READ THIS PAGE BEFORE YOU BEGIN THE EXAM.

1. Write your name on every page, in both packets of stapled-together pages. (5 points off for EACH unnamed page.)

2. Do NOT write on the BACK of any page unless you get a TA’s permission FIRST.

3. About writing answers:
   - All questions can be answered briefly.
   - For full credit, discuss mechanisms.
   - In problems asking for an answer and a reason, more credit is given for a correct reason.

4. Use a pen or pencil to write your answers, but do NOT use RED INK and DO NOT USE WHITE-OUT of any kind. However, if you use pencil, you cannot request a regrade.

5. All answers should be on pages in this packet. (Anything written on pages in the packet of multiple-choice questions will not be graded.)

6. Before you leave the testing room, turn in both packets of stapled-together pages.

POTENTIALLY USEFUL EQUATIONS:

\[ \pi = \sigma RT(C_a - C_i) \]
\[ F = \Delta V \Sigma \Delta X \]
\[ C_s = \frac{[S]_u}{[S]_p} \cdot \sqrt{V_u} \]
\[ R = \frac{8 \eta l}{\pi r^4} \]
\[ J = k[(P_{cap} + \pi_{int}) - (P_{int} + \pi_{cap})] \]
\[ V_m = \frac{G_{Na}}{\Sigma G} E_{Na} + \frac{G_{K}}{\Sigma G} E_{K} + \frac{G_{Cl}}{\Sigma G} E_{Cl} \]
\[ I_Y = G_Y (V_m - E_Y) \]
\[ I_{total} = \Sigma \{G_j [V_m - E_j]\} \]
\[ J = -PS(C_{out} - C_{in}) \]
\[ E = mc^2 \]

\[ \frac{1}{R_{Total}} = \Sigma \frac{1}{R_i} \]
\[ E_x = \frac{RT \ln ([X^+]_{out})}{ZF} \]

concentration = \frac{quantity}{volume}

\[ I_X = G_X (V_m - E_X) \]
\[ V = \frac{Q}{A} \]
\[ P = QR \]
\[ R_{Total} = \Sigma R_i \]
\[ R_{Total} = \Sigma R_i \]
\[ I_X = G_X (V_m - E_X) \]
\[ A = \pi r^2 \]
\[ V = IR \]

WAIVER: By signing this waiver I give permission that this exam can be left for me to pick up in the hall outside the elevators on the third floor of Pacific Hall. I realize that this procedure may expose my grade to public scrutiny and my exam to theft. If I do not sign this waiver, I understand I will be able to get my graded exam back only as described on the course Web site.

______________________________  ______________________
Signature  Date
Multiple choice answers:

<table>
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<tr>
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Scores and grade:

Final: MT1 __________
Final: MT2 __________
Final: New __________
Final: Total __________
Midterm 1 __________
Midterm 2 __________
Grand Total __________
Course Grade __________
1. (20 points total) Edema is swelling of the body—often the arms or legs—caused by increased levels of interstitial fluid. Edema is a condition, not a disease state: it can have many different causes.

For each of the causes of edema listed below, briefly explain the major physiological mechanism that causes it.

A. (5 points) Eating too much salt.

The ingested salt is taken up through the intestines into the plasma, making the plasma hyper-osmotic compared to normal. The plasma and interstitial fluid mix, as the plasma filters across the capillary walls in the near half of the capillaries, then returns in the far half. This mixing dilutes the plasma somewhat, but it remains hyper-osmotic, as does the interstitial fluid. The hyper-osmotic interstitial fluid draws fluid out of the cells into the extracellular fluid (water is in higher concentration inside the cells), which increases the volume of both the plasma and the interstitial fluid. The increased volume of the interstitial fluid is the edema.

