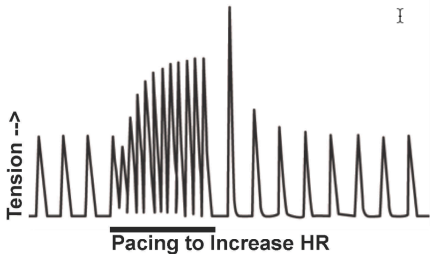
Exam KEY

NROSCI/BIOSC 1070 and MSNBIO 2070
Exam # 1
September 26, 2014

Total POINTS: 100 20% of grade in class

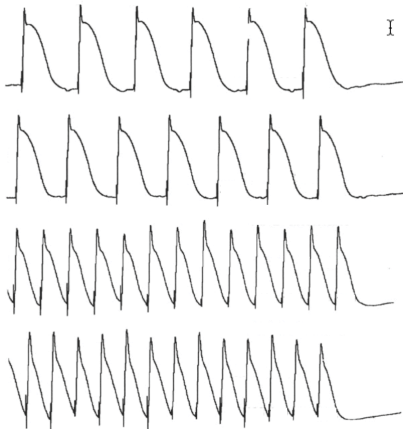
1) Heart cells are removed from an animal and placed into a tissue bath to keep them alive. Electrical stimulation of the heart muscle cells *(pacing)* induces their contraction.

a) When the rate of electrical stimulation of the heart cells increases by 10%, will the amount of shortening of the cells be altered? Discuss the physiological mechanism that accounts for your answer. ***(5 points).***



The amount of shortening increases due to the **Bowditch effect.** This is due to the impaired ability to remove Ca++ from the sarcoplasm. Some is removed at the cell surface by indirect active transport (1 Ca++ ion is exchanged for 3 Na+ ions; Na+ is normally low inside the cytoplasm due the actions of Na+/K+ ATPase). When contraction rates are high, the Na+/K+ ATPase is overwhelmed, and levels of Na+ climb in the cell near the plasma membrane. Thus, there is less driving force for indirect active transport, so intracellular Ca++ levels increase, but not to the point where contraction is induced. However, this additional Ca++ facilitates the contraction once an action potential occurs.

b) When the rate of electrical stimulation of the heart cells increases by 10%, will the cardiac action potential be altered? Discuss the physiological mechanism that accounts for your answer. ***(5 points).***



The cardiac action potential duration becomes shorter. The L-type Ca++ channel inactivates as a function of intracellular free Ca++ and membrane potential. Since the myocyte does a poorer job in eliminating Ca++ when heart rate is high, the persistent higher levels of calcium cause the channel to inactivate sooner.

Exam KEY

2) The following measurements are made for an individual:

Systemic vascular resistance = 20 mm L^{-1} min^{-1}
Heart rate = 100 beats/min
End diastolic volume = 150 ml
Systolic arterial pressure = 140 mmHg
Diastolic arterial pressure = 95mmHg
Right atrial pressure = 1 mmHg
Venous compliance is 16 times arterial compliance
Myocardial oxygen consumption is 35 ml/min

a) Determine the individual's ejection fraction; show your calculations. ***(8 points).***

Ejection Fraction (EF) = Stroke Volume (SV)/ End Diastolic Volume (EDV)

R=∆P/Q
20 mmHg/L/min =(MAP—1)/(SV*100)
MAP=(.67*95)+(.33*140)=109.85 mm Hg (round to 110 mm Hg)
∆P=(110-1)=109 mmHg

20 mmHg/L/min = 109 mmHg /(SV*100 beats/min)
SV*100= 109mmHg/20 mmHg/L/min
SV*100 beats/min=5.45 L/min
SV=.0545 L/beat or 54.5 ml/beat

EF=54.5/150
EF=0.36

Question Continues on the Next Page

b) Determine the individual's mean systemic filling pressure (P_{sf}); show your calculations. ***(7 points).***

$\Delta V_a = \Delta V_v$
$C_a = \Delta V_a / \Delta P_a$
$C_v = \Delta V_v / \Delta P_v$

