Please choose the BEST answer of those provided. For numerical answers, choose “none of the above” if your answer is not within ± 5% of the correct answer. Place your answers on the scantron sheet provided.

For Questions 1 – 3, please match the following graphs (A, B, C, D) or E for “None” to their respective equation below.

A

\[ B - 1. \quad C_p = C_p^0 e^{-kt} - 1 \text{ comp} \]

B

\[ \text{E} - 2. \quad C_p = A e^{-\alpha t} + B e^{-\beta t} \quad 2 \text{ comp} \]

C

\[ C - 3. \quad A = A_0 e^{-kt} + A_{ss} (1 - e^{-kt}) \quad \text{bolus + infusion} \]
For Questions 4 – 7, match the following points (4, 5, 6, 7) on the graphs to their respective equations below. TPA has a half-life of 5.2 minutes.

\[ Cp = \frac{R_0}{V_d k} = \frac{R_0}{Cp} = Cp_{SS} \]

A. \[ \text{multiple-iv. infusions for } \] \[ Cp_{SS} \]

B. \[ Cp = \frac{R_0}{Cl_p} \left( 1 - e^{-k_{inf}} \right) \]

C. \[ A = \frac{\text{Dose} \cdot F \cdot S}{1 - e^{-k_I}} \]

D. \[ A = \text{Dose} \cdot F \cdot S \left( \frac{1 - e^{-Nk_I}}{1 - e^{-k_I}} \right) \]

E. None of the above.
For questions 8 and 11, use the information below:

Sumycin® (tetracycline) is primarily used as a broad spectrum antibiotic for infections. Sumycin® is available in 250 mg and 500 capsules and is usually administered every 12 hrs. Tetracycline has the following pharmacokinetic parameters: 

\( F = 0.77, \; \text{fe} = 0.58, \; V_d = 105 \; \text{L}, \; \text{and} \; k = 0.0654/\text{hr} \). Assume one-compartment elimination kinetics and that absorption is instantaneous relative to its elimination.

\[
C_{p} = \text{fe} \times 8.67 \text{L/hr} \times (\text{Vd}/k) \Rightarrow t_{1/2} = 10.6 \text{hr}
\]

8. What is the renal clearance, \( Cl_r \)?

A. \( 60.9 \text{ L/hr} \)
B. \( 6.86 \text{ L/hr} \)
C. \( 3.98 \text{ L/hr} \)
D. \( 2.88 \text{ L/hr} \)
E. None of the above.

9. What is the area under the curve (AUC) following an oral dose of 250 mg tetracycline?

A. \( 21 \text{ mg*hr/L} \)
B. \( 28 \text{ mg*hr/L} \)
C. \( 36 \text{ mg*hr/L} \)
D. \( 2943 \text{ mg*hr/L} \)
E. None of the above.

\[
\text{AUC} = \frac{D \times F}{C_{p}} = \frac{250 \text{mg}}{6.8674 \text{L/hr}}
\]

\[
\text{AUC} = 28.03 \text{mg*hr/L}
\]

10. What fraction of the dose is remaining in the body after 3 half-lives?

A. \( 0.125 \)
B. \( 0.25 \)
C. \( 0.50 \)
D. \( 0.75 \)
E. None of the above

\[
\text{fraction remaining} = \left( \frac{1}{2} \right)^n
\]

\[0.125 = \left( \frac{1}{2} \right)^3\]

