

Instructor's Answer Key

Chapter 13: Heart and Circulation

Answers to Test Your Understanding of Concepts and Principles

1. During the resting period (diastole) of the heart, the fibers of the sinoatrial (SA) node region of the right atrium have unique channels that open in response to membrane *hyperpolarization* (approaching -60 mV) left over from the previous action potential. Since these channels (sometimes called HCN channels) are permeable to both Na^+ and K^+ , the predominate entry of Na^+ results in the net depolarization of these pacemaker cells producing spontaneous diastolic depolarization. Once threshold is reached, voltage-gated Ca^{2+} channels in the plasma membrane open resulting in the influx of Ca^{2+} that produces the upward phase of the action potential tracing and also results in contraction of these myocardial cells. After the spike, voltage-gated K^+ channels open and the outward diffusion of K^+ produces repolarization of the membranes that once again approach -60 mV with hyperpolarization that follows to repeat the cycle. The term “spontaneous” refers to the inherent property of myocardial pacemaker cells to beat automatically and on their own without the assistance of nerves or hormones. This property is known as *automaticity*. [Note: This question is also answered in the Student Study Guide.]
2. During diastole the cells of the SA node exhibit a slow spontaneous depolarization called the *pacemaker potential* or *diastolic depolarization*, that produce automatic action potentials as described in answer #1. Although other regions of the heart can potentially produce pacemaker potentials, their rate of spontaneous depolarization is slower than that of the SA node. Thus, other potentially excitable cardiac cells are depolarized by action potentials from the SA node before they can depolarize themselves. Action potentials spread from the SA node and from myocardial cell to myocardial cell through the gap junctions that connect them. In this way, action potentials will spread from the SA node through the atria and by means of conducting tissue, into the ventricles.
3. The contraction of the myocardium lasts about as long as the duration of its action potentials (250-300 ms). Since the myocardial cells are in a long absolute refractory period (followed by a shorter relative refractory period) while they produce action potentials, they must finish their action potentials, contract and relax before they can be stimulated again. As a result, the heart cannot be stimulated by successive action potentials. Summation of contractions is thus prevented, and the myocardium must relax after each contraction. This helps to ensure that the heart alternately contracts and relaxes; thus functions efficiently as a pump.

4. In diastole, pressure in the ventricles approaches 0 mmHg as they await the arrival of blood from the great veins and from the atrial systole. As ventricular systole begins, the intraventricular pressure rises, causing the AV valves to snap shut (creating the 1st heart sound). When ventricular pressures rise above pressures in the pulmonary artery (~ 25 mmHg) and the aorta (~ 80 mmHg), the semilunar valves are forced open and blood is ejected forcibly from the ventricles. With the contraction over, ventricular pressures start to fall. As pressures fall below the pressure in the aorta and pulmonary arteries, the back pressures cause the two semilunar valves to snap shut (creating the 2nd heart sound). Diastole begins as ventricular pressures return to 0 mmHg.
5. The answer is “no” to both questions. An ECG records and measures voltage changes produced by electrical conduction in the myocardium. Since the AV valves are not part of the pathway of electrical conduction, damage to them will not affect an ECG. Auscultation with a stethoscope will reveal vibrations produced by the mechanical action of the heart valves and resulting blood flow dynamics. Damaged AV valves will thus produce abnormal 1st heart sounds, but a partially damaged AV node—which conducts electrical current but does not participate in the mechanical action of the heartbeat—will not be evident by listening to the heart sounds.
6. The P wave is caused by depolarization of the atria; the QRS wave is caused by depolarization of the ventricles; and the T wave is caused by repolarization of the ventricles. The QRS wave occurs at the beginning of systole, and the T wave occurs at the beginning of diastole. The P wave occurs at the end of ventricular diastole (during atrial systole), just before the ventricles contract. The myocardium must first be depolarized electrically to contract mechanically; this is why the QRS wave is seen immediately before ventricular contraction when the AV valves close and the first heart sound is produced. The ventricles begin repolarization and relaxation after the period of depolarization and contraction; this explains why the second heart sound (caused by closing of the semilunar valves at the beginning of diastole) is heard when the T wave (ventricular repolarization) is seen in an ECG.
7. A cut in the skin initiates the intrinsic clotting pathway by exposing negatively charged collagen proteins to the blood plasma. Contact with these connective tissue proteins activates *Hageman factor* (factor XII) a protein-digesting enzyme, which initiates the intrinsic coagulation pathway. Damaged tissue cells may also release tissue *thromboplastin* (factor III), which starts the extrinsic clotting pathway. The extrinsic clotting pathway finishes first, because fewer steps are required to reach the common steps for both pathways where prothrombin is converted to active thrombin, which in turn converts fibrinogen to fibrin.
8. [Note: The **acid-base balance of the blood** section has been moved to chapter 16, but here is the answer anyway.] A fall in blood pH below 7.35 is called acidosis and a rise in blood pH above 7.45 is called alkalosis. Respiratory acidosis is caused by inadequate ventilation, which results in a rise in the plasma concentration of carbon dioxide, and thus carbonic acid, thereby lowering pH. Respiratory alkalosis by contrast, is caused by excessive ventilation, too little carbonic acid and a rise in pH. Metabolic acidosis can result from excessive production of nonvolatile acids, for example, as from excessive production of ketone bodies in uncontrolled diabetes mellitus. It can also result from a loss of bicarbonate. Metabolic alkalosis by contrast, could be caused by either too much bicarbonate or from inadequate nonvolatile acids.