$C_a \Delta P_a = C_v \Delta P_v$

$C_v = 16 C_a$

$C_a \Delta P_a = 16 C_a \Delta P_v$

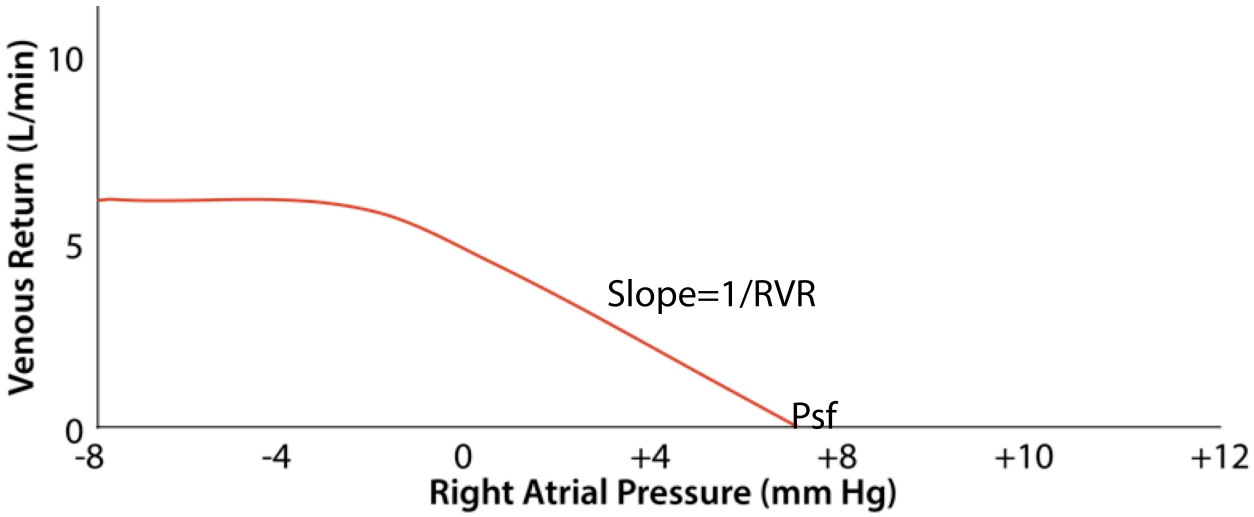
$\Delta P_a = 110 - X$
$\Delta P_v = X - 1$

$(110 - X) = 16(X - 1)$
$(110 - X) = (16X - 16)$
$126 = 17X$
$X = P_{sf} = 7.4$ mm Hg

Question Continues on the Next Page

c) The vascular function curve for a "normal" individual with the following cardiovascular parameters is plotted below. Plot (or indicate in words) how the vascular function curve would differ for the individual whose cardiovascular data are discussed above from this normal individual. ***(5 points).***

Mean arterial pressure = 102 mmHg
Central venous pressure=2 mm Hg
Cardiac output=5 L/min
Venous compliance=19 times arterial compliance



In this example:

