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

1. $\text{Cl}_p$ is unchanged, $V_d$ decreased, absorption kinetics are unchanged.
   (a) $T_{\text{max}}$ = decreased, $C_{\text{max}}$ = decreased, $\text{AUC}$ = decreased
   (b) $T_{\text{max}}$ = increased, $C_{\text{max}}$ = unchanged, $\text{AUC}$ = unchanged
   (c) $T_{\text{max}}$ = decreased, $C_{\text{max}}$ = increased, $\text{AUC}$ = increased
   (d) $T_{\text{max}}$ = decreased, $C_{\text{max}}$ = decreased, $\text{AUC}$ = unchanged
   (e) none of the above

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

3. $V_d$ unchanged, $\text{Cl}_p$ unchanged, $F$ is unchanged, $k_d$ increased, Dose unchanged
   (a) $T_{\text{max}}$ = decreased, $C_{\text{max}}$ = increased, $\text{AUC}$ = unchanged
   (b) $T_{\text{max}}$ = increased, $C_{\text{max}}$ = unchanged, $\text{AUC}$ = decreased
   (c) $T_{\text{max}}$ = increased, $C_{\text{max}}$ = increased, $\text{AUC}$ = increased
   (d) $T_{\text{max}}$ = decreased, $C_{\text{max}}$ = increased, $\text{AUC}$ = increased
   (e) none of the above

4. The volume of distribution of a drug:
   (a) Reflects the organs ability to remove drug from the blood.
   (b) Reflects the rate and extent of drug absorption.
   (c) Reflects the drug’s affinity to various tissues.
   (d) Reflects the extent of elimination.
   (e) None of the above.

5. Which of the following is true?
   (a) $\alpha$ is the distribution rate constant.
   (b) $\beta$ is the terminal half-life of a two-compartment model.
   (c) $k$ is the terminal elimination rate constant of a two-compartment model.
   (d) Disposition-limiting absorption kinetics occurs when the rate of elimination, $k$, is much greater than the rate of absorption, $k_{\alpha}$.
   (e) All of the above statements are false.
For questions 6 and 8, use the information below:

Noroxin® (norfloxacin) is primarily used for lower respiratory tract infections and urinary tract infections. Noroxin® is available in 400 -mg film-coated tablets and is usually administered every 12 hrs. Norfloxacin has the following pharmacokinetic parameters: \( F = 0.35, fc = 0.29, V_d = 224 \text{ L}, \) and \( t_{1/2} = 5 \text{ hrs}. \) Assume first-order absorption and elimination kinetics.

6. What amount of this drug will be remaining in the body 12 hours after an IV bolus dose of 800 mg?
   (a) 53 mg  
   (b) 150 mg  
   (c) 230 mg  
   (d) 650 mg  
   (e) None of the above.

7. What is the \( Cl_g \) of norfloxacin?
   (a) 1120 L/hr  
   (b) 325 L/hr  
   (c) 31 L/hr  
   (d) 9 L/hr  
   (e) None of the above

8. What is \( Cp \) of norfloxacin in a patient 8 hrs after a 400 mg oral ciprofloxacin dose.
   (a) 46 µg/L  
   (b) 132 µg/L  
   (c) 206 µg/L  
   (d) 590 µg/L  
   (e) None of the above

Use the following information to answer question 9 and 10.

Four different drug products containing the same antibiotic were given to 12 volunteer adult males (age 19 – 28 yrs, average weight is 73 kg) in a four-way crossover design. The volunteers were fasted for 12 hours prior to taking the drug product. Urine samples were collected up to 72 hours after the administration of the drug to obtain the maximum urinary drug excretion, \( A_{e,\infty} \). The data is presented below.

<table>
<thead>
<tr>
<th>Drug Product</th>
<th>Dose (mg/kg)</th>
<th>( A_{e,\infty} ) (mg, 0-72 hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV solution</td>
<td>0.2</td>
<td>20</td>
</tr>
<tr>
<td>Oral solution</td>
<td>4</td>
<td>380</td>
</tr>
<tr>
<td>Oral tablet</td>
<td>4</td>
<td>340</td>
</tr>
<tr>
<td>Oral capsule</td>
<td>4</td>
<td>360</td>
</tr>
</tbody>
</table>

9. What is relative bioavailability of the drug from the capsule compared to the oral solution \( (F_{\text{cap}}/F_{\text{sol}}) \)?
   (a) 0.89  
   (b) 0.95  
   (c) 1.05  
   (d) There is not enough information given.
   (e) None of the above.
10. What is absolute bioavailability of the drug from the tablet?
   (a) 0.85
   (b) 0.95
   (c) 17
   (d) There is not enough information given.
   (e) None of the above.