B. (5 points) Sunburn (which damages the capillary wall cells, allowing leakage of large molecules).

Normally, the hydrostatic pressure driving fluid out of the capillaries along the capillary bed is just balanced by the oncotic pressure pulling fluid back into the capillaries. Normally, the oncotic pressure is high because there are proteins in the plasma but none in the interstitial fluid. When the capillary walls are damaged in sunburn, proteins leak into the interstitial fluid, lowering the oncotic pressure difference. (In the extreme, the plasma proteins equilibrate between the plasma and interstitial fluid; in this case, the oncotic pressure is zero.) Lowering the oncotic pressure tips the balance in favor of fluid leaving the capillaries into the interstitial fluid, so the volume of the interstitial increases; this is edema.

C. (5 points) Failure of the valves in the veins of the legs.

The "muscle pump" in the legs helps to move blood along the veins back to the heart. Contractions of leg muscles squeeze the leg veins. Normally, this pushes blood toward the heart because the valves close in the veins on the side of the side of the contraction away from the heart, which prevents backward flow of the blood. If the valves do not close (this is what is meant by "failure"), the blood is forced backward into the veins. This builds up the hydrostatic pressure in the capillaries, so that more fluid comes out of the capillaries. Because there is no change in the oncotic pressure, excess fluid comes out of the capillaries in the legs; this is edema.

D. (5 points) Right heart failure.

When the muscles in the right ventricle weaken (this is what is meant by "right heart failure"), the right heart cannot pump all of the blood volume returning to it from the systemic system, so the blood backs up in the systemic vessels. This increases the pressure in the systemic veins, which builds up the hydrostatic pressure in the capillaries, so that more fluid comes out of the capillaries. Because there is no change in the oncotic pressure, excess fluid comes out of the capillaries into the interstitial fluid in the whole systemic system; this is edema.
2. (20 points total) Hyperosmotic laxatives cause diarrhea by drawing water from the bloodstream into the colon, which is then expelled from the body through the anus. The loss of water from the bloodstream increases the osmolarity of the plasma.

A. (8 points) Describe what happens to the volume and osmolarity of the other two body fluid compartments as a result of this hyperosmotic diarrhea, before there is any compensation by kidney mechanisms.

The loss of water from the plasma increases its osmolarity and decreases its volume. This hyper-osmotic fluid mixes with the interstitial fluid, across the capillary walls, so the interstitial fluid also loses some volume to the plasma and becomes more concentrated. The hyper-osmotic interstitial fluid causes water to move out of cells (rather than ions moving into the cells, because water moves across membranes faster than ions). At equilibrium, all three body fluid compartments would have a lower volume and a higher osmolarity. [NOTE: In all compartments, the volume would be decreased by the same percentage, and the osmolarity would be equal.]

B. (4 points) Is the release of ADH triggered by hyperosmotic diarrhea? Briefly explain.

Yes. The osmoreceptors in the hypothalamus would be activated by the increased osmolarity of the plasma, which triggers ADH release. [If the decrease in blood volume is sufficiently great, the blood pressure could decrease enough to slow the activity of the baroreceptors, which would also signal the release of ADH.]

C. (4 points) Would ADH help to reverse the changes in the body fluid volumes caused by hyperosmotic diarrhea? Explain your answer.

The ADH would minimize the loss of water through the kidney by increasing the permeability of the collecting ducts to water, so that as much water as possible would move out of the nephrons and, ultimately, back into the plasma. By forming a highly concentrated urine, excess salt would be lost, which would bring the osmolarity back toward normal levels. This mechanism does not, however, replace the water lost in the diarrhea; it can only minimize the loss of any additional water in the urine. Therefore, all three body fluid volumes would remain lower than normal.

D. (4 points) Describe one other important mechanism triggered by the changes in the fluid compartments that would help to compensate for the effects of this laxative.

The major physiological mechanism is that thirst is also triggered strongly by the increased activity of the osmoreceptors. After hyperosmotic diarrhea, you would become very thirsty. Drinking water would replace the water that was lost. As the water is absorbed in the intestine, all the steps in part A above would be reversed and all the volumes and osmolarities in the three fluid compartments would return to normal.

