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1. (30 pts) Consider a patient with the following physiologic values. Assume all measurements are taken at atmospheric pressure (760 mmHg) and at so-called "body temperature pressure saturated" (BTPS) conditions. Note that the vapor pressure of water at BTPS is 47 mmHg and that the mole fraction of oxygen in inhaled air is ~0.21.

Pulmonary function tests:
Tidal volume (V_T) = 0.5 L
Vital Capacity (VC) = 5 L
Inspiratory Capacity (IC) = 3.5 L
Forced expiratory volume after 1 sec (FEV_1) = 2.0 L
Breathing rate: 10 breaths/min
Fraction of CO2 in expired air (F_{ECO_2})= 0.05

Arterial Blood Gas:
pO2 = 80 mmHg
PCO2 = 40 mmHg
pH = 7.41
[HCO3-] = 23 mEq/L

A. Calculate this patient's inspiratory reserve volume. (5)

B. Calculate this patient's alveolar ventilation rate (mL/min). (10)

C. Calculate the partial pressure of this patient's alveolar oxygen (P_{AO_2}). Assume that the patient is consuming oxygen at 1.25 times the rate at which she is producing carbon dioxide. (10)

D. If this patient's breathing rate increases by a factor of two, and the rate of carbon dioxide production by the tissues increases by a factor of four, by what factor would you expect the alveolar pressure of carbon dioxide (P_{ACO_2}) to change? (5)

A. $IRV = IC - V_T = 3.5 - .5 = \boxed{3\ L}$

B. $V_D = V_T \times \dfrac{P_{aCO_2} - P_{ECO_2}}{P_{aCO_2}}$; $P_{ECO_2} = (P_B - P_{H_2O}) F_{ECO_2} = (760-47).05\ mmHg = 35.65\ mmHg$

$= (.5\ L)\dfrac{(40 - 35.65\ mmHg)}{40\ mmHg} = 54.4\ mL$

$\dot{V}_A = (V_T - V_D)\,BR = (.5 - .0544\ L)(10\ /min) = \boxed{4500\ mL/min}$

C. $P_{IO_2} = (P_B - P_{H_2O}) F_{O_2} = (760-47\ mmHg)(.21) = 149.73\ mmHg$

$P_{AO_2} = P_{IO_2} - \dfrac{P_{ACO_2}}{R}$; $R = \dfrac{CO_2\ prod}{O_2\ cons} = \dfrac{1}{1.25}$

$= 149.73 - \dfrac{40}{1/1.25}\ [mmHg] = \boxed{100\ mmHg}$

D. $\dot{V}_A = \dfrac{\dot{V}_{CO_2} K}{P_{ACO_2}}$; $\dfrac{(P_{ACO_2})_{new}}{(P_{ACO_2})_{old}} = \dfrac{(\dot{V}_{CO_2}/\dot{V}_A)_{new}}{(\dot{V}_{CO_2}/\dot{V}_A)_{old}} = \dfrac{(\dot{V}_{CO_2})_n}{(\dot{V}_{CO_2})_o} \cdot \dfrac{(\dot{V}_A)_o}{(\dot{V}_A)_n} = (4)(\tfrac{1}{2}) = \boxed{2}$

$(2 \times BR \Rightarrow 2 \times \dot{V}_A \Rightarrow (\dot{V}_A)_n/(\dot{V}_A)_o = 2)$

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2. (30 pts) Consider a patient's lungs and chest wall.

A. Suppose this patient develops extensive pulmonary fibrosis. What would you expect to happen to his functional residual capacity and why? (5)

B. Consider a terminal bronchiole of 200 µm diameter and 500 µm length in one of this patient's lungs that terminates into an alveolus of radius 50 µm. If the surface tension in the alveolar membrane is 30 mN/m, calculate the collapsing pressure on that alveolus. (10)

C. Calculate the flow rate through the bronchiole during inspiration. Assume that the pressure drop along the length of the bronchiole is 0.005 cm H_2O/µm and that the viscosity of the inhaled air is 18 x 10^{-6} Pa·s. Note that 1 cmH2O = 98 Pa = 0.736 mmHg. (10)

D. Consider two such bronchiole/alveolus pairs, one at the apex (top) of the lung, the other at the base (bottom) of the lung, and each associated with an alveolar capillary. Which capillary would have higher blood flow and why? (5)

A. Decrease. Pulmonary fibrosis ⇒ stiffening of the lungs, i.e. reduced compliance ⇒ ↑ collapsing tendency of lungs relative to expansion tendency of chest wall.

