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1. Suppose you are a physician conducting a spirometry study with an asthmatic patient, whose asthma is currently under excellent control. Under your instructions, the patient takes 4 tidal breaths, and at the end of inspiration of the fifth tidal breath exhales as much air as he possibly can. Following that maximal exhalation, the patient then inhales as much air as he can, after which the study ends.

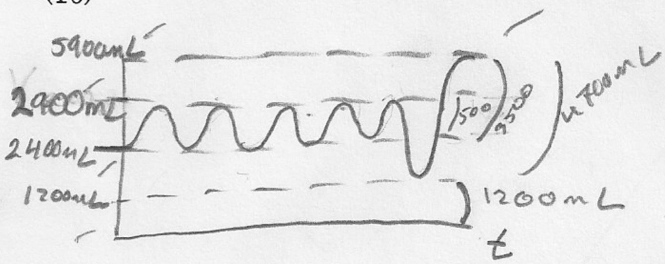
A. If the tidal volume is 500 ml, the inspiratory capacity is 3500 ml, and the vital capacity is 4700 ml, draw the spirometry curve (volume vs time) for the study above, and mark the numerical values of all local peaks and troughs on the curve. For problems A-B, estimate the residual volume to be 1200 ml. (10)

B. Calculate the inspiratory reserve volume. (5)

C. Briefly describe an additional study involving helium you could do to measure the total lung capacity. For full credit, give an equation or the name of a physical law that underlies this study. (5)

D. Suppose that in a separate spirometry study, you ask the patient to inhale as much as he can and then forcibly exhale as much as he can. A week later the patient develops an asthma attack and you repeat the forced-expiration study. On the same set of axes, plot the expiration curve (volume vs. time) before and after the patient develops the asthma attack. Mark the FEV_1 on both curves and clearly show which curve has the larger FEV_1 value. (10)

A) 10



B) 5

ERV=4700-3500-1200

IRV = IC - V_T = 3500-500mL
= 3000mL

C) 4

Helium dilution study

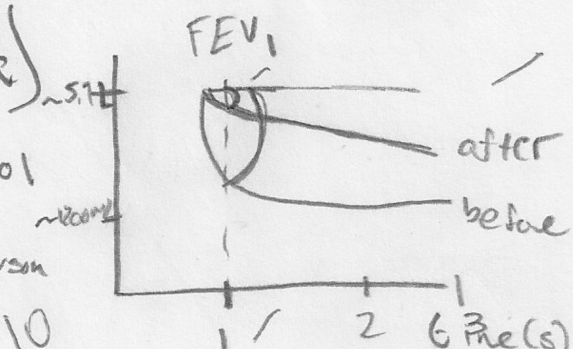
Ideal Gas equation PV=nRT

Henry's Law as well $P_x = f_x(P_{Tot})$

How use this? $P_1V_1 = P_2V_2$ ... how does this help

add known amount of helium to spirometer, allow equilibrium between helium tank and breathing person, take a full breath (full inhale), and measure concentration of helium of the original tank or canister that was used to administer the helium. As long as the lungs and canister are connected, they are at equilibrium, and the concentration of helium can be used to find total volume, then subtract the volume of the canister to find Total lung capacity.

d) 10



before has a much higher FEV1 (amount exhaled after 1 second)

2. Suppose that during the initial spirometry study in problem 1, the patient is breathing at a rate of 12 breaths per minute, and that the partial pressure of carbon dioxide in his exhaled breath and blood are 25 mmHg and 32 mmHg, respectively. 24/25

A. Calculate the patient's dead volume. (5)

B. Calculate the patient's minute ventilation and alveolar ventilation (10)

C. Calculate the rate at which he is producing CO_2. (5)

D. Suppose the patient is inspiring dry air at atmospheric pressure and has a body temperature of 37C, where the vapor pressure of water is 47 mmHg. Estimate the partial pressure of oxygen in the alveolus. Assume that dry air contains 20 mol% oxygen and that the respiratory exchange ratio (R) is 0.8. (5)

A) BR = 12 breaths/min $\quad P_{E,CO_2} = 25$ mmHg

4/5 $\quad V_D = V_T \left(\frac{P_{a,CO_2} - P_{E,CO_2}}{P_{a,CO_2}}\right)$ $\quad P_{a,CO_2} = 32$ mmHg $= P_{A,CO_2}$

$= 500\text{ mL}\left(\frac{32\text{ mmHg} - 25\text{ mmHg}}{25\text{ mmHg}}\right) = 140\text{ mL}$ −1

B) 10/10

$MV = V_T \times RR = 500\text{ mL} \times \frac{12\text{ breaths}}{\text{min}} = 6000\ \frac{\text{mL}}{\text{min}}$

$\dot{V}_A = (V_T - V_D) \times RR = (500 - 140) \times \frac{12\text{ breaths}}{\text{min}} = 4320\ \frac{\text{mL}}{\text{min}}$ X

C) 5/5

$\dot{V}_{CO_2} = \frac{\dot{V}_A \cdot P_{ACO_2}}{K} = \frac{4320\frac{\text{mL}}{\text{min}} \cdot 32\text{ mmHg}}{863\text{ mmHg}} = 160.18\ \frac{\text{mL}}{\text{min}}$ X