A second mechanism, of lesser importance, is that the lowered blood pressure could trigger the release of aldosterone, which would cause the distal tubules and collecting ducts to retain more NaCl, which would help to build up the blood volume. This retention of salt would, however, keep the osmolarity higher and would still depend upon drinking water to bring the osmolarity back to normal. In addition, the aldosterone mechanism is very slow, much slower than the ADH and thirst mechanisms.]
3. (10 points total) An increase in venous return to the right atrium (caused by either increased blood volume, increased blood pressure, or both) causes the release of a hormone called Atrial Natriuretic Peptide (ANP) from cells in the atrium. This hormone is part of a homeostatic system that involves both the cardiovascular system and the kidneys.

A. (5 points) ANP has a direct effect on the muscles of the veins and arterioles. Predict whether ANP would cause vasodilation or vasoconstriction, and explain your prediction.

To be homeostatic, the ANP must cause vasodilation, which would produce negative feedback: an increase in blood pressure would relax the muscles of the arteries and veins, lowering the blood pressure.

[In fact, this is exactly what happens: ANP relaxes smooth muscle cells in most blood vessels.]

[An alternative answer: if ANP caused vasoconstriction, an increase in blood pressure would result in a further increase in blood pressure, which is a positive feedback.]

B. (5 points) ANP also has an effect on the kidneys, acting primarily through aldosterone. Predict whether ANP would increase or decrease the amount of aldosterone in the blood, and explain your prediction.

Again, to be homeostatic, ANP must decrease the release of aldosterone. The trigger for ANP release is increased blood volume and blood pressure. The effect of aldosterone on the kidney is to retain NaCl, which would increase blood volume and blood pressure. Therefore, to be a negative feedback system, aldosterone must be inhibited.

[In fact, aldosterone is inhibited by ANP both directly (by acting on the cells in the adrenal cortex that release aldosterone) and indirectly (by decreasing the production of other hormones that release aldosterone).]
4. (18 points total) People with a disease called Fanconi’s Syndrome (FS) have malfunctions in the reabsorption of molecules in the proximal tubule of their nephrons. In the most extreme form, the proximal tubule cannot reabsorb glucose, amino acids, or Na\(^+\). The major symptoms of FS are polyuria (the production of huge amounts of urine) and polydipsia (extreme thirst).

A. (5 points) Explain the polyurea: how do the kidneys of a person with FS produce an abnormally high quantity of urine?

Because the proximal tubule cannot reabsorb the major components in the plasma (glucose, amino acids, or Na\(^+\)), they pass through the nephron in large quantities. In addition, because the proximal tubule allows water to pass freely through its walls, the fluid in the proximal tubule is isosmotic to the plasma, which means that a huge amount of water that normally is reabsorbed in the proximal tubule flows into the Loop of Henle in a person with FS. The remainder of the nephron cannot reabsorb the excess of substances, including the water, so large quantities of fluid are lost as urine.

[This is a condition known as ‘osmotic diuresis’.]

B. (5 points) Explain the polydipsia: why (i.e., by what mechanism) is a person constantly thirsty?

The huge water loss from the polyurea lowers the volume of blood, which activates the thirst center to produce drinking.

C. (4 points) Would the glomerular flow filtration rate (GFR) in a FS patient be higher, lower, or the same as the GFR of a normal person? Briefly explain why.

It would be the same. The amount of fluid that passes through the nephron would be much greater, but the amount that is filtered at the capsule would not change.

[An alternative explanation: the inulin clearance—which measure GFR—would be the same because the quantity of inulin that is filtered would not change. The concentration of inulin in the urine would be very low, but the volume of urine would be much greater because the quantity of inulin in the urine (which is concentration of inulin in the urine times the volume/minute of urine produced) would be the same.]

D. (4 points) How would the clearance of amino acids in an FS patient compare to a normal patient? State whether it would be higher, lower, or the same as the amino acid clearance in a normal person, and briefly explain why.

The clearance of amino acids would be much higher in an FS patient. Normally, no amino acids are in the urine, so their clearance = 0. In FS, all of the amino acids that are filtered make it past the proximal tubule. Because amino acids are neither reabsorbed nor secreted throughout the rest of the nephron, amino acids are handled exactly the same way as inulin in FS patients, so that:

\[ \text{clearance of amino acids} = \text{clearance of inulin} = \text{GFR} \]