MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Departments of Electrical Engineering, Mechanical Engineering, and the Harvard-MIT Division of Health Sciences and Technology

6.022J/2.792J/BEH.371J/HST542J: Quantitative Physiology: Organ Transport Systems

PROBLEM SET 10

SOLUTIONS

May 6, 2004

Problem 1

Inulin and para-amino hippuric acid are infused into the blood stream of a 40 kg ape. The following measurements were made during the course of the infusion, and were noted to be constant throughout the experiment: arterial plasma concentration of inulin 0.15 mg/ml, of para-amino hippuric acid 0.2 mg/ml; renal venous plasma concentration of para-amino hippuric acid 0.0015 mg/ml; urine flow 2 ml/min; urinary concentration of inulin 9.0 mg/ml, of para-amino hippuric acid 50 mg/ml.

$$\begin{aligned}
[IN]_p &= 0.15\ mg/ml \\
[PAH]_p &= .2\ mg/ml \\
[PAH]_v &= .0015\ mg/ml \\
\dot{U} &= 2\ ml/min \\
[IN]_u &= 9.0\ mg/ml \\
[PAH]_u &= 50\ mg/ml
\end{aligned}$$

A. What is the glomerular filtration rate?

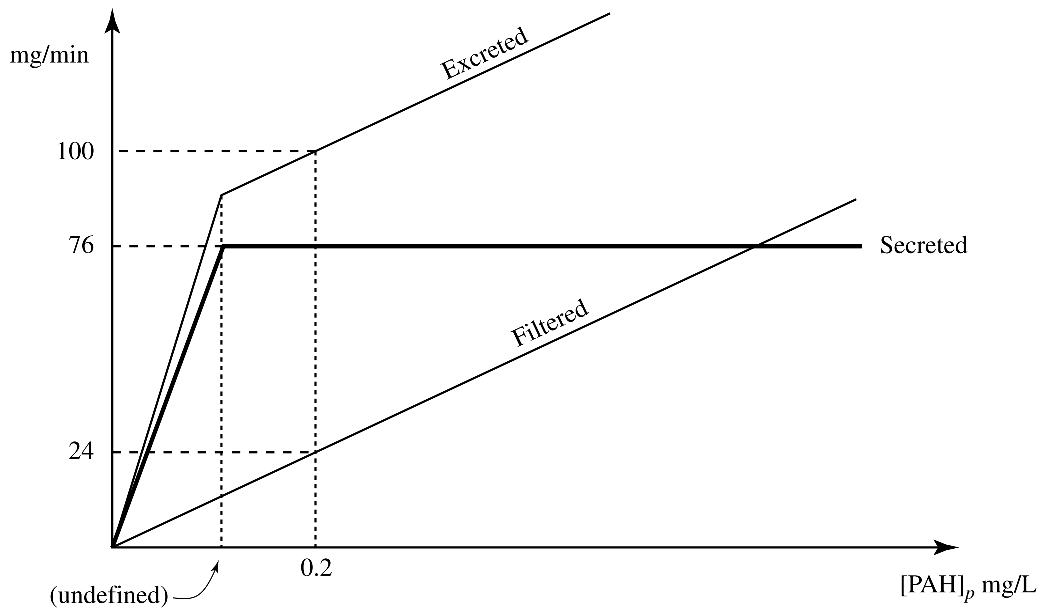
$$\begin{aligned}
GFR = inulin\ clearance &= C_L(IN) \\
&= \frac{\dot{U}[IN]_u}{[IN]_p} \\
&= \frac{(2)(9)}{.15} = 120\ ml/min
\end{aligned}$$

B. What is T_m (transport maximum) for PAH secretion?

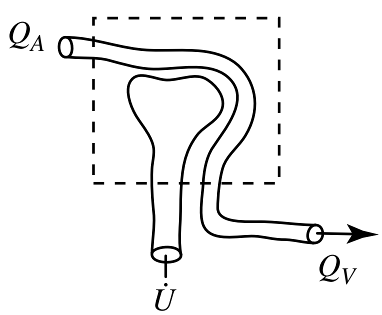
In this problem, some PAH is still found in venous blood from the kidney. This implies two important facts:

- *The tubular secretion mechanism is saturated; that is, the secretion rate is at T_m.*
- *Since $[PAH]_v$ is non-zero, the simple equation for renal plasma flow ($RPF = C_L[PAH]$) is not completely valid, and the more complete formula based on conservation of mass must be used.*

$$\begin{aligned}
secretion\ rate = T_m &= excretion\ rate - filtration\ rate \\
&= \dot{U}[PAH]_u - GFR[PAH]_p \\
&= (2)(50) - (120)(0.2) \\
&= 100 - 24 \\
&= 76\ mg/min
\end{aligned}$$



