

Exam KEY

NROSCI/BIOSC 1070 and MSNBIO 2070

Exam # 1

September 30, 2016

Total POINTS: 100	20% of grade in class
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- 1) Patients with very low blood potassium levels are often given potassium chloride to take in pill form. However, the patients are counseled never to take an overdose of potassium chloride, as this can induce sudden death.
 - a) Discuss the mechanism through which a large dose of potassium leads to sudden death. **(6 points)**.

Hyperkalemia can result in paralysis of skeletal and cardiac muscle and severe arrhythmia. This is because the repolarization phase of the cardiac and muscle action potentials and autorhythmic cells depends on a K^+ efflux from cells. If extracellular K^+ rises suddenly, then this repolarization does not occur, blocking subsequent action potentials as the muscle and autorhythmic cells remain in a depolarized state.

- b) If a patient were to take an overdose of potassium chloride that was not fatal, what adverse effects would be apparent? **(4 points)**.

Muscle weakness and paralysis are the main indicators. Bradycardia and changes in the ECG are also apparent.

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- 2) a) Which heart valves are open just *before* the second heart sound (S2) occurs? **(3 points)**.

Aortic valve + pulmonic valve

- b) In a “normal” individual at rest, what is the approximate volume of blood in the left ventricle at the time the second heart sound occurs? **(3 points)**.

This is end systolic volume: ~65 ml.

- c) Which wave of the ECG precedes the occurrence of the second heart sound? **(2 points)**.

T wave

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- 3) Patients with narrowed cardiac arteries due to atherosclerosis sometimes experience chest pain, called angina, when they exert themselves. This is because they cannot produce adequate ATP to meet the metabolic needs of the myocardial cells. Discuss three distinct, commonly-used drug treatments that act on the heart and serve to diminish angina (by reducing myocardial oxygen demand). Please provide the mechanism through which each drug exerts its effects. **(9 points)**.

Treatment 1:

β 1 blocker: lowers HR and contractility by preventing NE & EPI from binding to autorhythmic and myocardial cells.

Treatment 2:

Ca²⁺ channel blocker: inhibits Ca²⁺ movement through L-type calcium channels, thereby prolonging cardiac action potentials and slowing the rate of action potential generation by autorhythmic cells.

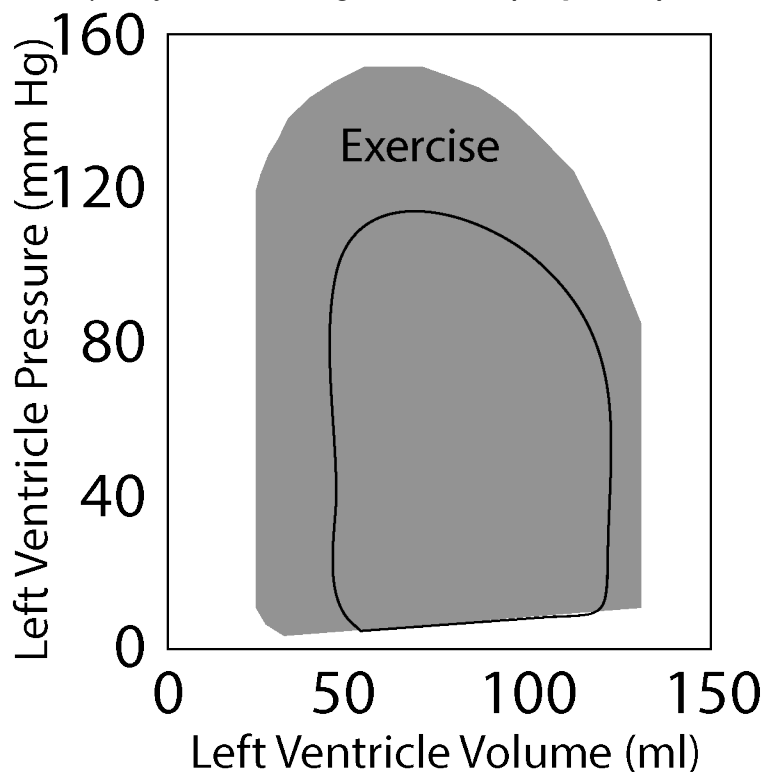
Treatment 3:

Nitroglycerine or similar drug that dilates the coronary vasculature via mimicking nitric oxide.

