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 $C_{\text{max}}$ and $\text{AUC}$?

1. $Cl_p$ is unchanged; $V_d$ unchanged; $F$ decreased; Dose, $S$, and $k_a$ are unchanged.
   - (a) $C_{\text{max}}$ = unchanged, $\text{AUC}$ = decreased
   - (b) $C_{\text{max}}$ = unchanged, $\text{AUC}$ = unchanged
   - (c) $C_{\text{max}}$ = increased, $\text{AUC}$ = increased
   - (d) $C_{\text{max}}$ = decreased, $\text{AUC}$ = decreased
   - (e) none of the above

2. $k_a$ decreased; $F$, $S$, and Dose are unchanged; disposition kinetics ($Cl_p$, $V_d$, $k$) are unchanged.
   - (a) $C_{\text{max}}$ = decreased, $\text{AUC}$ = decreased
   - (b) $C_{\text{max}}$ = increased, $\text{AUC}$ = increased
   - (c) $C_{\text{max}}$ = decreased, $\text{AUC}$ = unchanged
   - (d) $C_{\text{max}}$ = increased, $\text{AUC}$ = unchanged
   - (e) none of the above

3. $Cl_p$ is unchanged; $V_d$ decreased; absorption kinetics ($k_a$), $F$, $S$, and Dose are unchanged.
   - (a) $C_{\text{max}}$ = unchanged, $\text{AUC}$ = unchanged
   - (b) $C_{\text{max}}$ = unchanged, $\text{AUC}$ = decreased
   - (c) $C_{\text{max}}$ = increased, $\text{AUC}$ = unchanged
   - (d) $C_{\text{max}}$ = increased, $\text{AUC}$ = increased
   - (e) none of the above

4. If the volume of distribution exceeds 15 L, the drug is most likely to be distributed to the:
   - (a) Extracellular compartments
   - (b) Tissues
   - (c) Vascular compartment
   - (d) None of the above

5. Which of the following is the best definition of alpha, $\alpha$?
   - (a) $\alpha$ is the absorption rate constant.
   - (b) $\alpha$ is the terminal half-life of a two-compartment model.
   - (c) $\alpha$ is the distribution rate constant of a one-compartment model.
   - (d) $\alpha$ is the distribution rate constant of a two-compartment model.
   - (e) $\alpha$ is the terminal elimination rate constant of a two-compartment model.

6. Which of the following statements is true?
   - (a) For a drug that follows first-order elimination kinetics, a 2-fold decrease in dose will result in a 2-fold decrease in the volume of distribution and area under the curve.
   - (b) For a drug that displays saturation kinetics (non-linear kinetics) at high doses, the elimination half-life ($t_{1/2}$) will remain constant until the point of saturation then will decrease afterwards.
   - (c) Rate-limiting absorption kinetics occurs when the rate of elimination, $k$, is much greater than the rate of absorption, $k_a$ ($k >>> k_a$).
   - (d) All of the above statements are true.
   - (e) All of the above statements are false.
For Questions 7 – 11, please use the following graph. This graph represents plasma levels of pralidoxime after an i.v. dose (10 mg/kg) to a healthy male patient.

7. What is the equation that appropriately describes the data of pralidoxime?
   (a) \( C_P = 25.5 \mu g/mL \cdot e^{-0.513 \times t} \)
   (b) \( C_P = 31.1 \mu g/mL \cdot e^{-0.513 \times t} \)
   (c) \( C_P = 5.6 \mu g/mL \cdot e^{-0.378 \times t} + 25.5 \mu g/mL \cdot e^{-0.513 \times t} \)
   (d) \( C_P = 25.5 \mu g/mL \cdot e^{-0.378 \times t} + 5.6 \mu g/mL \cdot e^{-0.513 \times t} \)
   (e) None of the above

8. Calculate the overall elimination half-life for pralidoxime.
   (a) 1.35 minutes
   (b) 9.67 minutes
   (c) 10.98 minutes
   (d) 81.1 minutes
   (e) None of the above

9. Calculate the AUC.
   (a) 26.04 mg·hr/mL
   (b) 63.54 mg·hr/mL
   (c) 434 mg·hr/mL
   (d) 1059 mg·hr/mL
   (e) None of the above

10. Calculate \( k_{\text{obs}} \) and \( k_{\text{e}} \) for pralidoxime.
    (a) 1.44 hr\(^{-1}\) and 1.08 hr\(^{-1}\), respectively
    (b) 0.24 hr\(^{-1}\) and 4.59 hr\(^{-1}\), respectively
    (c) 4.59 hr\(^{-1}\) and 0.24 hr\(^{-1}\), respectively
    (d) 1.08 hr\(^{-1}\) and 1.44 hr\(^{-1}\), respectively
    (e) None of the above

11. What is the plasma level of the drug 30 min. after the i.v. dose?
    (a) 4.3 \( \mu g/mL \)
    (b) 5.5 \( \mu g/mL \)
    (c) 8.2 \( \mu g/mL \)
    (d) 29.5 \( \mu g/mL \)
    (e) None of the above
Questions 12 - 14:

Huang et al (1986) evaluated the bioavailability of 200 mg ketoconazole in solution, suspension, and tablet in 23 patients (Figure 1) and the resulting $C_{\text{max}}$, $T_{\text{max}}$, and AUC is shown in Table 2. They also evaluated how an increase in dose changes the plasma-concentration time curves (Figure 2). Please answer questions 12 – 14 using the information below.

