1. a. When you stand, the weight of the blood throughout the body (the “hydrostatic head”) pushes on the blood in your feet and ankles. This pressure head will increase the filtration of fluid through the walls of the capillaries in your feet and ankles, as described by the Starling equation.

b. Lymphatic fluid is propelled through the lymph vessels by contraction of skeletal muscles. If you walked all day, the muscle pump would push lymph fluid out of your feet and ankles and back toward the heart, reducing the swelling. But the best way to reduce the swelling is to put your feet above your heart, reversing the hydrostatic head and encouraging draining of lymph fluid into the thoracic duct.

2. a. Fluid transfer = $k[(P_{\text{cap}} - P_{\text{int}}) - (\pi_{\text{cap}} - \pi_{\text{int}})]$

   From the graph, at the arterial end of the capillary, $P_{\text{cap}} = 30$ mmHg. $P_{\text{int}}$ is very close to 0 under all normal circumstances. Therefore, across the arterial end of the capillary, the net fluid transfer = $k[30 - 0 - 25 + 15] = 20k$.

   A positive value indicates net transfer out of the capillary.

   From the graph, at the venous end of the capillary, $P_{\text{cap}} = 10$ mmHg. Therefore, at the venous end, net fluid transfer = $k[10 - 0 - 25 + 15] = 0k$.

   (Note: A negative value would have indicated net transfer into the capillary.)

   Hydrostatic pressure is assumed to drop linearly along the length of the capillary, so the net transfer would look like this:

   ![Graph showing net filtration out of the capillary](image)

   This graph shows that there is net filtration out of this capillary all along its length, so some volume will be lost to the tissues as the blood moves along the capillary.

b. Fluid transfer = $k[(P_{\text{cap}} - P_{\text{int}}) - (\pi_{\text{cap}} - \pi_{\text{int}})]$

   At the arterial end of the capillaries, net fluid transfer = $k[30 - 0 - 10 + 2] = 22k$.

   At the venous end of the capillaries, net fluid transfer = $k[10 - 0 - 10 + 2] = 2k$. 
All along the capillaries there will be a net filtration of fluid, and less volume of blood will enter the venules than entered the capillaries.

c. From the calculation of part b above, you would predict that starvation would be accompanied by tissue edema. Remember the pictures of children in famine-plagued parts of the world; they have spindly, matchstick arms and legs and swollen bellies. The swollen abdomen is caused by a build-up of fluid that has moved out of the capillaries in the abdominal cavity.

d. Fluid transfer = k[(P_{cap} - P_{int}) - (\pi_{cap} - \pi_{int})]

If the arterial pressure increased by 20%, the blood pressure at the arterial and venous ends of the capillaries might be expected to be 36 and 12 mm Hg. Then at the arterial end,

$$\text{net fluid transfer} = k[36 - 0 - 25 + 15] = 26 k.$$  

At the venous end,

$$\text{net fluid transfer} = k[12 - 0 - 25 + 15] = 2 k.$$  

There is no point along this capillary at which fluid is reabsorbed. Therefore, all along the capillary there is net filtration into the tissues.

[In clinical practice tissue edema often accompanies systemic hypertension.]

e. At the arterial end of the pulmonary capillaries,

$$\text{net fluid transfer} = k[10 - 0 - 25 + 15] = 0 k.$$  

At the venous end,

$$\text{net fluid transfer} = k[4 - 0 - 25 + 15] = -6 k.$$  

Diagramatically:
All along these capillaries the net fluid transfer is from the interstitial spaces into the capillaries and there is a net uptake of fluid. You would predict that the volume of blood entering the pulmonary venules would be larger than the volume entering the capillaries.

[This mechanism serves to keep fluid from accumulating along the linings of the lungs.]

