologic disorder symptoms and is also very common in Vegans.

To help someone experiencing a Vit B12 deficiency secondary to medicating with a PPI, I would first aim to take them off of the PPI. Acid reflux can often times be treated with household items such as Aloe Vera or apple cider vinegar. It can also be treated by consuming

healthy, nutritious fruits and vegetables with high levels of fiber and complex nutrients. I could also supplement the patient with a B12 tablet and IF.

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**

3. Shaving Lotion: find a toxicant in the shaving lotion and discuss it

Answer D2-

Aluminum Chlorohydrate, an antiperspirant chemical used in the majority of over-the-counter underarm deodorant/antiperspirants, is classified by the FDA in its safest category (big surprise).[5] A variety of symptoms have been reported following both acute and chronic exposures to Aluminum Chlorohydrate in the form of deodorant.

Aluminum is naturally found in the Earth's crust and is relatively non-toxic in its natural form. In antiperspirants, however, the aluminum is ionized, and this creates certain problems regarding toxicity. These ionic aluminum compounds react with sweat and produce clumping, which is what actually blocks and clogs your sweat glands which produce the desired effect of "less sweat".[6]

The most common symptoms/reactions caused by acute toxicity/exposure are the following: rash/dermatitis, acne, and itching. These will typically clear up and resolve after stopping use of the product.

Long-term health risks are also possible. Certain cancers, such as breast cancer, Alzheimer's, and other nodular masses have been documented. These complications/chronic toxicities are also linked with Vitamin D and Calcium deficiencies.

Many, many websites offer recipes for making your own deodorant/antiperspirant using mainly household items. Many use essential oils and coconut oil, though there are many different recipes which have proven to be both safe and effective.

E. 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

References

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3. Exposure assessment of heterocyclic amines (HCAs) in epidemiologic studies. - PubMed - NCBI. (n.d.). Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9202756
4. Widely Used Antacids Can Cause Vitamin B12 Deficiency. (n.d.). Retrieved from http://articles.mercola.com/sites/articles/archive/2014/02/05/antacids-vitamin-b12-deficiency.aspx
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6. The Effects of Aluminum on the Skin | LIVESTRONG.COM. (n.d.). Retrieved from http://www.livestrong.com/article/201752-the-effects-of-aluminum-on-the-skin/