Note: any drug that lowers HR and contractility is acceptable, including Class 2-4 anti-arrhythmic drugs.

Exam KEY

- 4) A “standard” pressure-volume curve for an individual at rest is illustrated below. Show how the pressure-volume curve changes during exercise, and describe (*in words*) why these changes occur. **(12 points)**.



During exercise, there is greater preload, as more ventricular filling occurs during diastole. This greater filling is due to a variety of factors, including lower venous compliance, skeletal muscle pumping, and more negative intrathoracic pressure (as ventilation becomes deeper).

Afterload is slightly higher during exercise as mean arterial pressure increases. Thus, the aortic valve opens at a slightly higher pressure.

Due to enhanced contractility, pressure in the ventricle becomes very high during systole, as does systolic blood pressure. Since systolic blood pressure becomes so high, the aortic valve closes at a higher pressure (the ventricular pressure drops below aortic pressure earlier).

ESV is lower during exercise (due to increased contractility).

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- 5) Systemic filling pressure (P_{sf}) is an important factor in determining cardiac output. Describe the two principal mechanisms/factors that control P_{sf} , and briefly discuss how each of these mechanisms/factors alters P_{sf} . **(6 points)**.

Fluid volume: with more fluid in the vessels, more pressure is generated by fluid pressing against the vessel walls.

Sympathetic activity (venoconstriction or vasoconstriction also OK): this in effect diminishes the intravascular volume, so the fluid is in a smaller space, and generates more pressure by pressing against the walls.

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- 6) An individual has a mutation such that the isoform of myosin ATPase in their cardiac myocytes is replaced with an isoform similar to that in type FF skeletal muscle fibers. In the tables below, indicate how this mutation alters cardiac function in the individual, and briefly explain why. Assume that the mutation has no effect on ventricular size or stiffness. **(9 points)**.

Contractility	<i>Less with mutation</i>	<i>Same with mutation</i>	More with mutation
<p>WHY? There will be more shorting per unit time, and thus contractility is increased.</p>			

MVO₂	<i>Less with mutation</i>	<i>Same with mutation</i>	More with mutation
<p>WHY? There will be more cross bridge cycles per unit time, each requiring an ATP. Since the ATP is made aerobically, oxygen demand increases.</p>			

End Systolic Volume	Less with mutation	<i>Same with mutation</i>	<i>More with mutation</i>
<p>WHY? Since contractility is higher, less blood is left in the ventricle at the end of systole.</p>			

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- 7) Another individual has a mutation such that the isoform of titin in their ventricular myocytes is replaced by one that is much stiffer. Assume that no compensatory changes in ventricular radius or contractility occur following the mutation. What effect would this mutation have on stroke volume, and why does this effect occur? **(5 points)**.

Stroke volume is reduced. Since the ventricle is stiff, considerable pressure builds as blood enters the chamber. The pressure in the ventricle comes to equal that in the atrium very quickly, so there is no more filling, even if the mitral valve is still open.

- 8) You are treating a patient with a mutation resulting in the enzyme phenylethanolamine N-methyltransferase (PNMT) being dysfunctional. What effects would this mutation have on the patient's capacity to exercise? Briefly explain why the changes in exercise capacity occur. **(6 points)**.

A patient without PNMT cannot produce epinephrine, and thus the adrenal medulla releases 100% norepinephrine under sympathetic stimulation. Without epinephrine to bind to β_2 receptors, increases in muscle blood flow are diminished. There is also a limitation to increases in coronary blood flow. This diminished muscle blood flow impacts the ability to make ATP aerobically, and thus performance is limited. Also OK to say that muscles fatigue more easily.

Exam KEY

- 9) The following physiological parameters are determined for two individuals. Which has the highest myocardial oxygen demand? Provide a brief justification for your answer. **(5 points)**.