$RVR=P_{sf}-P_v/Q$

Q = 5.45 L/min

RVR=(7.4-1) mmHg/5.45 L/min
RVR=1.17 mmHg/L/min

As calculated above,

P_{sf}= 7.4 mm Hg

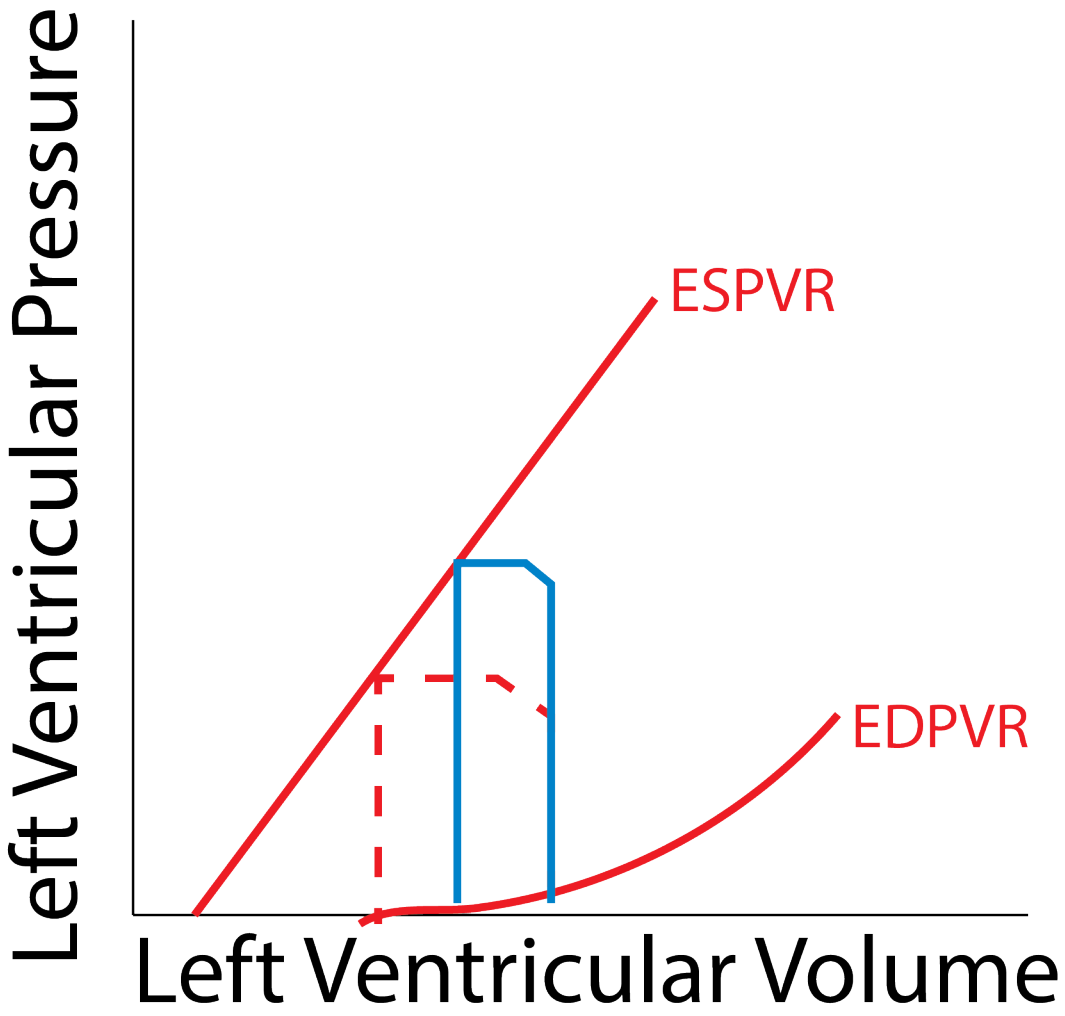
In a normal subject:

RVR = 1mmHg•min/L
P_{sf} = 7.4 mm Hg

Hence, the curves are virtually identical.