From $\dot{V}_A = \frac{\dot{V}_{CO_2} \times K}{P_{ACO_2}}$

D) 5/5

$P_{I,O_2} = (760\text{ mmHg} - 47\text{ mmHg}) \cdot (.20) = 142.6\text{ mmHg}$

$P_{A,O_2} = P_{I,O_2} - \frac{P_{A,CO_2}}{R} = 142.6\text{ mmHg} - \frac{32\text{ mmHg}}{.8} = 102.6\text{ mmHg}$

↑ correction factor can be ignored

3. In the inpatient setting, it is often desirable to have access to large "central" veins to facilitate the long-term administration of IV drugs. One of the most common ways this is done is to thread a catheter from just above the clavicle (collarbone) into the subclavian vein, which runs in the neck along the apex of the lung. Suppose you are inserting a right subclavian line into an obese patient, whose neck veins are difficult to see or palpate. Shortly after you insert the needle (but before you have any evidence you have entered the vein), the patient suddenly begins to breathe in a rapid, labored fashion. You realize, to your dismay, that you have inadvertently punctured the patient's right lung with your catheter needle.

A. What is the technical name for the condition you have induced? (5)

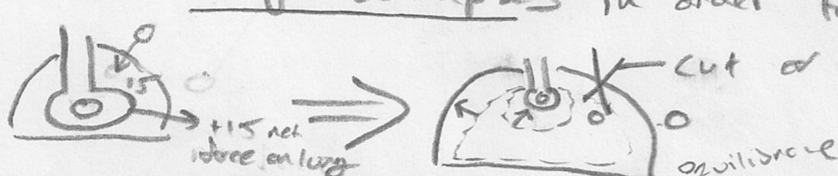
B. A quick examination reveals that the patient's right chest wall is noticeably expanded and x-ray reveals that his right lung has collapsed. Using the concepts of compliance and pleural pressure, explain both findings. (10)

C. Suppose this patient heals, and as a result of his 20-year history of smoking, later begins to show symptoms of emphysema. Draw the compliance curve (volume vs pressure) of his lung before and after the emphysema develops. Why, in molecular-level terms, does this shift occur? (10)

D. Consider two alveoli in this patient's left lung, one twice the diameter of the other. If both alveoli have the same surface tension, and the smaller alveolus requires 1 mmHg to inflate, how much pressure would be required to inflate the larger alveolus? (5)

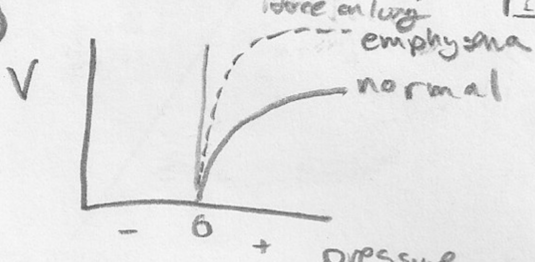
A) pneumothorax

B) the lung attempts to shrink due to low compliance
the chest wall attempts to expand
this creates a vaccum in the pleural space, with equilibrium lung volume being determined by opposing compliances (of the lung and chest wall)
when the vaccum is punctured, the chest wall expands and the lung collapses in order to relieve the pressure.



• dotted represents old lung and CW before puncture

C)



emphysema breaks down the elastic tissue in the lungs, raising compliance

D) $P = \frac{2T}{r}$

A: r B: $2r$

$P_A = \frac{2T}{r}$

$\frac{1\,mmHg}{2} \cdot r = T$

$P_B = \frac{2\left(\frac{1\,mmHg}{2} r\right)}{2r}$

$P_B = 1/2\ mmHg$

4. Consider a 24-year old woman who has just run a marathon. While she has of course perspired a great deal while running the race, she has not had the opportunity to drink adequate "replacement" amounts of water along the way.

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A. Describe what has happened to each of the 5 quantities, along with a ~1 sentence explanation of why: (1) total body water; (2) extracellular fluid volume; (3) extracellular fluid osmolarity; (4) intracellular fluid volume; (5) intracellular fluid osmolarity. (10)

sweat = hyperosmotic vol. contraction

B. Suppose that for drug testing purposes, urine samples were obtained from this woman before and after the race. Which urine sample would you expect to have the higher osmolarity? What hormone is primarily responsible for this difference in osmolarity and on what part(s) of the nephron does it chiefly act? (10)

C. Prior to running the race, suppose this woman's plasma concentrations of glucose, Na+, and blood urea nitrogen are 90 mg/dL, 135 mEq/L, and 14 mg/dL, respectively. If her urinary output is 1.4 L/day and her clearance of free water is 0, what is her urinary osmolarity? (10)

hyperosmotic contraction

A) TBW – decreased as sweat is excreted from ECF

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ECF vol – decreased, as hyposmotic fluid is lost from ECF as sweat

ECF osm – increased, as hyposmotic fluid is lost, leaving plasma as hyperosmotic.

