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Toxicology Final

6/15/15

A:

According to the class notes, polycyclic aromatic hydrocarbons (PAHs) are formed from partial combustion of coal, oil, gas, garbage, other organic substances, they can be found in soil, crude oil, coal, creosote and road and roofing tar. You are probably most likely to get exposed to PAH's through vehicle exhaust, coal ash, wildfires, agricultural field burns, hazardous waste sites, and foods particularly meat that is cooked at very high temperatures that causes charring. They typically occur as mixtures of two or more PAH's and overall there are more than 100 PAH's.

PAH's are highly lipophilic and is absorbed in the lungs, respiratory tract, skin as well as the GI tract from contaminated food and water. It is distributed and detected in all internal organs. Adipose tissue and the GI tract show highest accumulation. It is metabolized by the cytochrome p450 oxidase system where the CYP1 family is associated with metabolic activation of pro carcinogens. The PAH's conjugated metabolites are excreted by both biliary-fecal and urinary excretion. With urinary excretion glutathione conjugates are converted to mercapturic acid and then excreted in urine.

Metabolites of PAH's may be more reactive and alkylation appears to increase carcinogenesis. Some of the effects are tumors in the lungs or bladder, stomach cancer and irritation of the skin on the face or scrotum.

B:

Yellow #5 Dye- This dye was found to contain carcinogenic contaminants and cause allergic reactions. There were no studies linking yellow #5 to cancer or tumor growth but 6 out of 11 studies gene toxicity and hyperactivity in children. Yellow #5 is the second most commonly used dye in the United States. It is commonly found in packaged snacks like chips, crackers, cheese flavored items, sweets, cereals, and a variety of breakfast products (1).

Yellow #6 Dye- This dye was also found to contain carcinogenic contaminants and cause allergic reactions. Studies in rats also showed a possible increase in adrenal and testicular tumors in those rats that consumed yellow #6 dye (1).

You can use safe and healthy alternative yellow food dyes. Some great foods that you can use for natural yellow food coloring include turmeric powder, yellow carrots, lemon zest, saffron, and bee pollen. Each one of these natural food may be a little more expensive to buy and take a little longer to prepare but the benefits are priceless. Turmeric is great food fighting inflammation, carrots are great for your vision, and bee pollen is great for your immune system, so use these natural alternatives and say no to buying unsafe and unnatural food dye.

1. <http://cspinet.org/new/pdf/food-dyes-rainbow-of-risks.pdf>

C:

Some common medications that the general public takes every day can alter food intake, cause complications with food intake, and alter the absorption, metabolism, and excretion of nutrients. Antacids are one of these commonly consumed medications. According to the class notes, antacids work by reducing the gastric acidity and lowering the absorption of Vitamin B12, Folate, and Iron.

If I would first try to make a change in the patient's diet and have them stay away from the foods that tend to give them problems. If this did not work and they insisted on taking the antacids I would have them take a Vitamin B12 supplement and have them increase their food intake of natural and healthy foods that were high in Iron and Folate.

I would have my patients eat a diet high in leafy green vegetables and consume Brussels sprouts, avocados, asparagus, and broccoli as these all are good sources of folate and iron. Along with the B12 supplementation this change in diet could help counter the negative effects seen with antacid consumption.

E.

#### Sexual Dysfunction Therapy and Flibanserin

According to Sprout Pharmaceuticals Flibanserin Advisory Committee Briefing Document published on June 4, 2015, Flibanserin is a postsynaptic 5-HT<sub>1A</sub> agonist 5-HT<sub>2A</sub> antagonist developed as a novel, non-hormonal treatment for hypoactive sexual desire disorder (HSDD) in premenopausal women (1).

The document describes HSDD as the deficiency or absence of sexual fantasies and desire for sexual activity which causes marked distress or interpersonal difficulty, and is not better accounted for by another psychiatric disorder or due exclusively to the direct physiological effects of a substance or to the direct physiological effects of another medical condition.

The review committee also notes that CNS depression, presenting as sedation-related adverse effects (dizziness, somnolence, fatigue), is the hallmark adverse effect of Flibanserin and has been uniformly reported across the Flibanserin clinical development program.

Flibanserin has preferential affinity for serotonin 5-HT(1A), dopamine D(4), and serotonin 5-HT(2A) receptors. According to a drug review from 2002 on the pharmacology of Flibanserin, Flibanserin reduces neuronal firing rate in cells of the dorsal raphe, hippocampus, and cortex with the CA1 region being the most sensitive in the brain. Flibanserin-induced reduction in firing rate in the cortex seems to be mediated through stimulation of postsynaptic 5-HT(1A) receptors, whereas the reduction of the number of active cells seems to be mediated through dopamine D(4)

receptor stimulation. Flibanserin quickly desensitizes somatic 5-HT autoreceptors in the dorsal raphe and enhances tonic activation of postsynaptic 5-HT(1A) receptors in the CA3 region. Flibanserin preferentially reduces synthesis and extracellular levels of 5-HT in the cortex, where it enhances extracellular levels of NE and DA. The review goes on to state that Flibanserin may induce some sedation but does not induce observable toxic effects at pharmacologically relevant doses (2).

There are some ways to naturally increase libido and sexual satisfaction naturally and this is what I would first want my patients to try if they were having issues. The first would be exercise as this can help to naturally boost testosterone and thus increase sexual desire. The next thing I would have my patient do is to try to increase their intake of natural foods known to increase libido. According to Margarita R. Ochoa-Maya, MD, CDE, these are some of the best foods to try (3). Increase avocado consumption to help increase testosterone production and regulate the thyroid gland. Increase almond and nut intake in general because there are a primary source of essential fatty acids and they provide us the raw material we need for healthy production of hormones. I would have my patients increase their soy intake because it is a natural phytoestrogen and may improve hormone levels leading to improved sexual desire and pleasure. Eggs are also good to eat in order to balance hormone levels. Lastly I would have my patient consume more Liver as it is a great source of glutamine and glutamine is known to enhance sex drive (3).

There are a number of other foods thought to increase libido like oysters, basil, salmon, and celery and I would have my patient try to switch to a diet high in these foods before they look to a pill for intervention.

I would also want to express the importance of getting adjusted and how regular chiropractic care can help improve libido. During my evaluation I would pay close attention to the lumbar spine and the nerves that innervate reproductive areas. Removing subluxations in these areas will allow the brain and body to communicate effectively and help increase libido naturally.

1. <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM449090.pdf>
2. Borsini F1, Evans K, Jason K, Rohde F, Alexander B, Pollentier S. Pharmacology of Flibanserin. CNS Drug Rev. 2002 Summer;8(2):117-42. <http://www.ncbi.nlm.nih.gov/pubmed/12177684>.
3. <http://www.freedomtoheal.org/2010/11/what-foods-and-supplements-help-libido.html>