3 a. Glucose will be in higher concentration in plasma than in the extracellular fluid (ECF) around muscle cells, and it is likely that net fluid transfer will also be outward at the arterial end of muscle capillaries. Therefore, both diffusion and net fluid transfer will carry glucose out of the capillary and into the tissues.

b. O2 diffuses readily across capillary walls, and the O2 concentration is likely to be higher in blood within the arterial end of a skin capillary than it is in the tissues. (Arterial blood is oxygenated.) As a result, O2 will diffuse out of the capillary and into the tissues. Net fluid flow is also likely to be out of the arterial end of these capillaries, but it does not play a significant role in distributing O2.

c. Assuming the cake has been digested and the breakdown products (including glucose) are still in the intestine, glucose is at a higher concentration in the interstitial fluid of the gut than in the capillaries. Therefore, diffusion will drive glucose into the capillary from the interstitial fluid, so there would be a net uptake of glucose into blood flowing through the capillaries of the gut.

d. O2 will be in higher concentration in the fluid surrounding pulmonary capillaries than it is in the blood at the arterial end of these capillaries. Therefore, O2 will diffuse into the blood flowing through these capillaries. Net fluid flow also tends to be into pulmonary capillaries, but this flow is unlikely to be important in the transfer of O2 into the capillaries.

e. CO2 is produced in the tissues as a product of oxidative metabolism. It will, therefore, be more concentrated in the tissues than it is in the blood. Diffusion will move CO2 out of the tissues and into the blood at the arterial end of kidney capillaries.

f. Skin capillaries have conventional filtration/uptake profiles, with filtration at the arterial end and uptake at the venous end of the capillaries. There is, therefore, likely to be net transfer of water out of the arterial ends of capillaries in the skin.

g. Under normal conditions, the reflection coefficient for serum albumen in capillaries is high, and little or no albumen will be transferred across capillary walls.

h. CO2 will be more concentrated in the blood within the arterial end of pulmonary capillaries than it is in the fluid surrounding the capillaries. Therefore, diffusion will move CO2 out of the capillaries and into the interstitial fluids.

[Notice that CO2 will move out of the capillary, even though net fluid movement is into lung capillaries. This is a good example of the fact that, in most capillaries, diffusion is far more important in determining the movement of most dissolved substances than is net fluid movement.]

4. a. When skeletal muscle contracts, it squeezes the veins running through the muscle. Veins contain valves that prevent back-flow of the blood, so muscle contraction pushes venous blood back toward the heart. This effect has been called "the muscle pump."

b. When skeletal muscles contracts actively, the pressure that they produce on the veins pushes some of this blood back to the heart, increasing the venous return.

c. The stroke volume is the amount of blood ejected from a ventricle in a single contraction.

d. Increased venous return will mildly stretch the ventricular fibers, and this increased stretch will cause an increase in the vigor of ventricular contraction (Starling Law). As a result, the stroke
volume will increase. (PLEASE NOTICE: The correct answer to "why?" in this question describes the mechanism behind the change, not “because it is good for the body”!)

e. The increase in contractility of the heart will cause the heart to empty more completely, increasing the stroke volume.
f. Even if the atria were disabled, increased venous return would still increase the ventricular stroke volume because increased venous return would stretch the ventricular fibers. (Most of the blood ejected from the ventricles entered before the atria contract.)

5. At rest, in 25 minutes, your heart will pump:

\[70 \text{ ml/beat} \times 60 \text{ beats/min} \times 25 \text{ min} = 105 \text{ liters}\]

During exercise, your heart ejects 90% of its end-diastolic volume with each beat, which amounts to

\[160 \times 0.9 = 144 \text{ ml/beat}\]

In 25 minutes, your heart pumps:

\[144 \text{ ml/beat} \times 165 \text{ beats/min} \times 25 \text{ min} = 594.0 \text{ liters}\]

This shows that your heart pumps almost 6 times as much blood during this vigorous exercise as it does when you are being a couch potato.

6. When you are lying down, the pressures in your head and in your feet are about equal, and both are equal to the pressures in the aorta. When you stand up, gravity pulls blood away from your head and toward your feet. Thus the average blood pressure in the head will drop, while at the same time the blood pressure in the legs and feet rises.

[NOTE: Regulatory mechanisms cause the heart to generate enough pressure to counteract the hydrostatic forces pulling blood away from the head. If these mechanisms are sluggish or incapacitated, the blood supply to the brain becomes insufficient and the person faints.]