B. $$P = \frac{2T}{r} = \frac{2(.03\ N/m)}{(50\times10^{-6}\ m)} = \boxed{1200\ N/m^2}$$

C. $$R = \frac{8\eta l}{\pi r^4} = \frac{8(18\times10^{-6}\ Pa\cdot s)(500\times10^{-6}\ m)}{\pi(100\times10^{-6}\ m)^4} = 2.2918\times10^8\ \frac{Pa\cdot s}{m^3}$$

$$\frac{\Delta P}{l} = \frac{.005\ cm\ H_2O}{\mu m}\times\frac{98\ Pa}{1\ cm\ H_2O}\times\frac{1\ \mu m}{10^{-6}\ m} = 4.9\times10^5\ Pa/m$$

$$Q = \frac{\Delta P}{R} = \frac{(4.9\times10^5\ Pa/m)(500\times10^{-6}\ m)}{2.2918\times10^8\ Pa\cdot s/m^3} = 1.069\times10^{-6}\ m^3/s \times \frac{(1\ cm)^3}{(10^{-2}\ m)^3}$$

$$= \boxed{1.07\ cm^3/s}$$

D. Base. Here $P_a > P_v > P_A$ so capillary stays open. (At the apex, $P_A \geq P_a$ so capillary is squeezed smaller).

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3. (20 pts) Consider a blood sample from a patient living in San Francisco who has an oxygen saturation of 99%, and a hemoglobin concentration of 15 g hemoglobin/100 mL blood (note that these are both clinically normal values).

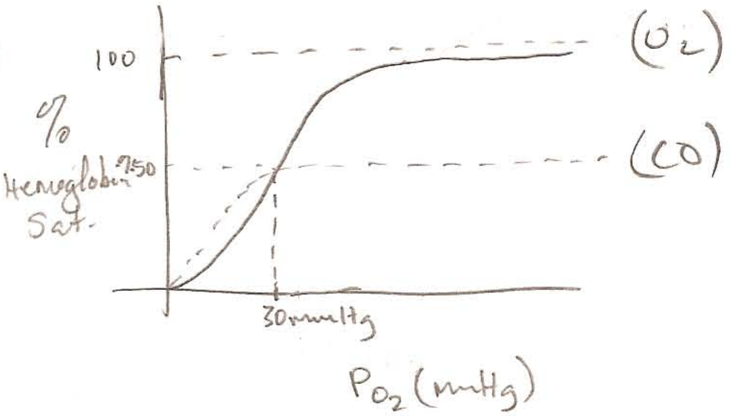
A. Sketch the % Hemoglobin saturation of this blood sample as a function of the partial pressure of oxygen (in mmHg), assuming that the P50 of the curve is 30 mmHg. (5)

B. On the same set of axes, sketch what the curve would look like in the presence of carbon monoxide at a partial pressure 1/250th that of oxygen. (5)

C. Suppose you take an second blood sample from this patient 2-3 weeks after he moves to Denver. How would you expect the P50 values of the two curves compare and why? (5)

D. Would you expect this patient's A-a gradient to change significantly in the move from San Francisco to Denver, and why? Incorporate the A-a gradient equation into your answer. (5)

A,B)



C) Denver is @ higher altitude, ↑ DPG production, ↓ affinity for O_2 ⇒ Curve shifts to Right ⇒ P_{50} ↑

D)

$$P_{A,O_2} - P_{a,O_2} = P_{I,O_2} - \frac{P_{A,CO_2}}{R} - P_{a,CO_2}$$

A-a gradient would change due to a change in P_{I,O_2}.