C. What is the renal plasma flow?



$$
\begin{aligned}
Q_A &= \dot{U} + Q_V \\
Q_A[X]_P &= \dot{U}[X]_U + Q_V[X]_V \\
&= \dot{U}[X]_U + (Q_A - U)[X]_V \\
\dot{U}[X]_U - U[X]_V &= Q_A[X]_P - Q_A[X]_V \\
Q_A\,(X_P - X_V) &= \dot{U}\,(X_U - X_V) \\
Q_A &= \frac{\dot{U}\,(X_U - X_V)}{(X_P - X_V)} \qquad X = PAH \\
&= \frac{(2)(50 - .0015)}{0.2 - .0015} = \frac{(2)(49.998)}{0.1985} \\
&= RPF = \frac{99.997}{0.1985} = 503.76 \text{ ml/min}
\end{aligned}
$$

D. Calculate the renal venous concentration of inulin.

Inulin is not secreted or reabsorbed, so its concentration in blood won't change:

$$[IN]_V = [IN]_P = 0.15$$

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Problem 2

In a particular experiment designed to determine rate of renal excretion of vitamin C, a human subject, after large doses of vitamin C, showed plasma concentration of the vitamin of 40 mg/liter. The vitamin C clearance was determined to be 60 ml/min. The inulin clearance which was measured simultaneously was 130 ml/min.

A. Calculate the excretion rate of the vitamin.

The excretion rate of vitamin C is given by:

$$\begin{aligned} \textit{Amount excreted} &= \textit{[concentration in urine][urine flow rate]} \\ &= \textit{[concentration in plasma][clearance of vitamin C]} \\ &= 40\ \textit{mg/L} \times 60\ \textit{ml/min} \\ &= 40 \times 10^{-3}\ \textit{mg/ml} \times 60\ \textit{ml/min} \\ &= 2.4\ \textit{mg/min} \end{aligned}$$

B. Calculate the reabsorption rate of the vitamin in the tubules.

The reabsorption rate is equal to the amount of vitamin C filtered less the amount excreted.

$$\begin{aligned} \textit{Reabsorption rate} &= \textit{[GFR][concentration in plasma]} - 2.4\ \textit{mg/min} \\ &= (130)(.04) - 2.4 \\ &= 5.2 - 2.4 \\ &= 2.8\ \textit{mg/min} \end{aligned}$$

C. It is known that vitamin C exhibits a transport maximum (T_m); i.e., the tubules cannot reabsorb a larger amount of the vitamin than T_m. What is the value of T_m for vitamin C? Find also the maximum blood concentration of the vitamin for which excretion of the vitamin will be close to zero.

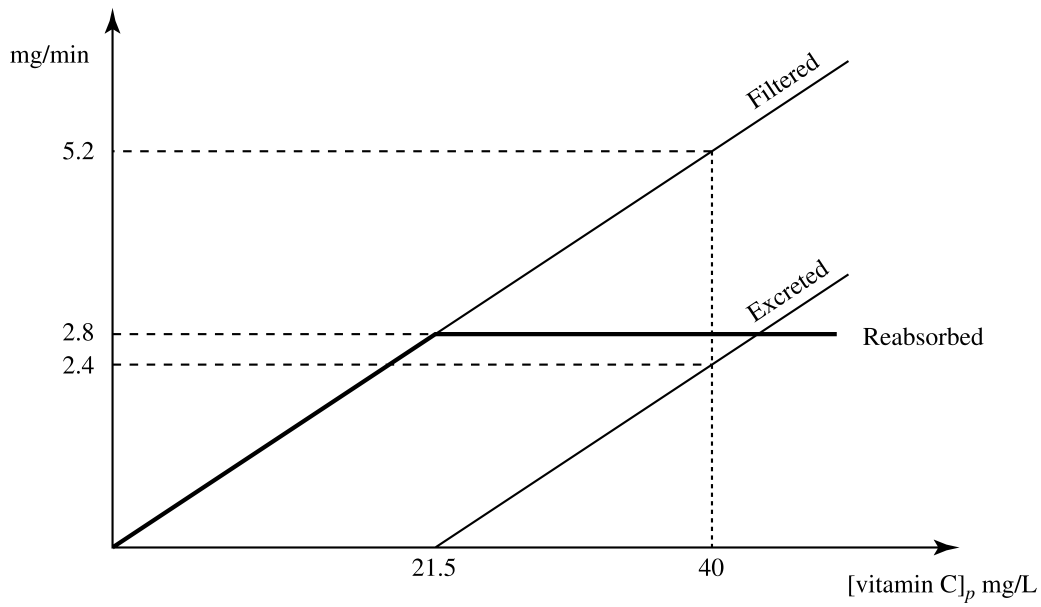
If vitamin C exhibits a classical transport maximum, then the amount reabsorbed must be equal to the T_m *whenever* any *vitamin C is excreted.*