7. a. Hanging upside down will reverse the usual hydrostatic forces acting on the circulation, so the pressure in your calf blood vessels would decrease relative to standing up or lying down.

b. Being upside down will increase the hydrostatic pressure measured by the baroreceptors in the aortic arch and the carotid sinus, which will trigger reflex responses that slow the heart and reduce the overall blood pressure. The blood pressure in your calves will already be reduced because of the hydrostatic head that tends to drain blood downward, and it will be reduced even more as a result of the baroreceptor reflexes.

[Our cardiovascular systems did not evolve to maintain constant blood pressure in our feet while we hang upside down, and they do a bad job of it. The arrangement of receptors does, however, effectively monitor blood flow to the brain in our usual upright posture.]

c. In 0 G, changing your body position would not change affect the distribution of blood, so the baroreceptors would not be affected by hanging “upside down”.

8. Because all of the baroreceptors are located either in the aortic arches or in the carotid sinuses, the input to all regulatory reflex loops comes only from those two locations. Thus, regulation of cardiovascular output occurs in response to changes in the amount of blood leaving the left ventricle and changes in the amount of blood going to the head (i.e., the brain). If the blood supply to parts of the body other than the head becomes compromised, there is no reflex response to bring it back to normal.

9. a. Anaphylaxis opens a very large volume of capillary beds, which greatly reduces peripheral resistance and therefore reduces diastolic pressure. It also reduces venous return to the heart, reducing the amount of blood pumped with each contraction. A low stroke volume reduces pulse pressure. Low diastolic pressure, coupled with a low pulse pressure, produces a very low systolic
pressure. This type of circulatory shock leads rapidly to fainting, because low pressures may make it impossible to send blood to the head against the hydrostatic pressure that exists between the head and the heart of a person who is standing up. As a result, the delivery of blood to the brain can be seriously compromised. [Even with the victim horizontal, however, death can ensue due to blockage of the airways and other problems.]

[NOTE: Anaphylactic shock is treated by laying the victim horizontal. This places the brain at the same level as the heart, thus reducing the amount of energy required to get blood to the brain [actually someone with anaphalaxis will probably collapse rapidly; you don't have to lay them down, just catch them!] and by injecting epinephrine, which causes vasoconstriction and increased cardiac output, which would increase the blood flow to the brain.

b. The sympathetic nervous system will increase vasoconstriction in most of your arterioles, therefore increasing peripheral resistance and raising diastolic blood pressure. It will also increase cardiac contractility, increasing the pulse pressure. Increased pulse pressure added on top of increased diastolic blood pressure will lead to an increased systolic pressure. The sympathetic nervous system will also increase your heart rate, which would further increase both systolic and pulse pressure.

10. a. (1) The plasma will rapidly become diluted (within minutes), so it will have a lower osmolarity than either the interstitial fluid or the intracellular fluid. As a result, water will move from the plasma into the interstitial fluid and from the interstitial fluid into the cells.

(2) The volume of all three compartments will rise and their final osmolarity will be lower. [Note that the time required for equilibration between the interstitial fluid and the intracellular compartment may be so long that water excretion may reduce the volume loading before the intracellular compartment can come into equilibrium with the other two compartments.]

(3) Water equilibration between the plasma and the interstitial fluid is tens of minutes; complete equilibration of water between interstitial fluid and intracellular fluid takes a comparable time.

b. (1) This iso-osmotic fluid will be absorbed from the gut into the intestinal capillaries, so the volume of the plasma will expand. There will be some movement of fluid from the plasma into the interstitial fluid compartment because the increased plasma volume will increase blood pressure, increasing the hydrostatic pressure driving fluid out of capillaries and into the interstitial fluid. Thus, the volumes of both the plasma and the interstitial fluid will expand. There will be no force that would lead to a change in the volume or osmolarity of the cellular compartment, so the cellular compartment will stay constant.

(2) The osmolarity of the plasma will not change, so the osmolarity of the interstitial and intracellular compartments will also remain the same. The volumes of the plasma and interstitial fluid will be higher than normal at equilibrium, but the intracellular will not change.