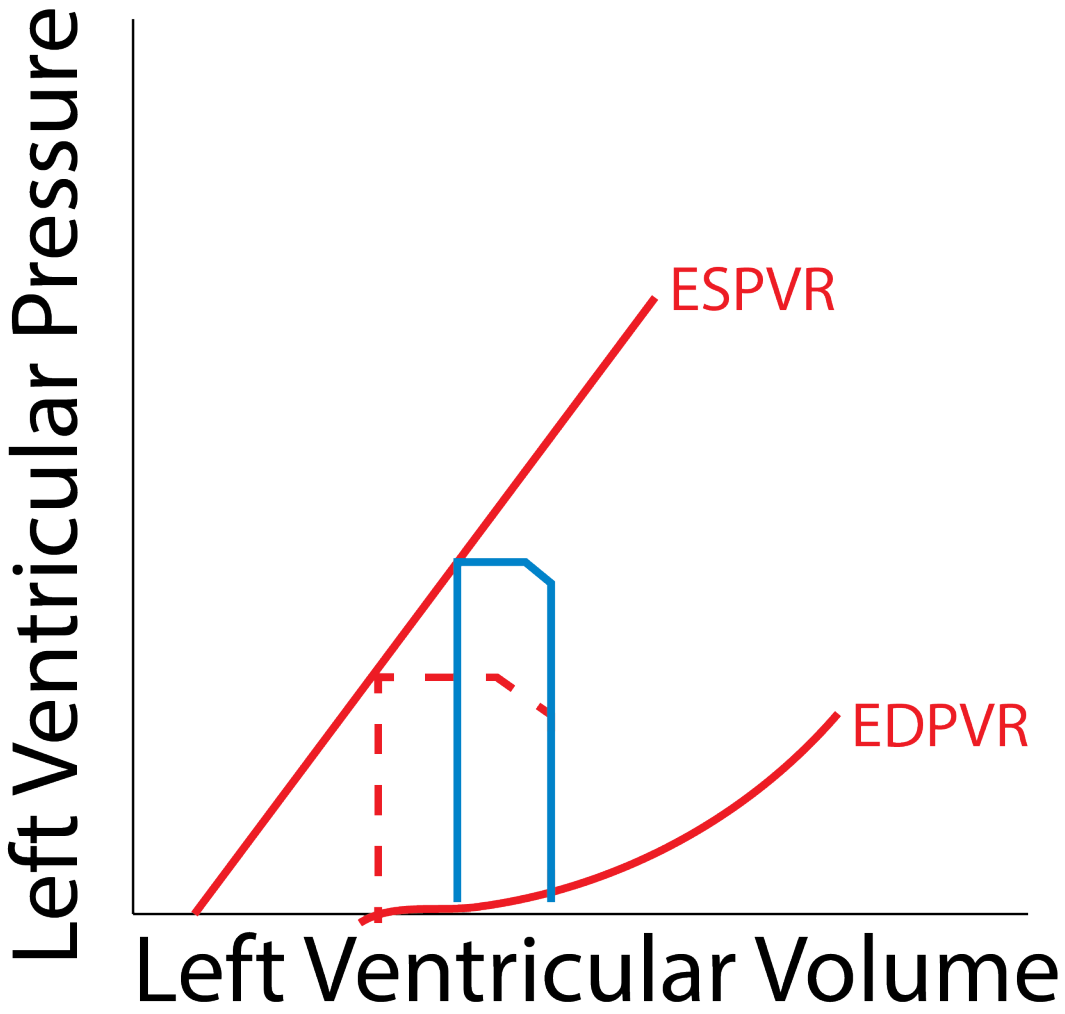
3) An unfortunate patient is diagnosed with severe aortic valve stenosis. As part of the evaluation of the patient a pressure-volume relationship is constructed for their left ventricle.

Dashed lines below show a normal pressure-volume relationship for the left ventricle. Draw the relationship differs in a patient with severe aortic valve stenosis. ***(5 points).***



4) An experimental animal is adrenalectomized (the adrenal glands are removed), and the nerves innervating the heart are cut. One week later, an experiment is conducted where the left ventricular pressure-volume relationship is monitored while an alpha-receptor agonist is injected intravenously.

Dashed lines below show a normal pressure-volume relationship for the left ventricle. Draw how the relationship differs in the experimental animal following injection of the alpha-receptor agonist. ***(5 points).***



5) Gonadotropin-releasing hormone (GnRH) antagonists are available, and are used to treat a variety of medical conditions.

a) Would GnRH antagonists serve as effective contraceptives (birth-control treatments) in women? Provide a brief justification for your answer. ***(5 points).***

Development of follicles and ovulation depends on the release of LH and FSH from the anterior pituitary. GnRH antagonists would completely block the release of these hormones, and thus would block ovulation. Hence, GnRH antagonists would be very effective contraceptives.

b) In fact, GnRH antagonists are rarely administered to reproductive age women because they are associated with an undesired side effect. Discuss the major side effect of administration of GnRH antagonists in reproductive age women. ***(5 points).***

Without the release of LH and FSH from the anterior pituitary, there will be no progesterone and estrogen release from the ovary. Thus, a woman taking a GnRH antagonist would have no circulating sex steroids, and thus would effectively be in menopause.

Most conventional contraceptives are a combination of progesterone and estrogen, which block the release of FSH and LH from the anterior pituitary via feedback inhibition. This prevents ovulation, but since the sex steroids are being administered, they are present in the bloodstream.

6) Generally in the body, blood flow is laminar. However, under some conditions laminar flow can be disrupted and become turbulent. When this occurs, blood does not flow linearly and smoothly in adjacent layers, but instead the flow can be described as being chaotic.