The plasma concentration at which excretion begins is obtained from the geometry of the graph below (Figure 1), or by noting that at that point

$$T_m = \textit{GFR (threshold concentration)}$$

Either way, the answer is 21.5 mg/L.

Figure 1:



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Problem 3

From electron-microscopic studies it was estimated that the wall thickness of the glomerular capillaries through which filtration occurs is about 500Å. The individual pore diameter is 80 Å. Using the values for glomerular filtration rate (GFR), viscosity of the fluid, μ, and the filtration pressure, Δp, of: GFR = 125 ml/min, μ = 0.01 g/cm-sec, and Δp = 30 mmHg, estimate the total number of pores and the cross-sectional area of a single pore which would provide an equivalent resistance. (Assume laminar viscous flow.)

Total flow rate through glomerulus = GFR 125/60 ml/sec.
By conservation of mass, GFR $= nQ_p$ *where* Q_p *is the flow rate through one pore.*
Since the flow is viscous and fully developed inside one pore

$$Q_p = \frac{\Delta P A_p^2}{8\mu\pi L}$$

using Poiseuille's Law.

$$\begin{aligned}
\Delta P &= 30 \text{ } mmHg = 30 \times 1330 = 39,900 \text{ } dynes/cm^2 \\
A_p &= \text{area of one pore} = \pi \left(40 \times 10^{-8}\right)^2 = 5.03 \times 10^{-13} \text{ } cm^2 \\
\mu &= 0.01 \text{ } poise = 0.01 \text{ } g/cm\text{-}sec \\
L &= 500 \times 10^{-8} \text{ } cm
\end{aligned}$$

Therefore

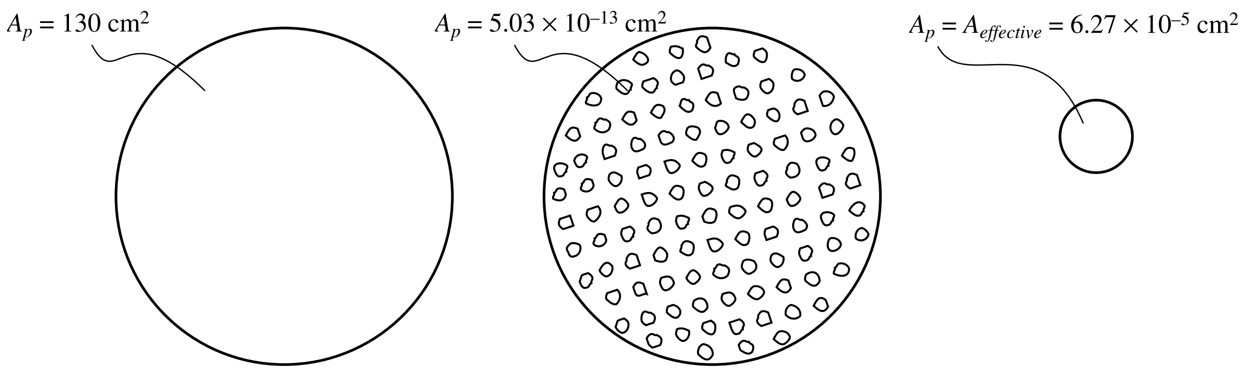
$$n = \frac{GFR}{Q_p} = \frac{\left(\frac{125}{60}\right) 8(0.01)\pi(500 \times 10^{-8})}{(39,900)\left(5.03 \times 10^{-13}\right)^2} = 2.59 \times 10^{14}$$

The total equivalent *(or effective) area is the area of one tube or pore, throgut which you would get an equivalent total flow rate. Therefore,*

$$\begin{aligned}
GFR &= \frac{\Delta P A_{eq}^2}{8\mu\pi L} \Rightarrow A_{eq} = \sqrt{\frac{GFR \cdot 8\mu\pi L}{\Delta P}} \\
A_{eq} &= 2.95 \times 10^{-4} \text{ } cm^2
\end{aligned}$$

