Exam Key

NROSCI/BIOSC 1070 and MSNBIO 2070
Final Exam
December 19, 2015

Total POINTS: 100 20% of grade in class

1) Zollinger-Ellison syndrome results from a gastrin-secreting tumor, producing increased numbers of parietal cells and increased acid output in the stomach. The large quantity of acid produced leads to gastrointestinal mucosal ulceration. It also leads to diarrhea and malabsorption. Briefly explain why Zollinger-Ellison syndrome is associated with malabsorption. ***(5 points).***

In the small intestine, enzymes need an alkaline environment to function properly. The acid production in Zollinger-Ellison syndrome is so extensive that bicarbonate secretion in the small intestine and pancreas cannot achieve an alkaline pH. Hence, the pancreatic and intestinal enzymes become dysfunctional, such that chyme is incompletely digested, resulting in malabsorption.

Key point: enzymes in intestine require alkaline environment, impossible if stomach acid secretion is exaggerated.

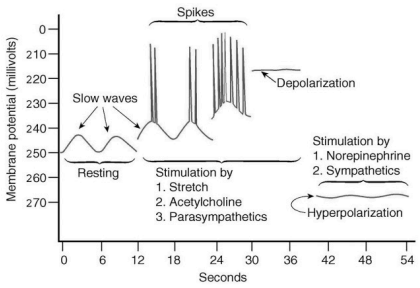
2) Metabolic acidosis can lead to a change in plasma potassium levels. Does metabolic acidosis result in hyperkalemia or hypokalemia? Provide a brief explanation for your answer. ***(7.5 points).***

Metabolic acidosis results in hyperkalemia. The proton pump exchanges H^+ for K^+. In the kidney and other tissues, the proton pump is used to eliminate H^+ from the plasma, and in doing so plasma K^+ levels rise.

Key points: Metabolic acidosis results in hyperkalemia *(3 points)* due to the actions of the proton pump (H^+—K^+ exchanger) *(4.5 points)*.

Exam Key

3) Earlier in the class, we discussed the use of calcium channel blockers such as verapamil to treat hypertension, angina, and cardiac arrhythmias. The most common side effect reported for such drugs is constipation. Briefly discuss the mechanism through which commonly-used calcium channel blockers produce constipation. ***(4 points).***



Smooth muscle contraction in the GI tract results from opening of L-type Ca^{2+} channels at the crest of slow waves. Calcium channel blockers reduce this Ca^{2+} influx, so motility is reduced.

Key point: must indicate that the Ca^{2+} entry that results in smooth muscle contraction in GI tract is reduced by calcium channel blockers.

4) One of the earliest markers for liver failure in adults is Jaundice, a yellowish pigmentation of the skin, the conjunctival membranes (whites of the eyes), and other mucous membranes. The yellowish color is due to accumulations of bilirubin in these tissues. Briefly discuss why liver failure leads to Jaundice, and include in your answer a discussion of how the liver normally processes bilirubin. ***(5 points).***

Old and damaged red blood cells are removed by several tissues (including the spleen), and the breakdown product of hemoglobin (bilirubin) is transported to the liver for removal. The liver excretes bilirubin in bile, which is deposited into the lumen of the intestine. In liver disease, damage to the liver prevents the elimination of bilirubin in bile, so levels accumulate in the blood and a number of tissues, causing the yellow skin coloration associated with Jaundice.

Key points: bilirubin is eliminated by the liver in bile and in liver failure this no longer occurs.

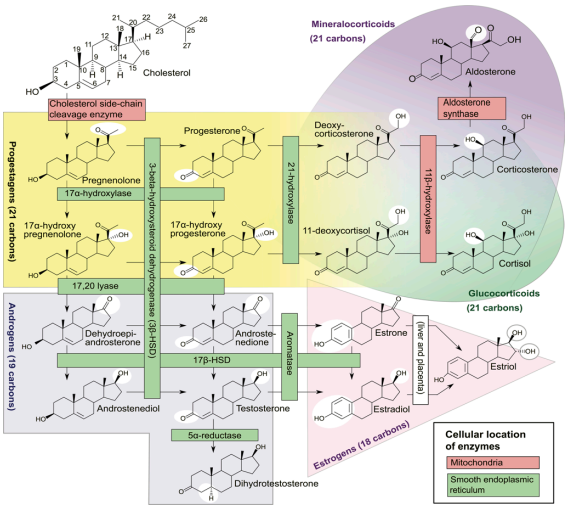
5) During pregnancy, use of all over-the-counter drugs is usually discouraged. However, if a pregnant woman has a fever, she is usually told to take acetaminophen (e.g., Tylenol) instead of acetylsalicylic acid (e.g., Aspirin). Based on your knowledge about the pharmacology of NSAIDs, describe why low doses of Tylenol may be safer for a pregnancy than low doses of aspirin ***(7.5 points).***