**TABLE 2. Summary of pharmacokinetic and bioavailability data after administration of 200-mg doses of ketoconazole in 23 volunteers.**

<table>
<thead>
<tr>
<th>Formulation</th>
<th>$C_{\text{max}}$ (µg/mL)</th>
<th>$T_{\text{max}}$ (h)</th>
<th>AUC (µg - h/mL)</th>
<th>$F_{\text{rel}}$ (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablet</td>
<td>4.22</td>
<td>1.7</td>
<td>16.74</td>
<td>7.9</td>
</tr>
<tr>
<td>Suspension</td>
<td>5.04</td>
<td>1.2</td>
<td>15.64</td>
<td>7.9</td>
</tr>
<tr>
<td>Solution</td>
<td>6.17</td>
<td>1.9</td>
<td>18.11</td>
<td>75.5</td>
</tr>
</tbody>
</table>

12. What is the RELATIVE bioavailability of Tablet compared to the Solution ($F_{\text{tablet}}/F_{\text{solution}}$)?
   
   (a) 0.81
   (b) 0.87
   (c) 0.93
   (d) 1.23
   (e) none of the above

13. What is the RELATIVE bioavailability of Suspension compared to the Tablet ($F_{\text{suspension}}/F_{\text{tablet}}$)?

   (a) 0.81
   (b) 0.87
   (c) 0.93
   (d) 1.07
   (e) none of the above

14. Using Figure 2, which of the following statements is true?

   (a) Ketoconazole displays first-order elimination at all doses.
   (b) Ketoconazole displays non-linear (saturation) kinetics at all doses.
   (c) Ketoconazole displays non-linear (saturation) kinetics at high doses.
   (d) The half-life of ketoconazole remains the same at all doses.
   (e) None of the above are true.
15. When developing an iv bolus multiple dose regimen, doubling both the dosing interval (tau) and the dose will result in the same average plasma concentration.  
True or False = B

16. The graph below demonstrates which of the following pharmacokinetic concepts:

a. Steady State  
b. The principle of superposition  
c. Plateau  
d. An iv bolus multiple dosing regimen  
e. None of the above

![Graph showing concentration over time](image)

17. 500 mg of tetracycllin is administered by iv bolus every 6 hours to a patient with an elimination t\(_{1/2}\) of 12 hrs and a volume of distribution of 60 L. The expected C\(_{\text{max}}\) at steady state would be:

a. 16.83 mg/L  

b. 28.82 mg/L  
c. 11.78 mg/L  
d. 8.3 mg/L  
e. none of the above
18. The time from point A to point B in the graph below during a short iv infusion regimen with a drug exhibiting 1st order elimination kinetics is which of the following:

a. tau  

b. time of infusion  

c. half-life  

d. rate of accumulation to plateau  

e. none of the above

19. 250 mg penicillin is given by iv bolus injection every 12 hours. Because the t₁/₂ is approximately 6.0 hours, steady state is reached after the first dose. True or False

20. Ertapenem (INVANZ, Merck) is a new once-a-day parenteral beta-lactam antimicrobial shown to be effective as a single agent for treatment of various community-acquired and mixed infections. Multiple-dose pharmacokinetics of ertapenem at doses of 3000 mg were examined in a healthy volunteer. The plasma concentration of ertapenem was 175 mg/L at the end of a 30-min infusion, the plasma half-life (t₁/₂) was 4.4 hr. Clearance is calculated to be which of the following:

a. 2.57 L/hr  

b. 34.29 L/hr  

c. 17.14 L/hr  

d. 1.29 L/hr  

e. none of the above
21. If 500 mg ertapenem is administered as an iv bolus every 6 hours the $A_{max}$ and $A_{min}$ after the 3rd dose would be:
   a. 1500 mg and 1000 mg
   b. 1206 mg and 470 mg
   c. 770 mg and 300 mg
   d. 2312 mg and 901 mg
   e. none of the above

22. The elimination half-life for ciprofloxacin, Cipro, ($F = 0.6$) is approximately 4 hours. What percent of this drug would be still remaining in the body 16 hours after an IV bolus dose?
   a. 6.25%
   b. 12.5%
   c. 25%
   d. 50%
   e. 93.75%

23. For the drug in question #22, how long will it take for 500 mg of the drug to decompose by 45%? (Assume first-order kinetics and constant temperature.)
   a. 35.9 hr
   b. 4.6 hr
   c. 3.5 hr
   d. 3.1 hr
   e. None of the above

24. How much drug in question #22, will be remaining in a patient 8 hrs after a 750 mg ciprofloxacin dose.
   a. 115 mg
   b. 185 mg
   c. 240 mg
   d. 560 mg
   e. None of the above