11. Which of the following is true?
   (a) Steady state concentrations can be attained quicker if the dose is doubled.
   (b) Steady state concentrations can be attained quicker if the dose is given more frequently.
   (c) Steady state concentration is independent of the plasma clearance, Clp.
   (d) All of the above are true.
   (e) All of the above statements are false.

12. A doctor would like to increase a patient’s theophylline plasma concentration from 6.0 mg/L to 25 mg/L. What does the new i.v. infusion rate need to be adjusted to if the old infusion rate to produce 6.0 mg/L at Cpss was 20.8 mg/hr?
   (a) 86.6 mg/hr
   (b) 70.0 mg/hr
   (c) 7.2 mg/hr
   (d) 3.5 mg/hr
   (e) None of the above

For questions 13 and 16, please use the information below:

Retrovir® (zidovudine) a pyrimidine nucleoside analogue active against human immunodeficiency virus (HIV). Retrovir® is available in 300-mg film-coated tablets and is usually administered as 600 mg every day. Zidovudine has the following pharmacokinetic parameters: \( F = 0.63, fe = 0.18, V_d = 1.4 \text{ L/kg, and } t_{1/2} = 1.1 \text{ hr.} \) Assume first-order absorption and elimination kinetics and that the absorption is instantaneous relative to the elimination.

13. A 75 kg male patient is given an I.V. infusion at an infusion rate, \( R_o \), of 25 mg/hr for 10 hrs. At what time will steady state occur?
   (a) 1.1 hr
   (b) 5.5 hrs
   (c) 11 hrs
   (d) 22 hrs
   (e) None of the above
14. What is the plasma concentration of zidovudine, $C_p$, at 6 hrs for the patient in question #13?
   (a) 24.4 mg/L  
   (b) 17.4 mg/L  
   (c) 0.369 mg/L  
   (d) 0.232 mg/L  
   (e) None of the above

15. What is the plasma concentration of zidovudine, $C_p$, at 13 hrs for the patient in question #13?
   (a) 0.057 µg/L  
   (b) 2.70 µg/L  
   (c) 3.78 µg/L  
   (d) 57.1 µg/L  
   (e) None of the above

16. If the patient in question #13 only received an oral 900 mg loading dose of Retrovir® (no iv infusion), what will the plasma concentration of zidovudine, $C_p$, be at 3 hrs for the patient?
   (a) 136 mg/L  
   (b) 97 mg/L  
   (c) 61 mg/L  
   (d) 0.82 mg/L  
   (e) None of the above

Use the following information to answers questions 17 through 20.

Park and associates (1983) studied the pharmacokinetics of amrinone after a single i.v. bolus injection (75 mg) in 14 healthy adult male volunteers.  The pharmacokinetics of this drug followed a two-compartment open model and the equation best describing amrinone kinetics in humans was:

$$C_p = 4.62 \, \mu g/mL \, e^{-(8.94/hr)^t} + 0.64 \, \mu g/mL \, e^{-(0.19/hr)^t}$$

17. What is the elimination rate constant from the entire body.
   (a) 0.08 hr$^{-1}$  
   (b) 1.70 hr$^{-1}$  
   (c) 1.35 hr$^{-1}$  
   (d) 3.65 hr$^{-1}$  
   (e) None of the above

18. What is the elimination rate constant from the central compartment ($k_d$).
   (a) 0.19 hr$^{-1}$  
   (b) 1.35 hr$^{-1}$  
   (c) 3.65 hr$^{-1}$  
   (d) 9.13 hr$^{-1}$  
   (e) None of the above
   (a) 0.5 L 
   (b) 3.9 L 
   (c) 14.3 L 
   (d) 27.7 L 
   (e) None of the above

20. Calculate $k_{12}$ and $k_{21}$.
   (a) 1.04 hr$^{-1}$ and 7.87 hr$^{-1}$, respectively for $k_{12}$ and $k_{21}$.
   (b) 7.87 hr$^{-1}$ and 1.04 hr$^{-1}$, respectively for $k_{12}$ and $k_{21}$.
   (c) 6.52 hr$^{-1}$ and 1.26 hr$^{-1}$, respectively for $k_{12}$ and $k_{21}$.
   (d) 1.26 hr$^{-1}$ and 6.52 hr$^{-1}$, respectively for $k_{12}$ and $k_{21}$.
   (e) None of the above