9. Aspirin inhibits the cyclo-oxygenase enzyme associated with plasma membranes that catalyzes the conversion of arachidonic acid into prostaglandins, thereby inhibiting the platelet release reaction and the consequent formation of a platelet plug. Heparin, a mucoprotein, activates a plasma protein called antithrombin III, which combines with and inactivates thrombin. Coumarin drugs (dicumarol and warfarin) prevent blood clotting indirectly by competing with and inactivating vitamin K, thereby causing a vitamin K deficiency at the cellular level. EDTA and sodium citrate are chelating agents since they tightly bind to plasma Ca^{2+} and thereby prevent activation of the clotting pathways. Both EDTA and heparin are effective when added to test tubes while aspirin and coumarin drugs are not. This is because EDTA and heparin directly block events in the clotting cascades while aspirin and coumarin drugs act indirectly.
10. Blood moves through arteries, capillaries, and veins due to the pumping action of the heart and from higher pressures to lower pressures. Exercise can increase the strength of contraction of the heart, which will increase the flow of blood into the arterioles. Exercise also dilates the arteriole smooth muscle especially in skeletal muscle leading to greater flow through those tissue capillaries and veins before returning to the heart. Due to the extensive cross-sectional area of capillaries, blood flow through these vessels not only slows down but loses its pulsatile characteristics. Venous flow will continue quietly as laminar flow is silent.
11. Atherosclerosis usually begins with injury “fatty streaks” to the endothelium.. Then monocytes and lymphocytes move into the tunica intima, where monocytes are converted into macrophages that engulf lipids, becoming “foamy cells.” Progression of the disease involves a wide variety of cytokines and other paracrine regulators secreted from the endothelium and by other participating white blood cells. Smooth muscle cells then proliferate and become “synthetic” as they secrete extracellular matrix leading to the formation of localized fibrous plaques, or atheromas. Atheromas can protrude into the lumen of the artery where it can reduce blood flow and serve as a site for thrombus formation. Antioxidants may help reduce the progression of this disease by inhibiting the oxidization of LDL cholesterol that contributes to endothelial cell injury and other events in the progression of the disease. Atherosclerosis is promoted by inactivity, smoking, hypertension, high plasma cholesterol concentration, and diabetes. A regimen of exercise and diet (including one oily fish meal a week) can significantly lower blood cholesterol, which can then decrease the chances of atherosclerosis.

Answers to Test Your Ability to Analyze and Apply Your Knowledge

1. The recombinant cytokines that might be used prior to harvesting stem cells would include: *multipotent growth factor-1*, *interleukin-1*, and *interleukins-3* for general leucopoiesis. Specific cytokines would include: *granulocyte colony-stimulating factor* (G-CSF) and *granulocyte monocyte colony-stimulating factor* (GM-CSF). The former cytokine, G-CSF, acts in a highly specific manner to stimulate the development of neutrophils, whereas the latter cytokine, GM-CSF, stimulates the development of monocytes and eosinophils. Together, these two cytokines stimulate the bone marrow to release more stem cells for subsequent harvesting from the donor. Perhaps, injection of the cytokine, *thrombopoietin* would be useful in stimulating the proliferation of megakaryocytes and their maturation into platelets.

2. The patient's low RBC count (anemia) was due to the loss of blood into the digestive tract through a bleeding ulcer. Reticulocytes are derived from differentiating normoblasts cells after losing their nuclei during erythropoiesis in the bone marrow. Normally reticulocytes stay in the bone marrow for the first two days and then enter the circulation on the third day as mature erythrocytes. The high proportion of reticulocytes in the blood of this patient indicates the exaggerated homeostatic response of the body (especially the kidneys) to restore the loss of blood by secreting high levels of the hormone erythropoietin to stimulate erythropoiesis. The result is the abnormal acceleration of red blood cell production and the early release of immature reticulocytes into the blood stream.
3. The infusion of EDTA prevents both clotting pathways by chelating or binding to calcium ion, which is given the title of *factor IV*. EDTA directly blocks the extrinsic pathway by binding the Ca^{2+} that serves as a cofactor for the conversion of factor VII to factor X; and similarly blocks the intrinsic pathway by interrupting the conversion of factor IX to factor X. Furthermore, the activation of factor X and subsequent conversion of prothrombin to thrombin along the common clotting pathway is inhibited in the absence of calcium ion. Aspirin by contrast, exerts its effects on the blood platelets and has no direct effect on the blood-clotting cascade. Aspirin retards clotting by inhibiting the cyclooxygenase enzyme that catalyzes the conversion of arachidonic acid into the prostaglandins responsible for the platelet release reaction and therefore, slows the formation of platelet plugs.
4. Since the upper limit of normal for the PR interval is 0.20 seconds, this student's PR interval of 0.24 seconds indicates first-degree AV node block. Her subsequent second and third ECG strip readings indicate perhaps second-degree AV node block as the PR interval becomes progressively longer and longer, leading to a "dropped" QRS complex. Further analysis of the ECG strip can then show a normal pattern until the AV node conduction damage reappears, the PR interval lengthens and another QRS is dropped once again.
5. Typically yes, because the septal defect in the heart wall of a two year-old baby, like that of the newborn, interferes with the circulation of deoxygenated blood from the right heart to the lungs. As venous blood from the vena cavae returns to the right side of the heart, some deoxygenated blood can be abnormally shunted through the defect to the left side without routing as usual through the pulmonary circulation. If this shunted blood volume is great enough the blood pumped out the aorta will be not be fully oxygenated and will cause the visible bluish coloration (cyanosis) in capillaries of the skin. However, since left heart pressures are normally higher than right heart pressures, the actual volume of deoxygenated blood that shunts to the left side of the heart may be minimal and a child may live for two years with this defect without symptoms. With this type of less severe septal defect the child may not show cyanosis.