11. What is \( C_p \) of tetracycline in a patient 6 hrs after a 1 gram oral dose of tetracycline?

A. \( 675 \text{ mg/L} \)
B. \( 520 \text{ mg/L} \)
C. \( 6.43 \text{ mg/L} \)
D. \( 4.95 \text{ mg/L} \)
E. None of the above

\[
C_p = \frac{1000 \text{mg} \times 0.77 \text{e}^{-0.0654 \times 6 \text{hr}}}{105 \text{L}}
\]

\[
C_{p_6} = 4.95 \text{ mg/L}
\]
Indocin® (indomethacin) is an anti-inflammatory drug used for the treatment of rheumatoid arthritis. Indocin® is available in 25-mg, 50-mg immediate release capsule and as a 75-mg sustained release capsule. Indomethacin displays one-compartment model pharmacokinetics and has the following pharmacokinetic parameters:

\[ F = 0.98, \quad V_d = 0.29 \text{ L/kg, and } t_{1/2} = 2.4 \text{ hrs.} \text{ Assume that absorption is instantaneous relative to its elimination.} \]

\[ t = \frac{0.289}{\ln 2} \Rightarrow 12 \text{ hrs to SS} \]

\[ V_d = \frac{0.29}{0.60} = 17.4 \text{ L} \quad \text{Cl}_{\text{p}} = 5.024 \text{ L/hr} \]

12. What is the accumulation ratio, \( R_{\text{acc}} \), in a 60 kg female patient who has been receiving 50 mg orally every 8 hrs for 3 days?

A. 1.00  
B. 1.11  
C. 10.10  
D. Not enough information is given to determine \( R_{\text{acc}} \).  
E. None of the above

\[ R_{\text{acc}} = \frac{1}{1 - e^{-\frac{t}{t_{1/2}}}} = \frac{1}{1 - e^{-\frac{8}{2.4}}} = \frac{1}{1 - e^{-3.33}} = 0.90 \]

13. What is the “average concentration of indomethacin in the body, \( C_{\text{pave}} \)” in the above patient who has been receiving 50 mg orally every 8 hrs for 1 day?

A. 73 mg/L  
B. 21 mg/L  
C. 22 mg/L  
D. The patient has not reached steady state; thus, the \( C_{\text{pave}} \) cannot be determined.  
E. None of the above

\[ C_{\text{pave}} = \frac{D \cdot S \cdot F}{C_{\text{p}} \cdot t} = \frac{(50 \text{ mg})(0.98)}{(5.024 \text{ L})(8 \text{ hrs})} = 1.23 \text{ mg/L} \]

14. What will the patient’s “minimum amount, \( A_{\text{min}} \)” in question #12 be following a 50-mg oral dose of Indocin® given every 4 hours for 7 days?

A. 1.3 mg  
B. 4.4 mg  
C. 22.5 mg  
D. 50.0 mg  
E. None of the above

\[ A_{\text{SS min}} = A_{\text{SS max}} e^{-\frac{t}{t_{1/2}}} = \frac{D \cdot S \cdot F}{(1 - e^{-\frac{t}{t_{1/2}}})} = \frac{(50 \text{ mg})(0.98)}{(1 - e^{-\frac{4}{2.4}})} \cdot (2.89 \text{ L/hr})(4 \text{ hrs}) = 2.25 \text{ mg/g} \]

\[
\frac{2.25 \text{ mg}}{g} = 71.51 \text{ mg}(0.3147)
\]
Please use the following information to answer questions 15 – 18.

Inocor® (amrinone) is a cardiac inotrope used for the short term management of severe congestive heart failure. Inocor® is available as a solution for i.v. administration for bolus doses or continuous infusions. Amrinone has the following first order pharmacokinetic parameters: \( \text{fe} = 0.25, \text{Cl}_p = 16.8 \text{ L/hr}, t_{1/2} = 4.4 \text{ hr} \).

\[ t_{ss} = 22 \text{ hrs} \]

15. At what TIME will steady state occur?
   A. 8.8 hrs
   B. 22 hrs ✓
   C. 5 half-lives
   D. A and C
   E. B and C

16. What INFUSION RATE, \( R_o \), is needed to maintain \( C_{pss} \) of 300 \( \mu \text{g/L} \) for a 70 kg male?
   A. 5.040 mg/hr
   B. 47.25 mg/hr
   C. 5.04 mg/hr ✗
   D. None of the above.