ICF vol – decrease as fluid shifts to ECF in order to equilibrate osmolarities

ICF osm – increases as ICF vol decreases, but the amount of solute in the ICF remains the same

10/10 B) afterwards. Antidiuretic hormone (ADH) acts on the principal cells of the late distal tubule and collecting duct. During exercise, an increase in ADH increases the H_2O permeability of those principal cells, allowing more H_2O reabsorption, making the urine more hyperosmotic, (higher osmolarity).

C)

10/10

$$\text{Plasma Osmolarity} = 2[Na^+] + \frac{[glucose]}{18} + \frac{[BUN]}{2.8}$$

$$= 2\left(135 \frac{mEq}{L}\right) + \frac{90\ mg/dL}{18} + \frac{14\ mg/dL}{2.8} = 280 \frac{mOsm}{L}$$

$$C_{H_2O} = \dot{V} - C_{osm} = \dot{V} - \frac{[U]_{osm} \times \dot{V}}{[P]_{osm}}$$

$$0 = 1.4\ L/day - \frac{[U]_{osm} \times 1.4\ L/day}{280 \frac{mOsm}{L}}$$

$$[U]_{osm} = 280 \frac{mOsm}{L}$$

The same osmolarity as the $[P]_{osm}$

as urinary output is isosmotic b/c $C_{H_2O} = 0$

5. Consider a patient with a hematocrit of 0.45, a plasma creatinine of 3 mg/dL, a urine creatinine of 50 mg/dL, and a urinary output of 1 L/day.

A. What is this patient's glomerular filtration rate? (5)

1 dL = .1 L

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B. Consider a substance X with a plasma concentration of 10 mg/dL and a urine concentration of 200 mg/dL. What is the clearance ratio of X? Based on this answer, predict how X is handled in the nephron with respect to filtration and net reabsorption/secretion. (10)

C If the patient has a filtration fraction of 0.2 (20%), what is this patient's renal plasma flow and renal blood flow? (10)

A) $GFR = C_{creatinine} \approx \frac{[U]_{creat} \times \dot{V}}{[P]_{creat}} = \frac{50\,mg/dL \times 1\,L/day}{3\,mg/dL} = 16.66\ \frac{L}{day}$

B) $[P]_x = 10\frac{mg}{dL}$ $[U]_x = 200\,mg/dL$

$C_x = \frac{[U]_x \cdot \dot{V}}{[P]_x} = \frac{200\,mg/dL \cdot 1\,L/day}{10\,mg/dL} = 20\,L/day$

$C_x/GFR = \frac{20\,L/day}{16.66\,L/day} = 1.2$

C.R. > 1, so it is fully filtered and net secreted

C) $FF = .2 = GFR/RPF$

$.2 = 16.66\,L/day / RPF$ $RPF = 83.33\,L/day$

$RBF = RPF/1-hct = 83.33\,L/day / (1-.45) = 151.51\,L/day$

6. Answer the following questions about solute handling in the kidney:

thiazide diuretic

A. A patient who has recently been placed on the drug hydrochlorothiazide for hypertension begins to complain of muscle weakness and palpitations; analysis of serum electrolytes reveals a serum potassium level of 3.1 (the normal range is 3.5-5.5 mEq/L). Explain why this patient is hypokalemic, justifying your answer with a specific molecule and a specific region of the nephron. (5)

B. Suppose you discover a drug that has the ability to inhibit the Na^+/valine co-transporter in the early proximal tubule of the nephron. If you administered this drug, what would you expect to happen to urinary valine levels and why? (5)

C. Say whether the following statement is true or false, and briefly explain why: The ability of the kidney to generate the corticopapillary osmotic gradient depends on the fact that both the ascending and descending limbs of the Loop of Henle are freely permeable to water. (5)

D. Say whether the following statement is true or false, and briefly explain why: Hormones that constrict the efferent arterioles more strongly than the afferent arterioles reduce renal blood flow but increase glomerular filtration rate. (5)

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A) hydrochlorothiazide is a thiazide diuretic, which inhibits the activity of the Na^+/Cl^- cotransporter in the early distal tubule. This means less Na^+ reabsorption occurs here, and the tubular fluid is of higher concentration of Na^+ once the late distal tubule is reached, causing a higher influx of Na^+ into the principal cells, making intracellular Na^+ concentration higher. This allows for higher activity of the Na^+/K^+ atpase, pumping more Na^+ into serum and more K^+ out of plasma, leading to hypokalemia

B) Increase, as Na^+/amino acid transporters are responsible for reabsorption of amino acids, so inhibition of this cotransporter would lead to more valine being excreted instead of reabsorbed

C) False, the descending limb is permeable, allowing equilibration between the kidney and tubular fluid. The ascending limb is not permeable. The thick ascending limb moves NaCl out (via $Na^+/K^+/2Cl^-$ transporter) of tubular fluid. After equilibration again occurs in the descending loop, the movement of fluid pushes the very concentrated fluid into the ascending limb, where the process occurs again. This process is called countercurrent multiplication as the individual properties continually repeat to create a very high osmolarity at the more inner region (medulla) of the kidney.

D) ON BACK OF this sheet