NSAIDs inhibit the cyclooxygenase enzymes, and prevent prostaglandin synthesis. Both Tylenol and Aspirin are NSAIDS, but Aspirin is a much stronger inhibitor of the Cox-1 enzyme. The prostaglandins that prevent closure of ductus arteriosus and trigger parturition are produced by Cox-1, and thus aspirin can result in premature closure of ductus arteriosus and prolonged pregnancy.

Key points: Aspirin inhibits Cox-1 more than Cox-2, and prostaglandins produced by Cox-1 play key roles in pregnancy *(3.5 points)*, including preventing closure of ductus arteriosus *(2.5 points)* and triggering parturition *(1.5 points)*.

Exam Key

6) Congenital adrenal hyperplasia is an inherited disease (autosomal recessive) where one enzyme (21-hydroxylase) is ineffective. Loss of this single enzyme results in loss of both cortisol and aldosterone synthesis, as well as overproduction of sex steroids. Briefly explain how loss of one enzyme can cause a change in the synthesis of so many hormones ***(4 points).***



21-hydroxylase converts Progestogens into Glucocorticoids, which are in turn converted to mineralocorticoids. Without, 21 hydroxylase, neither glucocorticoids or mineralocorticoids can be synthesized. Thus, cells that normally produce glucocorticoids and mineralocorticoids will release Progestogens. The rise in plasma Progestogens will serve as a substrate for production of androgens and estrogens.

Key points: the missing enzyme plays a key role in synthesis of glucocorticoids and mineralocorticoids *(3 points).* Progesto-gens thus rise, and also serve as a substrate for estrogen and testosterone synthesis *(1 points).*

7) The smell and taste and expectation of food will sometimes cause "lightheadedness." Briefly discuss why expecting food results in this cognitive effect. ***(5 points).***

During the cephalic phase, the expectation of food causes an increase in blood insulin levels (3 points), and thus lowers blood sugar (1 point). This results in lightheadedness (1 point).

Exam Key

8) Historically, iodine deficiency in the diet has been one of the most common causes of birth defects. Briefly discuss the consequences of iodine deficiency on the developing fetus, including the mechanism through which iodine deficiency leads to birth defects. ***(4 points).***

Iodine is essential for synthesis of thyroid hormone (3 points), which in turn is necessary for microtubule assembly (1 point). Hence, a mother without proper iodine in the diet will be hypothyroid, and her child will have neurological damage.

9) Bisphosphonates such as Fosamax and Boniva are now the standard treatment for postmenopausal women suffering from osteoporosis. Bisphosphonates have no action on estrogen receptors, but prevent bone loss through another mechanism. Discuss the mechanism through which Bisphosphonates act to treat osteoporosis. ***(3.5 points).***

Bisphosphonates inhibit the activity of osteoclasts.

Exam Key

10) Evista (raloxifene), which was patented by Eli Lilly, is another drug used to treat osteoporosis in postmenopausal women. Unlike bisphosphonates, Evista is also used for reduction of the risk of invasive breast cancer in postmenopausal women at high risk (e.g., with a family history of breast cancer). Briefly describe the action of Evista to produce these effects. ***(4 points).***

Evista is a SERM, which inhibits (blocks) the estrogen receptor in the breast and stimulates the estrogen receptor in bone. Note that many breast cancers are simulated by estrogen, so the cancer risk decreases when the breast estrogen receptors are blocked.

Key points: Evista is an agonist for the estrogen receptor in bone *(2.5 points)* and an antagonist for the receptor in the breast *(2.5 points).*

11) Analogs of gonadotropin-releasing hormone (GnRH) can be used to either prevent ovulation or to enhance ovulation, depending on how the hormone is administered. Discuss how GnRH must be administered to produce each effect. ***(5 points).***

GnRH must be provided in a pulsatile fashion to induce LH and FSH release in the anterior pituitary. A computer controlled pump can provide pulsatile GnRH and enhance FSH secretion, but providing the hormone continuously prevents FSH release and the LH surge, so there is no ovulation.

