Possible Clinical Application Questions for Exam III

1. Explain what a heart murmur is and describe the difference between an innocent and abnormal heart murmur. How is a heart murmur diagnosed?

A heart murmur is an extra or unusual sound heard during a heartbeat as a result of abnormal turbulent blood flow through the heart. The two types of heart murmurs are innocent (functional) and abnormal. Innocent heart murmurs aren't caused by heart problems and they don't cause adverse symptoms. Having one doesn't require you to limit your physical activity or do anything else special. They can occur when blood flows more rapidly through the heart as occurs during physical activity, pregnancy, fever, hyperthyroidism, anemia, and aging. These murmurs are common in healthy children and can be simply due to the chest wall being relatively thin making it easier to hear the sounds of the blood flowing through the heart. Abnormal heart murmurs may have signs or symptoms of heart problems. Most abnormal murmurs in children are caused by congenital heart defects such as a hole between the chambers (septal defect) or valve abnormalities. Congenital defects are problems with the heart's structure that are present at birth. In adults, heart murmurs most often are caused by heart valve disease that develops as the result of another condition. Infections such as rheumatic fever and endocarditis; stenotic (stiff) valves associated with atherosclerosis where the valve doesn't open completely, and insufficient (incompetent) valves that do not close completely and heart changes associated with aging. Heart murmurs are usually diagnosed by listening to the heart with a stethoscope. A more detailed test includes an Echocardiography (ultrasound), a test that uses sound waves to create pictures of your heart. They are not diagnosed with an ECG.

2. Draw and label a typical electrocardiogram (ECG). Describe what an ECG is and what each wave is the result of.

- Electrocardiogram (ECG or EKG) is a record of the electrical activity conducted through the heart during a cardiac cycle.
  - The waves of the ECG are produced by the combined effects of action potentials generated by myocardial cells
  - Each cardiac cycle produces three distinct waves:
    1. P wave: Period during which the atria are depolarizing.
      - The spread of an action potential from the SA node through the two atria
    2. QRS wave (complex): The period during which the ventricles are depolarizing, which precedes their contraction.
    3. T wave: Period during which the ventricles are repolarizing.
      - Indicates ventricular relaxation and repolarization
  
Note: There is no wave to show atrial relaxation because the stronger QRS wave masks this event.
3. Discuss four common characteristics of the many types of anemia.

1) reduced RBCs/hematocrit; reduced hemoglobin
2) fatigue (lack of oxygen needed for ATP production)
3) cold intolerance (lack of oxygen needed for heat production)
4) skin appears pale (low content of red-colored hemoglobin)

4. Describe the structural features of a mature red blood cell that help it function in gas transport.

a) It has the shape of a biconcave disc which helps make the cell flexible and increases its surface area for diffusion of gases
b) It lacks a nucleus and some organelles such as endoplasmic reticulum and thus has more space for gas transport.
c) The cytosol contains hemoglobin.
d) There are no mitochondria, and therefore the cell metabolizes anaerobically, and does not use up any of the carried oxygen.

5. A person with ketoacidosis may hyperventilate. Explain why this occurs, and explain why this hyperventilation can be stopped by an intravenous fluid containing bicarbonate.

Ketoacidosis is a type of metabolic acidosis, and the fall in arterial pH stimulates the aortic and carotid bodies to signal the medulla oblongata which increases ventilation. This type of hyperventilation is referred to as Kussmaul's respirations. Hyperventilating reduces the level of carbon dioxide in the bloodstream and, as shown in the following equation, will cause more HCO$_3^-$ and H$^+$ to bind together to form H$_2$CO$_3$, which will be converted to CO$_2$ and H$_2$O. This effectively removes more H$^+$ ions from the bloodstream, thus raising the pH of the blood and partially compensating for the decrease in pH by the ketoacidosis.

$$\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-.$$ Administration of bicarbonate can buffer the H$^+$ released from the ketoacidosis and help to return the blood pH to normal. As this occurs, the amount of hyperventilation will decrease.

6. You Do NOT have to write on each of these in the clinical application short answer portion of the test. I have included them for you to read through and will be required to identify each in the form of a multiple choice or fill in the blank question. You goal is to be able to explain how each of the following antihypertensive drugs would lower arterial blood pressure: Note, for this section you are not expected to remember the drug names in parenthesis, but instead, you are expected to know how the antihypertensive drugs work given the following descriptions.

a. Drugs that block $\alpha1$-adrenergic receptors (for example, phentolamine).