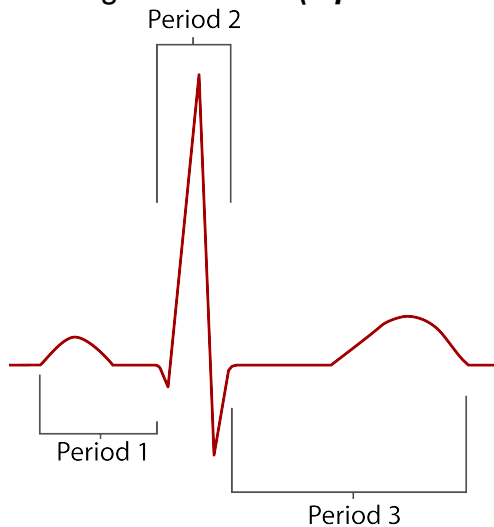
Individual 1	Individual 2
Systolic Pressure → 120 mmHg	Systolic Pressure → 100 mmHg
Diastolic Pressure → 80 mmHg	Diastolic Pressure → 75 mmHg
Heart Rate → 60 beats per minute	Heart Rate → 50 beats per minute
Cardiac output → 6 L/min	Cardiac output → 5.75 L/min

Answer: **Individual 1 has the highest oxygen demand.**

Justification: **The largest contributor to MVO_2 is afterload. Individual 1 has a much higher afterload (bp is higher, tpr is higher). In addition, there are more cardiac cycles per unit time, each requiring the same amount of oxygen.**

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- 10) A standard ECG waveform is provided below, with several “periods” demarked. Circle or underline the period in which an abnormal heart sound would occur during each of the following conditions: **(1 point each; 4 points total)**.



Mitral Valve Stenosis	Period 1	Period 2	Period 3
Mitral Valve Regurgitation	Period 1	Period 2	Period 3
Aortic Valve Stenosis	Period 1	Period 2	Period 3
Aortic Valve Regurgitation	Period 1	Period 2	Period 3

Note: for the second and third rows, indicating BOTH Period 2 and Period 3 is acceptable. However, Period 3 must be included.

Exam KEY

11) The drug hexamethonium completely suppresses both sympathetic and parasympathetic nervous system activity.

a) Describe how this drug must work to suppress the firing rate of both sympathetic and parasympathetic postganglionic neurons. **(3 points)**.

The only way of doing this is by blocking the nicotinic receptors in the autonomic ganglia (nicotinic antagonist).

b) Would administration of hexamethonium alter heart rate? If so, describe the changes in heart rate that would occur. **(3 points)**.

Yes! By eliminating both sympathetic and parasympathetic influences, HR would increase to the intrinsic firing rate of SA node cells, about 100/min.

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- 12) Which blood vessel type (*aorta, large artery, small artery, arteriole, capillary, venule, vein, vena cava*) contributes the most to producing total peripheral resistance in the cardiovascular system? Briefly describe the main property of these vessels that generates resistance to blood flow. **(5 points)**.

Arterioles; first vessels encountered with a small diameter, so friction is generated as blood moves through them.

- 13) In which blood vessel type (*aorta, large artery, small artery, arteriole, capillary, venule, vein, vena cava*) does systolic pressure appear to be highest? Why is systolic pressure highest in this vessel type? **(5 points)**.

Either large or small arteries is OK. Systolic pressure is higher there than in the aorta due to reflection of pressure waves at more distal branch points.

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14) A patient has extremely high levels of both thyroid hormones (thyroxine) and thyroid-stimulating hormone (TSH) in their bloodstream.

a) What is the most likely explanation for this imbalance in hormones? Provide a brief explanation for your answer. **(4 points).**

A TSH-secreting tumor (also OK if they say high TRH release). Feedback regulation is abnormal. Must be a TSH tumor, since both TSH and Thyroid Hormone are high.

b) Would it be feasible to measure blood levels of thyrotropin-releasing hormone to determine if overproduction of this hormone leads to high levels of thyroxine and TSH? Provide a brief explanation for your answer. **(3 points).**

No. Although TRH is in high levels in the hypothalamus-pituitary portal system, the levels in the venous blood are too low to detect.

c) Could an alternate test be done to determine if thyrotropin-releasing hormone levels are normal? What would you look for in such tests? **(3 points).**

Could assay prolactin levels, since TRH stimulates both prolactin and TSH release