(3) Equilibrium between the plasma and the interstitial fluid will be reached within 10 - 30 minutes.

c. (1) This is a combination of salt and volume loading. The plasma compartment will initially expand because the salt water will move into the plasma. Because body fluids are about 300 mOsm, sea water is more than 3 times more concentrated than body fluids, so the expanded plasma compartment will also be more concentrated than the rest of the body fluids. Therefore, water will move from the interstitial fluid into the plasma, leaving the interstitial fluid more concentrated and leading to the movement of water out of cells and into the interstitial fluid. As a result, the plasma compartment will initially expand due to the water ingested and to water that was pulled from the interstitial compartment and (indirectly) from the cells. At the same time that water is moving, salt will follow its concentration gradient and move into the interstitial fluid, increasing its solute content. The major solute in sea water is NaCl, which will not enter the cells. So at equilibrium, the cellular compartment will be smaller, because it will have lost water, and the
plasma and interstitial fluid will compartments will both be larger. All three compartments will be at the same concentration, which will be greater than normal.

(2) The volume of the interstitial compartment will increase at the expense of the volume of the cellular compartment. The plasma compartment will be expanded by even more than the volume of water that you drank, because of water moving out of the cells.

(3) Water and salt will equilibrate between the plasma and the interstitial fluid in 10-30 minutes. Water will equilibrate between the cells and the other two compartments over hours. One of the net effects of drinking this amount of sea water is a very uncomfortable edema, due to volume expansion of the interstitial compartment.

d. (1) Beer is hypo-osmotic to plasma, so the plasma becomes diluted. As a result, water will move from the plasma into the interstitial compartment and from there into cells.

(2) The volume of the plasma will expand, as will the volume of the interstitial compartment. The osmolarity will be reduced in all compartments. [If you avoid eating lots of salty chips or peanuts with your beer, excretion will probably get rid of the volume expansion before enough time has elapsed for osmotic equilibration between the plasma and the intracellular compartment.]

(3) As in (a), water equilibrates between the plasma and interstitial fluid in tens of minutes, and water equilibration between interstitial fluid and intracellular fluid takes several hours.

In fact, drinking beer eventually leads to a net loss of body water, because the alcohol in beer stimulates the excretion of water more than it stimulates the excretion of solute. Thus, ingesting alcohol leads to a net dehydration over several hours and produces a reduction in the volume and an increase in the osmolarity of the fluid compartments. One hypothesis concerning the etiology of a hangover is that cells become dehydrated as a result of this net loss of water and this dehydration produces the malaise.

11. a. The cytoplasm of red blood cells (RBCs) is about 300 mOsm, with the same mix of ions and proteins found in other cells. Initially the glycerol solution is isotonic to the RBCs even though the solutes inside the cell are different from the solutes outside of the cell. However, the cell membrane is permeable to glycerol, and there is no glycerol in the cell. Following its concentration gradient, glycerol will enter the cell, but when that happens, there will now be more solute inside the cell than outside and, as a result, the cell will be hyper-osmotic to the external solution, and water will enter the cell. At the same time, some K+ and Cl− may move out of the cell, following their concentration gradient. Because permeating ions make up only part of the osmotically active solute inside the cell, while glycerol makes up the entire osmotically active solute outside of the cell, glycerol entering the cell will eventually add more and more solute to the interior of the cell, drawing in more and more water, causing the cell to swell and finally to burst. So, although this glycerol solution is iso-osmotic to the RBC cytoplasm, it is hypotonic, because it caused the cells to swell and burst.