P_{I,O_2} ↓, P_{A,O_2} & P_{a,O_2} ↓ proportionally.

A-a gradient remains Normal

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4. (35 pts) Consider a patient who receives an IV infusion of inulin and para-aminohippuric acid (PAH), and then 24 hours later is subject to urine and blood collection. Suppose those tests reveal the following values:

<u>Urinalysis</u>
Urine output over 24-hour period: 1800 ml
Urine concentration of PAH: 80 mg/dL
Urine concentration of inulin: 400 mg/dL
Urine concentration of K+: 50 mEq/L
Urine concentration of Na+: 20 mEq/L
Urine osmolarity: 800 mEq/L

<u>Blood work</u>
Blood concentration of inulin: 10 mg/dL
Blood concentration of PAH: 0.5 mg/dL
Blood concentration of K+: 3.6 mEq/L
Blood concentration of Na+: 135 mEq/L
Blood concentration of BUN: 17 mg/dL
Blood concentration of Glucose: 100 mg/dL
Hematocrit: 0.47

A. Calculate the clearance ratio of K+. How would you expect this value to change in someone who begins to take furosemide and why? (10)

B. Determine the filtered load of Na+ (in mEq/hr), the rate of elimination of Na+ through the urine (mEq/hr), and the % of Na+ that is reabsorbed. (10)

C. Calculate the osmolarity of this patient's blood (mOsm/L) and determine the clearance of free water (mL/min). (10)

D. If this patient suffered head trauma and developed the syndrome of inappropriate ADH, what would you expect to happen to his free water clearance and why? (5)

A) $$C_K = \frac{[U]_K \cdot \dot{V}}{[P]_K} = \frac{[50 \text{ mEq/L}] \cdot (1800 \text{ ml}/24\text{ hr})}{[3.6 \text{ mEq/L}]}$$

$$\boxed{C_K = 1041.67 \frac{\text{ml}}{\text{hr}} = 17.36 \frac{\text{ml}}{\text{min}}}$$

$$C_{Inulin} = GFR = \frac{[U]_I \cdot \dot{V}}{[P]_I} = \frac{[400 \text{ mg/dl}] \cdot 1800\text{ ml}/24\text{ hr}}{[10 \text{ mg/dl}]}$$

$$\boxed{C_{Inulin} = 3000 \text{ ml/hr}}$$

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$$CR = \frac{C_K}{C_I} = \frac{1091.67 \text{ ml/hr}}{3000 \text{ ml/hr}} = \boxed{0.347 = CR}$$

Furosemide - blocks $Na^+/K^+/2Cl^-$ cotransporter $\Rightarrow$ K^+ Not reabsorbed which leads to an ↑ CR.

B) Filtered load = $GFR \cdot [P]_{Na} = C_{Inulin} \cdot [P]_{Na}$

$$FL = \left(3000 \frac{ml}{hr}\right)\left(135 \frac{mEq}{L}\right)\left(\frac{1 L}{1000 ml}\right)$$

$$\boxed{FL = 405 \frac{mEq}{hr}}$$

$$\text{Elimination Rate} = \dot{V} \cdot [U]_{Na^+} = \left(\frac{1800 ml}{24 hr}\right)\left(20 \frac{mEq}{L}\right)\left(\frac{1 L}{1000 ml}\right)$$

$$\boxed{ER = 1.5 \frac{mEq}{hr}}$$

$$\% \text{ reabsorbed} = \frac{FL - ER}{FL} = \frac{\left(405 \frac{mEq}{hr}\right) - \left(1.5 \frac{mEq}{hr}\right)}{405 \text{ mEq/hr}} \cdot 100 = \boxed{99.6\%}$$