Key point: Must indicate that GnRH has to be provided in pulses to trigger LH/FSH release.

12) A male is born with an inability to produce the aromatase enzyme. Answer the questions below regarding the physiological effects of loss of the aromatase enzyme in a male.

a) What would be the most overt (clearly-observable) manifestation of the aromatase deficiency? ***(3 points).***

Aromatase converts androgens into estradiols. The man will be extremely tall (as the epiphyseal plate never closes since no estrogen is produced in bone).

b) List three hormones whose levels are altered in an adult male with an aromatase deficiency. Indicate whether the levels are increased or decreased. ***(6 points).***

- *Estrogen levels are very low*
- *LH levels are very high (since feedback inhibition is diminished)*
- *Testosterone levels are usually elevated (high LH; limited feedback inhibition)*
- *Also acceptable: FSH levels are high, although the mechanism is unclear*

Key point: 2 points for indicating each hormone and the change that occurs. 0 points for listing the hormone but incorrectly indicating the change (example: decreased LH levels gets no points).

Exam Key

13) Answer the following questions regarding the medical use of progesterone receptor antagonists.

a) What is the main medical usage for progesterone receptor antagonists? ***(5 points).***

To cause a loss of the uterine lining (endometrium) along with any implanted blastocyst/fetus. This is usually done as part of emergency contraception or to induce an abortion in the first two months of pregnancy.

b) Often progesterone receptor antagonists are administered along with misoprostol, a synthetic analog for prostaglandin E_1 (PGE_1). Why are the drugs often combined? ***(5 points).***

Prostaglandins trigger uterine contractions, so this facilitates shedding the endometrium and blastocyst.

c) Misoprostol is also used in the treatment of stomach ulcers. What action of misoprostol makes it effective in this therapy? ***(5 points).***

Prostaglandins (particularly PGE_1) trigger the formation of stomach mucus, so giving misoprostol causes more mucus formation in the stomach, which protects the stomach lining.

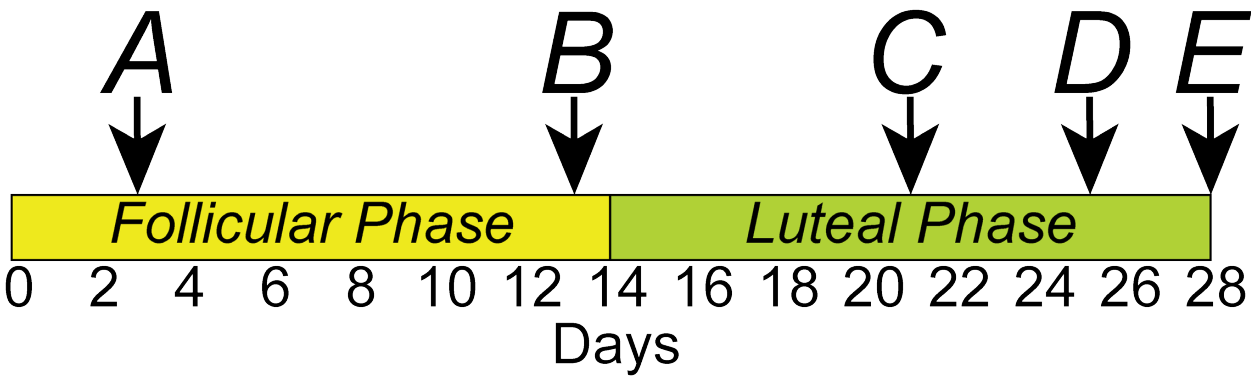
14) Could either a dopaminergic agonist or antagonist serve to stimulate lactation in a nursing mother? Which (an agonist or antagonist), if either, would be effective? How would the drug work to promote lactation? ***(7.5 points).***

Antagonists of the D2 receptor in the anterior pituitary promote lactation. This is because hypothalamic dopamine inhibits prolactin secretion. Thus, a dopaminergic antagonist can increase prolactin levels, which facilitates lactation.

Key points: Dopamine antagonists are effective *(2.5 points)* as they promote prolactin secretion *(5 points).*

Exam Key

15) Refer to the diagram below regarding the menstrual cycle, and indicate which letter designates when peak and minimal plasma values occur of particular hormones. ***(2 points each; 14 points total).***



a) Peak LH: B
b) Peak FSH: B
c) Minimal FSH: D
d) Peak Estrogen: B
e) Minimal Estrogen: E
f) Peak Progesterone: C
g) Minimal Progesterone: E