[NOTE: the assumption in this problem that the osmolarity of the external solution was not changed by the solute movements, even though the intracellular osmolarity was changed. This would be true if the volume of the solution were so much larger than the intracellular volume that the solute and water movements do not change the concentrations of the external solution even though they have very dramatic results on the intracellular solution. To be answerable unambiguously, this problem should have told you the relative volumes of the blood sample and the solution.]

b. The sucrose solution, like the above glycerol solution, is initially iso-osmotic to the RBCs. However, there are several concentration gradients to consider here. There is a concentration gradient driving sucrose into the cells, because there is no sucrose in RBCs and there are 300 mOsmoles of it outside per liter of solution. But sucrose is too large to enter cells. In contrast, there are organic ions and molecules along with inorganic ions (such as K+ and Cl−) inside the cell, and none of these solutes outside of the cell. At least some of the inorganic ions can move across the plasma
membrane, and the sucrose outside of the cell cannot move in to compensate. As a result, there will be a net movement of osmotically active particles out of the cell and into the surrounding fluid. When the solutes leave the cell, following their concentration gradients, they will leave the inside of the cell less osmotically concentrated, producing a driving force on water to move outside of the cell. As water leaves, the cells will shrink. Thus, this iso-osmotic solution of sucrose was hypertonic to the cytoplasm of the cells. [The loss of ions from the cell is quite slow, so that it takes many minutes for the cells to show any shrinkage.]

[NOTICE again the assumption that the volume outside of the cells is so large that when K⁺ or Cl⁻ move out of the cell, they don't significantly modify the properties of the outside solution.]

12.a. Proteins contribute heavily to the osmotically active solute in the intracellular compartment. Plasma proteins like serum albumen are important in regulating plasma volume and supply osmotic activity to counteract the hydrostatic pressure in capillaries, but they make up a relatively small fraction of the total solute in plasma. [They play such an important role in controlling the movement of fluid out of capillaries because, unlike most of the other solutes in the plasma, they cannot move out of the capillaries.]

b. Under normal conditions, all three compartments are in osmotic equilibrium, so they have exactly the same osmolarity.

c. The intracellular compartment is the main storage site for K⁺, because it has the highest K⁺ concentration and is the largest fluid compartment.

d. Infusing iso-osmotic NaCl into the blood stream would have no effect on intracellular volume, because Na⁺ cannot enter cells (so no extra solute would enter the cells) and there would be no driving force on water to move into the cells. It would increase the volume of the extracellular volumes, both the plasma and the interstitial fluid.

[An “intravenous drip” of isotonic saline—NaCl at 150 mM—is often used on patients who are having trouble eating or drinking as a way to maintain their plasma volume.]

e. Infusion of an iso-osmotic glucose solution might increase the intracellular volume, depending upon how the glucose was handled by the cells. Glucose is transported into cells, even against a concentration gradient. (1) If glucose moves into cells and is stored as glycogen or glucose, it will increase the total amount of solute in the cells, drawing water in with it and maintaining osmotic equilibrium. The result would be an expansion of the intracellular compartment. (2) If the glucose were metabolized immediately to CO₂ and H₂O, however, these two substances would rapidly equilibrate across the plasma membrane, there would be no net increase in the amount of solute in the cells, and there would be no net increase in the intracellular compartment as a result.

13. a. You would want a marker molecule that is held within the circulatory system, so you would choose Evans blue, which binds to proteins too large to pass through normal capillary walls.

b. The sample just needs to be big enough for you to analyze. If you could analyze 1 ml, that would be fine; it is the concentration of the marker that is important.

c. You injected 50 ml of a 1 molar solution, or 50 mMoles of Evans blue (0.050 moles is equal to 50 mMoles). After equilibration, you determined that there was a concentration of 23 mMoles/l. Therefore:

\[
\text{the volume of plasma} = \frac{\text{quantity}}{\text{concentration}} = \frac{50\text{mMoles}}{23\text{mMoles per liter}} = 2.17 \text{ liters.}
\]

Remembering that this is just the plasma volume, you realize that you need to convert this number to the volume of whole blood in order to know whether the person has lost blood. You would need to measure the hematocrit in order to figure out how much whole blood this plasma volume corresponds to. You weren't told the hematocrit in this problem, but 50% is a good guess. That would mean that
the person has 4.34 liters of whole blood. This volume is slightly under the normal volume of 5 liters, so you might suspect some slight blood loss, but 5 liters is an average number and lacking baseline data on this individual it would be difficult for you to decide for sure whether the person has lost blood.

d. Inulin can move freely across most capillary walls and would, therefore, equilibrate in both the plasma and the interstitial fluid. Therefore, inulin would allow you to measure the entire extracellular volume.