

Case Study 3
PHA 5127

Assume GFR is 130 mL min^{-1} and urine flow is 1.5 mL min^{-1} . For the following situations, indicate whether the drug is:

- only filtered
- filtered and reabsorbed through passive diffusion
- filtered and actively secreted

- 1a) A drug with $f_u = 0.04$ and a $Cl_{REN} = 40 \text{ mL min}^{-1}$ **filtered and actively secreted**
b) A drug with $f_u = 0.20$ and a $Cl_{REN} = 26 \text{ mL min}^{-1}$ **only filtered**
c) A drug with $f_u = 0.30$ and a $Cl_{REN} = 30 \text{ mL min}^{-1}$ **filtered and reabsorbed through passive diffusion**

2.) A drug is eliminated through glomerular filtration (no other clearance mechanism is observed). The drug is 50% bound to plasma proteins. Glomerular filtration rate is normal (130 mL/min). No active renal secretion and passive or active reabsorption after renal filtration is observed. The volume of distribution is 50L .

What is the clearance of the drug? What is the elimination rate constant of the drug?

$$CL = GFR * f_u = 130 \text{ mL/min} * 0.5 = 65 \text{ mL/min}$$

$$CL = k_e * V \quad 65 \text{ mL/min} = k_e * 50,000 \text{ mL} \quad k_e = 0.0013 \text{ min}^{-1}$$

3.) Complete the following statements for a low molecular weight drug which does not bind to plasma proteins.

A. The maximum value which renal clearance can approach that of **Renal Blood Flow**

B. If this drug is hydrophilic and not interacting with transporters the largest possible renal clearance is that of **GFR**

C. If this drug is lipophilic, neutral drug and not interacting with transporters the smallest possible renal clearance is that of **Urine Flow**

D. Assuming that the lipophilic drug is a base, renal clearance can be reduced by **increasing pH**

4.) An investigational new drug is eliminated entirely by liver (hepatic) metabolism, with a clearance of 1.40 L/min in subjects with an average liver blood flow of 1.50 L/min . What would be its expected clearance in a congestive heart failure patient with a liver blood flow of 1.10 L/min but no change in hepatic enzyme activity?

$$CL_H = Q_H * E$$

$$E = CL_H / Q_H = 1.4 \text{ L/min} / 1.5 \text{ L/min} = 0.933$$

For CHF patient: $Q_H = 1.10 \text{ L/min}$

$$CL_H = Q_H * E = 1.10 \text{ L/min} * 0.933 = 1.03 \text{ L/min}$$

5.) J.P. is a 40 y.o. man, height 5'6" with a serum creatinine level of 1.3 mg/dL. S.G. is a 20 y.o. female, height 5'2", weight with a serum creatinine level of 1.5 mg/dL.

Determined the creatinine clearance for each person. What can be deduced about the GFR for each of these people?

$$\text{For J.P.: } Cl_{\text{creat(male)}} = ((140 - \text{age}) * \text{IBW}) / (72 * C_{\text{pcreat}})$$

$$\text{IBW(male)} = 50 \text{ kg} + 2.4 \text{ kg for every inch above 5 ft}$$

$$\text{IBW for JP: } 50 \text{ kg} + 2.4(6) = 64.4 \text{ kg}$$

$$\text{Creat Clearance} = ((140 - 40)(64.4)) / (72 * 1.3) = 68.8 \text{ ml/min}$$

$$\text{For S.G.: } Cl_{\text{creat(female)}} = ((140 - \text{age}) * \text{IBW}) / (85 * C_{\text{pcreat}})$$

$$\text{IBW(female)} = 45.5 \text{ kg} + 2.3 \text{ for every inch over 5 ft}$$

$$\text{IBW for S.G.: } 45.5 \text{ kg} + 2.3(2) = 50.1 \text{ kg}$$

$$\text{Creat Clearance} = ((140 - 20)(50.1)) / (85 * 1.5) = 47.1 \text{ ml/min}$$

Creatinine is eliminated from the body via glomerular filtration and shown no protein binding. Thus, calculating creatinine clearance is a means of obtaining the GFR. Since the creatinine clearance was very low for these patients (normal value is 125 ml/min), it may be deduced that there is some kidney failure.