C)

$$P.O. = 2[Na^+] + \frac{[glu]}{18} + \frac{[BUN]}{2.8} = 2\left[135 \frac{mEq}{L}\right] + \frac{[100 mg/dL]}{18} + \frac{[17 mg/dL]}{2.8}$$

$$P.O. = 270 \frac{mOsm}{L} + 5.55 \frac{mOsm}{L} + 6.07 \frac{mOsm}{L}$$

$$\boxed{P.O. = 281.62 \frac{mOsm}{L}}$$

$$C_{H_2O} = \dot{V} - \frac{[U]_{osm} \dot{V}}{[P]_{osm}} = \frac{1800 ml}{24 hr} - \frac{800 \frac{mEq}{L} \cdot \frac{1800 ml}{24 hr}}{281.63 \frac{mEq}{L}}$$

$$C_{H_2O} = 1.25 \frac{ml}{min} - 3.55 \frac{ml}{min} = \boxed{-2.3 \frac{ml}{min} = C_{H_2O}}$$

D) SIADH ⇒ ↓ C_{H_2O} because SIADH leads to H_2O reabsorption & decreased C_{H_2O} & more hyperosmotic urine.

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5. (15 pts.) Consider the problem of sodium reabsorption in the nephron.

A. Suppose you discovered a toxin that inhibited co-transport of sodium and glucose. At which portion of the nephron would you expect this toxin to have its greatest effect, and what would you expect the effect of this toxin to be on urinary glucose? (5)

B. Suppose a patient develops a glomerular basement membrane disorder that causes filtration of significant amounts of protein. How would you expect the rate of sodium and water reabosrption in the proximal tubule to change and why? (5)

C. If you obtained a sample of a patient's kidney's cortex, inner medulla, and outer medulla, rank the expected osmolarity of these three regions from lowest to highest. Explain what would happen to medullary osmolarity in the case of (1) water deprivation, and (2) the presence of a drug that makes the cortical collecting ducts freely permeable to urea. (5)

A) The toxin would have the greatest effect on the early PCT (most active Na^+ adsorption, location of Na^+-glucose cotransporter. This would ↑ urine glucose due to lack of reabsorption.

B) Filtration of protein = ↓ π_{GC}, ↓ in reabsorption of isosmotic fluid ⇒ ↓ Na^+ & H_2O in proximal tubule because π_{GC} is a driving force for isosmotic reabsorption

C) High: Inner Medulla > Outer Medulla > Cortex :Low

1) ↑ ADH, ↑ medullary osmolarity due to H_2O reabsorption

2) CD permeable to urea - No more urea recycling leads to ↓ in corticopapillary osmotic gradient & ↓ in Inner medullary osmolarity

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6. (20 pts) Consider a patient with the following arterial blood values:

pO2 = 95 mmHg
PCO2 = 38 mmHg
[HCO3-] = 25 mEq/L

A. Calculate the expected arterial pH, assuming bicarbonate is the dominant buffer. (5)

B. Suppose this patient's breathing rate was cut in half as a result of a medication. Assuming the rate of carbon dioxide production remained constant, calculate how high the bicarbonate concentration would need to rise to keep the pH from dipping below 7.35. (10)

C. Suppose the medication in B was discontinued, and the patient was instead placed on the diuretic acetazolamide. Identify the chemical reaction, enzyme, and location in the nephron where acetazolamide primarily acts, and explain what would happen to this patient's blood pH (and why). (5)

A. $pH = pK + \log \frac{HCO_3^-}{.03\,P_{CO_2}} = 6.1 + \log \frac{25\ mOsm/L}{.03(38\ mmHg)} = \boxed{7.44}$

B. $\dot{V}_A = \frac{\dot{V}_{CO_2} K}{P_{ACO_2}}$; $\dot{V}_{CO_2}$ const, K const ; BR ↓½ ⇒ $\dot{V}_A$ ↓½

$\dot{V}_A = (V_T - V_D)\,BR$

∴ P_{ACO_2} ↑ by factor of 2.

$7.35 = 6.1 + \log \frac{x}{.03(38\ mmHg \times 2)} \Rightarrow x = \boxed{40.54\ mEq/L}$

C. $H_2O + CO_2 \overset{CA}{\rightleftharpoons} H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$

CA = carbonic anhydrase enzyme

acetazolamide is a CA inhibitor acting on the brush border of the proximal tubule, interfering with HCO_3^- reabsorption. Thus, more HCO_3^- is excreted, and the patient's blood pH ↓.