Turbulent flow can occur in large arteries at branch points. Provide the physiological rationale why branch points in large vessels can generate turbulent flow. ***(5 points).***

At branch points, there is a sudden increase in the diameter of the vessel (as it splits into two). Hence, there is a sudden increase in Reynolds number:

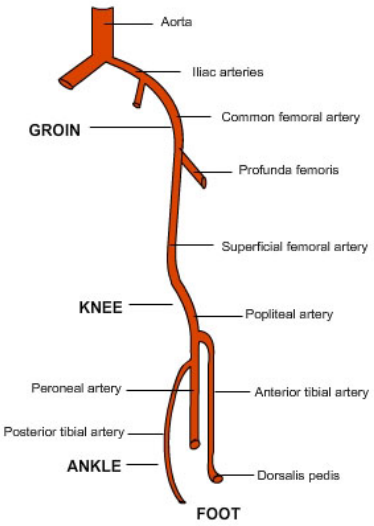
$$Re = dvD/\eta \ .$$

A high Reynolds number is correlated with turbulent blood flow.

Exam KEY

7) The femoral artery, a large artery in the leg, is a tributary (branch) of the aorta. The femoral artery has a much smaller diameter than the aorta.

Assuming that an individual is lying down (and there is no gravitational gradient between the aorta and femoral artery), would one vessel have a higher surface tension along the inner wall than the other? Provide a brief explanation for your answer. ***(5 points).***



The Law of Laplace describes surface tension in vessels:

$T=Pr$

The pressure in the aorta and femoral artery would be similar in this scenario, but the femoral artery has a much smaller radius. Thus, surface tension is higher in the aorta, which needs a thicker wall to sustain this surface tension.

8) During aging, a number of changes occur in the large arteries and veins. The changes alter the compliance of the vessels. The following questions relate to changes in blood vessel compliance that occur during aging.

a) Discuss how compliance changes in large arteries during aging. As part of your answer, indicate how these compliance changes affect arterial blood pressure. ***(7 points).***

Arterial compliance decreases during aging, and as a result pulse pressure increases: (pulse pressure ~ stroke volume/C)

The larger transients in pulse pressure in the elderly have been shown to be an important cardiovascular risk factor.

b) Discuss how compliance changes in large veins during aging. As part of your answer, discuss how these changes affect the ability of an older individual to maintain stable blood pressure. ***(8 points).***

Aging alters the structure of the vein wall, leading to an increase in compliance. This increase in compliance increases the tendency for blood to pool in the veins, thereby reducing venous return. As a result, the tendency for orthostatic hypotension to occur increases during aging.

9) Would a muscarinic receptor antagonist have any effect on the contraction of skeletal muscle? Provide a brief explanation for your answer. **(5 points).**

Skeletal muscle fibers have no muscarinic receptors, and thus muscarinic antagonists have no effects on them.

10) Would creatine phosphate levels be higher, lower, or the same in skeletal muscle following an intense bout of exercise than an rest? Provide a brief explanation for your answer. **(5 points).**

Creatine phosphate donates a high-energy phosphate to ADP, thus rapidly replenishing ATP in skeletal muscle cells. Thus, creatine phosphate levels are very low after exercise: the creatine phosphate has been converted to creatine.

11) In 1962, Sir James W. Black discovered propranolol, the first pharmacological treatment for hypertension. Propranolol blocks all beta-receptors, and produces a number of unwanted side effects. Today, selective beta-1 antagonists (such as metoprolol) are used as antihypertensive treatments, since most of the negative side effects of propranolol are avoided.

In the table below, indicate for each function the possible negative effect *(if any)* that might result in a patient taking propranolol, but not one taking metoprolol. ***(15 points).***

Vision	Binding of epinephrine to beta-2 receptors causes relaxation of the ciliary muscle (flattening the lens for far vision). Propranolol will block this effect, and thus far vision may be impaired.
Micturition	Binding of epinephrine to beta-2 receptors relaxes the smooth muscles in the bladder wall, to prevent micturition. This effect is blocked by propranolol, increasing the risk of urine leaking from the bladder.
Digestion	In general, the sympathetic nervous system inhibits gastrointestinal motility. Blocking these effects with propranolol can cause diarrhea, nausea, and vomiting
Skeletal muscle performance	Epinephrine binding to beta-2 receptors on skeletal causes increased contractility. Thus, blocking this effect with propranolol can decrease muscular performance.
Breathing	Epinephrine binding to beta-2 receptors in bronchial smooth muscle causes bronchodilation. Thus, blocking this effect with propranolol can increase airway resistance. This is particularly a problem in people with respiratory problems such s asthma.