1. Quinidine gluconate \((S = 1.0, F = 0.71)\), a drug used for arrhythmia, was given as an oral 1 gram dose to a 73 kg male patient every 12 hours to maintain a \(C_{pss}\) of 5 \(\mu\)g/mL. Quinidine has an elimination rate constant of 0.11 hr\(^{-1}\) and a \(V_d\) of 197.1 L in this patient. \(\tau_f = 6.3\) hr

What is the patient’s \(C_p^o\)?

\[
\text{L.D.} = \frac{(C_{pss}) \cdot C_p^o \cdot \tau_f}{F \cdot S}
\]

(a) 0.20 L/min

(b) 0.28 L/min

(c) 16.7 L/min

(d) 11.8 L/min

(e) None of the above

2. What would be the loading dose of quinidine gluconate for the patient in question #1 to achieve a \(C_p\) of 3.6 \(\mu\)g/mL?

\[
\text{L.D.} = \frac{V_d \cdot C_p}{S \cdot F}
\]

(a) 700 mg

(b) 1000 mg

(c) 875 mg

(d) 1500 mg

(e) None of the above

3. If the above patient in question #1 has congestive heart failure, the quinidine \(C_p\) decreases to 4.0 mL/min*kg. How often does the patient need to be dosed 750 mg quinidine gluconate to maintain a \(C_{pss}\) of 2.8 \(\mu\)g/mL?

\[
\text{m.D.} = \frac{(C_{pss}) \cdot (C_p) \cdot \tau}{F \cdot S}
\]

(a) 1 hr

(b) 8 hr

(c) 11 hr

(d) 12 hr

(e) None of the above

4. As you fill the above prescription, you have 750 mg quinidine sulfate \((S = 1.0, F = 0.8)\) instead of quinidine gluconate. How often does the patient need to be dosed 750 mg quinidine sulfate to maintain a \(C_{pss}\) of 2.8 \(\mu\)g/mL? \(\) (Assume that the patient has congestive heart failure)

\[
\text{\(\tau\)} = \frac{(750 \text{mg}) \cdot (1)(0.8)}{(2.8 \text{mg/L})(0.292 \text{L/min})}
\]

(a) 1 hr

(b) 8 hr

(c) 11 hr

(d) 12 hr

(e) None of the above

\[
\text{\(\tau\)} = \frac{(733.9 \text{min})(\frac{1 \text{hr}}{60 \text{min}})}{(10.9 \text{hr} = \tau)}
\]

\[
\tau = 12.2\text{hr}
\]
5. A drug has an elimination half-life of 4.8 hours and follows one-compartment first-order kinetics. If a single 250 mg dose is given to an adult female patient (52 kg) by intravenous injection, how much of the dose is lost in 12 hours?

\[
\frac{t}{2} = 4.8 \text{ hr} \quad k_e = 0.693 \quad \frac{1}{4.8 \text{ hr}} = 0.144 \text{ hr}^{-1} = f_u \]

\[
\text{Fraction lost} = \left(1 - e^{-k_e t}\right) \quad t = 12 \text{ hr}
\]

(a) 44.25 mg
(b) 125 mg
(c) 189.5 mg
(d) 205.8 mg
(e) None of the above

\[
0.693 = \left(1 - e^{-1.728}\right) = \left(1 - e^{\ln(0.522)}\right) = \left(1 - e^{\ln(0.522)}\right)
\]

6. Will dapsone (pKa = 1.0), a weak base, have great difficulty crossing the biological membranes in the small intestine (pH 4-6)? What is its state of ionization?

(a) No, ionized
(b) Yes, ionized
(c) No, un-ionized
(d) Yes, un-ionized
(e) None of the above

\[
\text{Dapsone = weak base, pKa = 1.0}
\]

For a single extravascular dose of a drug that exhibits monoeponential disposition and first order absorption, how do the following changes in absorption or disposition kinetics affect \(C_{\text{max}}\), \(T_{\text{max}}\) and AUC.

\[
\text{AUC} = \frac{F \times \text{Dose}}{C_{\text{pe}}} \quad Cl_p = \frac{V_d \times K_d}{C_{\text{pe}}}
\]

7. \(Cl_p\) is increased, \(V_d\) unchanged, absorption kinetics (F, Dose, and \(k_a\)) unchanged.

(a) \(C_{\text{max}} = \text{decreased}\), \(T_{\text{max}} = \text{decreased}\), AUC = decreased
(b) \(C_{\text{max}} = \text{unchanged}\), \(T_{\text{max}} = \text{decreased}\), AUC = unchanged
(c) \(C_{\text{max}} = \text{decreased}\), \(T_{\text{max}} = \text{increased}\), AUC = increased
(d) \(C_{\text{max}} = \text{unchanged}\), \(T_{\text{max}} = \text{increased}\), AUC = increased
(e) none of the above

8. \(Cl_p\) is decreased, \(V_d\) unchanged, absorption kinetics (F, Dose, and \(k_a\)) unchanged.

(a) \(C_{\text{max}} = \text{increased}\), \(T_{\text{max}} = \text{decreased}\), AUC = unchanged
(b) \(C_{\text{max}} = \text{unchanged}\), \(T_{\text{max}} = \text{decreased}\), AUC = unchanged
(c) \(C_{\text{max}} = \text{decreased}\), \(T_{\text{max}} = \text{increased}\), AUC = increased
(d) \(C_{\text{max}} = \text{unchanged}\), \(T_{\text{max}} = \text{increased}\), AUC = increased
(e) none of the above

9. \(F\) is unchanged, \(k_a\) increased, Dose increased, disposition kinetics (\(Cl_p\), \(V_d\), \(k_d\)) unchanged.