\[ C_{pss} = \frac{R_o}{\text{Cl}^p} = \frac{300 \mu \text{g}}{16.8 \text{ L/hr}} = \frac{R_o}{16.8 \text{ L/hr}} \]

\[ R_o = 5.040 \mu \text{g/hr} \]

17. If the above patient in question #16 was given an I.V. infusion at an infusion rate, \( R_o \), of 15 \( \mu \text{g/min} \times \text{kg} \) for 48 hrs, what is the CONCENTRATION of amrinone, \( C_p \), at 30 hrs?
   A. 400 mg/L
   B. 62.5 mg/L
   C. 3.75 mg/L
   D. 0.063 mg/L
   E. None of the above

\[ C_{p30} = C_{pss} = \frac{R_o}{\text{Cl}^p} = \frac{15 \mu \text{g}}{16.8 \text{ L/hr}} = \frac{15 \mu \text{g}}{16.8 \text{ L/hr}} = \frac{3750 \mu \text{g}}{L} \]

18. What is the AMOUNT of amrinone, \( A \), at 12 hours if the patient in question #16 is given an I.V. loading dose of 150 mg at the same time an I.V. infusion begins at a \( R_o \) of 42 mg/hr?
   A. 2.33 mg
   B. 63 mg
   C. 225 mg
   D. 250 mg
   E. None of the above.

\[ A_{12} = A^o e^{-\frac{t}{t_{1/2}}} + A_{ss} \left[ 1 - e^{-\frac{t}{t_{1/2}}} \right] \]

\[ = 150 \text{ mg} e^{-\frac{12 \text{ hr}}{4.4 \text{ hr}}} + \frac{42 \text{ mg/hr}}{0.1573 \text{ hr}} \left( 1 - e^{-\frac{12 \text{ hr}}{4.4 \text{ hr}}} \right) \]

\[ = 249.2 \text{ mg} \]

\[ = 22.797 \text{ mg} + 226.38 \text{ mg} \]
Tenormin® (atenolol) is a cardiac beta-blocker used for hypertension and chest pain. Tenormin® is available in 25-mg, 50-mg, and 100-mg tablets. Atenolol has the following first order pharmacokinetic parameters: \( f_e = 0.56, \ \text{Cl}_p = 7.2 \text{ L/hr}, \ \text{t}_{1/2} = 6.1 \text{ hr} \). \( \text{t}_k = 0.114/\text{hr} \) not included.

19. What is the \( C_p \) of atenolol, at 14 hrs in a patient that is receiving multiple i.v. infusions of 75 mg atenolol over 30 minutes every 6 hours?

A. 1.02 mg/L
B. 1.38 mg/L
C. 1.62 mg/L
D. 2.03 mg/L
E. None of the above.

\[
C_{p,14} = \frac{C_p}{\text{max}} e^{-\frac{\text{t}_k}{\text{t}_1/2}}
\]

\[
= \frac{75 \text{ mg}}{0.5 \text{ hr}} \times 150 \text{ mg/hr}
\]

\[ t = 6 \text{ hrs} \]

3 - Dose past \( N = 3 \)

\[ t' = 14 \text{ hr} - 12 \text{ hr} = 2 \text{ hr} \]

\[
C_{p,14} = C_{p,\text{max}} e^{-\frac{2}{0.114}}
\]

\[
= \frac{7.24 \text{ L/hr}}{1 - e^{-0.114/0.5 \text{ hr}}} \times \left[ 1 - e^{-0.114/6 \text{ hr}} \right] e^{-0.114/2 \text{ hr}}
\]

\[
= 20.833 \text{ mg} \left( \frac{0.055406 \times 0.09747 \times 0.79612}{0.49541} \right) (0.79612)
\]

\[
= 20.833 \text{ mg} \left( 0.09747 \right) (0.79612)
\]

\[
C_{p,14} = 1.62 \text{ mg/L}
\]