Note that $A_{eq} \neq nA_p$, $A_{eq}^2 = nA_p^2 \Rightarrow A_{eq} = \sqrt{n}A_p$, *and* $A_{eq} \ll nA_p$ *where* $nA_p = 130 \text{ } cm^2$*!*

This problem basically points out that if you took one pore with cross-sectional area = 130 cm^2 *and divided it into* 2.59×10^{14} *pores of cross-sectional area equal to* 5.03×10^{-13} cm^2*, then your flow rate would drop by 14 orders of magnitude! (for the same* ΔP*)*



$$\begin{aligned} n &= 1, \quad nA_p = 130\ cm^2 \\ Q &= \frac{39,900 \times 130^2}{8(0.01)\pi(500 \times 10^{-8})} \\ &= 5.36 \times 10^{14}\ ml/sec \\ &= 3.2 \times 10^{16}\ ml/min \end{aligned}$$

$$\begin{aligned} n &= 2.59 \times 10^{14} \\ nA_p &= 130\ cm^2 \\ Q &= 125\ ml/min \end{aligned}$$

$$\begin{aligned} n &= 1 \\ nA_p &= 6.27 \times 10^{-5} \\ Q &= 125\ ml/min \end{aligned}$$

These flow rates were calculated assuming $\Delta P = 30$ mmHg, $\mu = 0.01$ poise, $L = 500$ Å in all three cases.

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Problem 4

A 70 kg patient in the hospital was found to have a plasma Na^+ concentration of 112 mEq/liter. (Normal is 140 mEq/l.) It is decided that this abnormality must be corrected rapidly because of altered mental status. If it is desired to raise the plasma Na^+ concentration to 132 mEq/liter, how much 5% NaCl solution must be administered? (The molecular weight of NaCl is 58.) Ignore changes in TBW due to administration of NaCl solution.

Since all body fluid compartments are in osmotic equilibrium, we have (approximately)

$$\frac{(Na)}{ECW} = \frac{(K)}{ICW} = \frac{(Na + K)}{TBW}$$

where

(Na)	=	*total body stores of sodium (mostly extracellular)*
(K)	=	*total body potassium (intracellular)*
TBW	=	*total body water*
ECW	=	*extracellular water*
ICW	=	*intracellular water*

In this case, TBW = (0.6)(70 kg) = 42 L
Initially

$$\begin{aligned} \frac{Na + K}{42} &= 112 \\ (Na + K)_i &= (112)(42) \end{aligned}$$

Final situation (ignoring any changes in TBW)

$$\begin{aligned} \frac{Na + K}{42} &= 132 \\ (Na + K)_f &= (132)(42) \end{aligned}$$

Net change in sodium (no change in K) = (132-112)(42) = 840 mEq. Thus, we must supply 840 mEq of Na^+ intravenously.

$$\begin{aligned} 5\%\ NaCl &= \frac{(50\ gm\ NaCl)}{liter\ H_2O} = \frac{(50/58\ moles)}{L} \qquad \text{(The molecular weight of NaCl is 58.)} \\ &= 862\ mEq\ Na^+/L \end{aligned}$$

Thus, we need 840/862 = .974 liters or .974 ml of 5% NaCl to bring the serum sodium from 112 to 132.

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Problem 5

An elderly patient who weighed 50 kg when in good health became ill and stopped eating and drinking. Several days later the patient was taken to the hospital where serum electrolytes were measured. The serum sodium concentration was 160 mEq/liter. (Normal = 140 mEq/L). Estimate the approximate volume of water which must be administered to the patient to restore normal osmolarity. (Use the approximate "20–40–60" percent rule. Assume the patient had lost pure water.)

$$\begin{array}{ll} \textit{Baseline: } 50\ kg & TBW = 30\ L \\ \textit{Dry: } [Na^+] = 160 & TBW' \textit{ (less than } 30\ L) \end{array}$$

$$\begin{aligned} \textit{Total cation (dry)} &= (160\ mEq/L)TBW' \\ \textit{Total cation (baseline)} &= (140\ mEq/L)30\ L \end{aligned}$$

Thus:

$$\begin{aligned} 160\ TBW' &= 140 \cdot 30 \\ TBW' &= \frac{140 \cdot 30}{160} = 26.25\ L \\ \Delta\ water &= 30 - 26.25 = 3.75\ Liters \end{aligned}$$

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