The $\alpha1$ receptors are found in the smooth muscle of all arterioles with the exception of the brain and heart vasculature. The binding of epinephrine and norepinephrine to $\alpha1$ receptors leads to vasoconstriction and increased arterial blood pressure. Blockage of $\alpha1$-adrenergic receptors results in vasodilation thereby lowering arterial blood pressure.
b. Drugs that block β1-adrenergic receptors (for example, metoprolol).

β1 receptors are found primarily on the SA node, AV Node and heart muscle cells. Activation of β1-adrenergic receptors with epinephrine and norepinephrine increases heartrate and strength of cardiac contraction. Drugs that block β1 receptors decrease heart rate and force of contraction resulting in a reduction of cardiac output and blood pressure.

c. Drugs that directly relax arteriolar smooth muscle (for example, hydralazine).

Drugs that directly relax arteriolar smooth muscle by decreasing the phosphorylation of smooth muscle myosin light chain thereby lower arterial blood pressure by promoting arteriolar vasodilation and reducing total peripheral resistance.

d. Drugs that block release of norepinephrine from sympathetic endings (for example, guanethidine).

Sympathetic neuron innervating blood vessels release norepinephrine which activates α1 receptors found in the smooth muscle causing arteriolar vasoconstriction. This results in an increase in total peripheral resistance and arterial blood pressure. Drugs that block the release of norepinephrine from sympathetic endings lower blood pressure by preventing this vasoconstrictor effect.

e. Drugs that act on the brain to reduce sympathetic output (for example, clonidine).

Sympathetic neuron innervating blood vessels release norepinephrine which activates α1 receptors found in the smooth muscle causing arteriolar vasoconstriction. This results in an increase in total peripheral resistance and arterial blood pressure. Drugs that act on the brain to reduce sympathetic output lower blood pressure by preventing the effect of sympathetic activity on promoting arteriolar vasoconstriction and the resultant increase arterial blood pressure.

f. Drugs that block calcium channels of smooth muscle cells in blood vessels (for example, verapamil).

Drugs that block calcium channels reduce the entry of calcium into the vascular smooth muscle cells from the extracellular fluid in response to excitatory input. Because the level of contractile activity in vascular smooth muscle cells depends on their cytosolic calcium concentration, drugs that block calcium channels reduce the contractile activity of these cells by reducing calcium entry and lowering their cytosolic calcium concentration. Total peripheral resistance and, accordingly, arterial blood pressure are decreased as a result of reduced arteriolar contractile activity.

g. Drugs that interfere with the production of angiotensin II (for example captopril, an ACE inhibitor).

Blocking the production of Angiotensin II will stop it from the following activities and thus lower blood pressure. Angiotensin II does the following: 1) Is a powerful vasoconstrictor of small arteries and arterioles which increases blood pressure (BP). 2) Stimulates the adrenal cortex to release aldosterone, a hormone that promotes Na⁺ and water resorption at the kidneys and thus increases blood volume and BP. 3) Stimulates ADH release by the posterior pituitary which increases absorption of water at the kidneys.
increasing blood volume and thus BP. 4) Activates the body’s thirst center within the hypothalamus which causes a person to drink more - increased fluid intake causes an increase in blood volume and BP.

h. Drugs that block angiotensin II receptors (for example, losartan).

Drugs that block angiotensin II receptors prevent angiotensin II from activating the following activities and thus lower blood pressure. Angiotensin II does the following: 1) Is a powerful vasoconstrictor of small arteries and arterioles which increases blood pressure (BP). 2) Stimulates the adrenal cortex to release aldosterone, a hormone that promotes Na+ and water resorption at the kidneys and thus increases blood volume and BP. 3) Stimulates ADH release by the posterior pituitary which increases absorption of water at the kidneys increasing blood volume and thus BP. 4) Activates the body’s thirst center within the hypothalamus which causes a person to drink more - increased fluid intake causes an increase in blood volume and BP.

i. Diuretic drugs that increase urinary output (for example, furosemide).

Diuretic drugs reduce the plasma volume, thereby lowering arterial blood pressure, by increasing urinary output. Salt and water that normally would have been retained in the plasma are excreted in the urine.