

Homework 4
PHA 5127 Fall 2007
(Total 10 Points)

1. For the physiological changes listed below, determine what will happen on the pharmacokinetic parameters for a lipophilic, protein bound, high extraction drug cleared by liver. (3 pts)

$$Cl = \frac{Q_H \cdot f_u \cdot Cl_{int}}{Q_H + f_u \cdot Cl_{int}} \approx Q_H \quad E = \frac{f_u \cdot Cl_{int}}{Q_H + f_u \cdot Cl_{int}} \approx 1 \quad F = 1 - E \approx \frac{Q_H}{f_u \cdot Cl_{int}}$$

scenarios	<i>Cl</i>	<i>E</i>	<i>F</i>
a) plasma protein binding ↑	↔	↔	↑
b) liver blood flow ↓	↓	↔	↓
c) metabolic liver enzyme ↑	↔	↔	↓

2. Carlo is a 25-year-old, 5'5", 80kg male with a serum creatinine concentration of 1.2mg/dL. He is going to receive an antibiotic A for his infection. Knowing this drug is mainly eliminated by Glomerula filtration and has no protein binding, finish the following questions with appropriate units. (2 pts)

a) Calculate the "Ideal Body Weight" and "Adjusted Body Weight". State which of these two weight measurements should be used for the estimation of the *Cl_{cr}* (note: if one's total body weight is over 120% of his IBW, he is an obese patient); (1 pts)

Solution : $IBW = 50 + 2.3 \times 5 = 61.5kg$

$TBW > 120\% IBW = 73.8$, we will use ABW for CL_{cr} calculation

$ABW = 61.5 + (80 - 61.5) \times 0.4 = 68.9kg$

b) Estimate the CL of this drug (with Cockcroft-Gault Equation); (1 pts)

$$CL \approx CL_{cr} = \frac{(140 - 25) \times 68.9}{72 \times 1.2} = 91.7 \text{ ml/min} = 5.5L/hr$$

3. Drug D is mainly eliminated by kidney and 90% of this drug is binding to plasma proteins. For patient A, his last 24-hour urine collection volume is 2.8 L with the drug concentration in urine of 1.2 mg/L. Knowing his drug concentration in plasma for the last 24 hrs is 0.1 mg/L, estimate his *Cl*. Does the elimination involve partial re-absorption, complete passive diffusion re-absorption or secretion? Explain! (2 pts)

$$\frac{2.8 \cdot 1.2 / 0.1}{24} = 1.4 \text{ L/hr} > 130 \cdot 10\% = 13 \text{ ml/min} = 0.78 \text{ L/hr}$$

∴ involves secretion

4. Mark whether the following statements are True or False (0.5 points each)

- T F** a. The maximum value of renal clearance is that of the glomerula filtration rate. (F)
- T F** b. The degree of tubular reabsorption might be affected by the pH of the urine. (T)
- T F** c. Reducing liver blood flow may significantly increase the extraction rate and clearance of a low extraction drug. (F)

A renal clearance of 300 ml/min may suggest the following:

- T F** d. The drug is eliminated by tubular secretion (T)
- T F** e. The drug is extensively reabsorbed in renal tubules (F)
- T F** f. Drug interactions in renal tubules are likely (T)