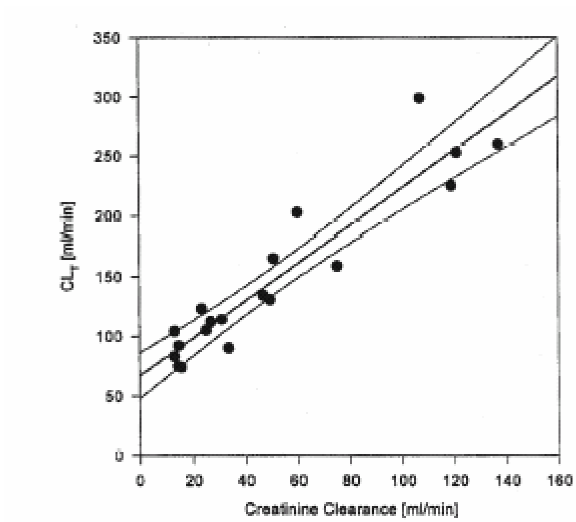
PHA 5127 – Fall 2003
Case Study # 4 – Answers

1. In a study in patients with various degrees of renal impairment the following relationship was found for piperacillin:



The volume of distribution in the elimination phase (Vd_{area}) was 19L and independent of renal function.

For a patient with normal renal function (CrCL 130 mL/min) and a patient with impaired renal function (CrCL 25mL/min), estimate the clearance, half-life and the percentage of the dose excreted into urine.

Parameter	**Normal**	**Impaired**
CL (mL/min)	250	100
CL_{renal} (mL/min)	180	30
$CL_{non-renal}$ (mL/min)	70	70
t1/2 (h)	0.9	2.2
k_e (h^{-1})	0.79	0.32
F_R (%)	72	30

For a normal patient:

The total clearance can be estimated from the graph using the creatinine clearance.

The non-renal clearance can be estimated from the graph as well. The intercept (CrCL 0 mL/min) gives the value of the non-renal clearance as creatinine is eliminated only renally.

The renal clearance can then be calculated as:

$$CL_{renal} = CL_{total} - CL_{non-renal}$$

The elimination rate constant can be calculated using the following equation:

$$k_e = \frac{CL_{total}}{Vd_{area}} = \frac{15L/h}{19L} = 0.79h^{-1}$$

The half-life is then calculated as:

$$t_{1/2} = \frac{0.693}{k_e} = \frac{0.693}{0.79} = 0.9h \qquad \text{or} \qquad t_{1/2} = \frac{0.693 \cdot Vd_{area}}{CL} = \frac{0.693 \cdot 19}{15} = 0.9h$$

The fraction excreted into the urine is calculated as:

$$F_R(\%) = \frac{CL_{renal}}{CL_{total}} \cdot 100 = \frac{180}{250} \cdot 100 = 72$$

For the impaired renal patient:

The total clearance can be estimated from the graph using the creatinine clearance.

The non-renal clearance can be estimated from the graph as well. The intercept (CrCL 0 mL/min) gives the value of the non-renal clearance as creatinine is eliminated only renally.

The renal clearance can then be calculated as:

$$CL_{renal} = CL_{total} - CL_{non-renal}$$

The elimination rate constant can be calculated using the following equation:

$$k_e = \frac{CL_{total}}{Vd_{area}} = \frac{6L/h}{19L} = 0.32h^{-1}$$

The half-life is then calculated as:

$$t_{1/2} = \frac{0.693}{k_e} = \frac{0.693}{0.32} = 2.2h \qquad \text{or} \qquad t_{1/2} = \frac{0.693 \cdot Vd_{area}}{CL} = \frac{0.693 \cdot 19}{6} = 2.2h$$

The fraction excreted into the urine is calculated as:

$$F_R(\%) = \frac{CL_{renal}}{CL_{total}} \cdot 100 = \frac{30}{100} \cdot 100 = 30$$

2. B.G., a 62-year-old, 50 kg female is admitted to the hospital. Her serum creatinine is 3.0 mg/dL and she is about to be started on drug A. She receives an i.v. bolus of 750mg of drug A. What will be B.G.'s plasma concentration after 3.5h? Also calculate B.G.'s half-life.

   $CL = (0.8mL/\min/kg \cdot weight) + CrCL(mL/\min)$

   $Vd = 3.8 \cdot weight + 3.1 \cdot CrCL(mL/\min)$

$$CrCL = 0.85 \cdot \frac{(140 - age) \cdot weight}{72 \cdot SeCr} = 0.85 \cdot \frac{(140 - 62) \cdot 50}{72 \cdot 3.0} = 15.3mL/\min$$

$$CL = 0.8 \cdot 50 + 15.3 = 55.3mL/\min \approx 3.32L/h$$

$$Vd = 3.8 \cdot 50 + 3.1 \cdot 15.3 = 237.4L$$

$$k_e = \frac{CL}{Vd} = \frac{3.32}{237.4} = 0.012h^{-1}$$

$$t_{1/2} = \frac{0.693}{k_e} = \frac{0.693}{0.012} = 57.8h$$

$$C_p = \frac{Dose}{Vd} \cdot e^{-k_e \cdot t} = \frac{750}{237.4} \cdot e^{-0.012 \cdot 3.5} = 3.03mg/L$$