(a) \(C_{\text{max}} = \text{unchanged}\), \(T_{\text{max}} = \text{decreased}\), AUC = unchanged
(b) \(C_{\text{max}} = \text{increased}\), \(T_{\text{max}} = \text{decreased}\), AUC = increased
(c) \(C_{\text{max}} = \text{increased}\), \(T_{\text{max}} = \text{increased}\), AUC = increased
(d) \(C_{\text{max}} = \text{unchanged}\), \(T_{\text{max}} = \text{increased}\), AUC = unchanged
(e) none of the above

10. \(Cl_p\) is unchanged, \(V_d\) increased, absorption kinetics (F, Dose, and \(k_a\)) unchanged.

(a) \(C_{\text{max}} = \text{increased}\), \(T_{\text{max}} = \text{decreased}\), AUC = unchanged
(b) \(C_{\text{max}} = \text{unchanged}\), \(T_{\text{max}} = \text{decreased}\), AUC = unchanged
(c) \(C_{\text{max}} = \text{increased}\), \(T_{\text{max}} = \text{increased}\), AUC = unchanged
(d) \(C_{\text{max}} = \text{unchanged}\), \(T_{\text{max}} = \text{increased}\), AUC = increased
(e) none of the above
11. F is unchanged, $k_a$ increased, Dose unchanged, disposition kinetics ($Cl_p$, $V_d$, $k_d$) unchanged.
   (a) $C_{\text{max}}$ = unchanged, $T_{\text{max}}$ = decreased, $\text{AUC}$ = unchanged
   (b) $C_{\text{max}}$ = unchanged, $T_{\text{max}}$ = decreased, $\text{AUC}$ = increased
   (c) $C_{\text{max}}$ = increased, $T_{\text{max}}$ = increased, $\text{AUC}$ = increased
   (d) $C_{\text{max}}$ = unchanged, $T_{\text{max}}$ = increased, $\text{AUC}$ = unchanged
   (e) none of the above

12. F is unchanged, $k_a$ decreased, Dose unchanged, disposition kinetics ($Cl_p$, $V_d$, $k_d$) unchanged.
   (a) $C_{\text{max}}$ = unchanged, $T_{\text{max}}$ = decreased, $\text{AUC}$ = unchanged
   (b) $C_{\text{max}}$ = unchanged, $T_{\text{max}}$ = decreased, $\text{AUC}$ = increased
   (c) $C_{\text{max}}$ = increased, $T_{\text{max}}$ = increased, $\text{AUC}$ = increased
   (d) $C_{\text{max}}$ = decreased, $T_{\text{max}}$ = increased, $\text{AUC}$ = unchanged
   (f) none of the above

Questions 13 - 17:

When a 184 mg dose of ceftriaxone was given i.v. to a newborn infant, the following plasma concentration-time relationship ($C_p$ in mg/L and $t$ in hours) was observed,

$$C_p = 140 \text{ mg/L} \cdot e^{-(0.0256/\text{hr})t}$$

13. Calculate the total AUC.
   (a) 5.47 g*hr/L
   (b) 7.19 g*hr/L
   (c) 5469 g*hr/L
   (d) 7188 g*hr/L
   (f) none of the above

14. Calculate the elimination half-life.
   (a) 0.113 days
   (b) 1.13 days
   (c) 2.71 days
   (d) 27.1 days
   (f) none of the above

15. What would be the plasma concentration be after 190 minutes of the i.v. dose?
   (a) 1.1 mg/L
   (b) 5.9 mg/L
   (c) 129 mg/L
   (d) 352 mg/L
   (e) none of the above

   $$C_p = 140 \text{ mg/L} \cdot e^{-(0.0256/\text{hr})(3.167 \text{ hr})}$$

   $$C_p = 140 \text{ mg/L} \cdot e^{-(0.0256/\text{hr})(0.0511)}$$

   $$C_p = 129 \text{ mg/L}$$
16. Ceftriaxone is most effective when its plasma concentration exceeds 20 μg/mL but results in unacceptable toxicity when the plasma concentration exceeds 150 μg/mL. What is the greatest i.v. bolus dose that could be administered to this patient without producing toxicity?

(a) 5 mg
(b) 26 mg
(c) 200 mg
(d) 7676 mg
(e) none of the above

17. How much time would the plasma concentration remain in the therapeutic range following a 50 mg dose in the patient?

(a) 5.6 hr
(b) 20.5 hr
(c) 25 hr
(d) 76 hr
(e) none of the above

Questions 18 - 20:
Mitenko and Ogilvie (1973) demonstrated the theophylline (S = 1.0, F = 1.0) followed a two-compartment pharmacokinetic model in human subjects. After administering a single intravenous dose (5.6 mg/kg) in nine normal volunteers (average weight, 76 kg), these investigators demonstrated that the equation best describing theophylline kinetics in humans was:

$$\text{Cp} = 12 \mu\text{g/mL} e^{(5.8/\text{hr})t} + 18 \mu\text{g/mL} e^{-(0.16/\text{hr})t}$$

18. What is the plasma level of the drug 15 min. after the i.v. dose? (15min × 1 hr = 0.25 hr)

(a) 0.148 μg/mL
(b) 17.28 μg/mL
(c) 30.0 μg/mL
(d) 12.0 μg/mL
(e) None of the above

19. Estimate the Area Under the Curve

(a) 6.87 μg/hr/mL
(b) 114.6 μg/hr/mL
(c) 0.115 μg/hr/mL
(d) 6874 μg/hr/mL
(e) None of the above

20. Estimate the Clp

(a) 3.28 L/hr
(b) 3.72 L/hr
(c) 30.5 L/hr
(d) 50.3 L/hr
(e) None of the above