Circle your final answers. Use the following information to answer questions 1 – 3 (3 pts each).

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 $C_{\text{max}}, T_{\text{max}}$ and AUC.

1. $Cl_p$ is unchanged, $V_d$ unchanged, $F$ unchanged, Dose increased, and $k_a$ unchanged.

   $AUC = \frac{D \cdot F \cdot t_s}{Cl_p} = \uparrow AUC \quad \text{Cmax} = \uparrow \quad T_{\text{max}} \text{ (no change)}$

2. $F$ is decreased, $k_a$ unchanged, Dose unchanged, disposition kinetics ($Cl_p$, $V_d$, $k$) unchanged.

3. $Cl_p$ is decreased, $V_d$ unchanged, Dose unchanged, absorption kinetics ($F$, Dose, $k_a$) unchanged.

   $AUC = \frac{D \cdot F}{Cl_p} \downarrow AUC \quad \text{Cmax} \downarrow \quad \text{Tmax (no change)}$

4. Which of the following parameters was not discussed in lecture as being used to calculate hepatic clearance? (3 points)
   A. Hepatic blood flow
   B. Fraction of drug unbound in the plasma
   C. Fraction of drug bound in the plasma
   D. Intrinsic clearance
   E. All of the above were discussed in lecture as being used to calculate hepatic clearance.

5. Disease states a patient may have may have a significant affect on: (2 points)
   A. Hepatic blood flow
   B. Hepatic clearance
   C. Plasma protein binding
   D. A and B
   E. A, B, and C

6. If an oral dose of a drug with a high extraction ratio ($E > 0.8$) is 100% absorbed, what fraction of the dose is able to reach systemic circulation? (2 points)
   A. < 0.2
   B. > 0.8
   C. 0.8
   D. 0.2
   E. None of the above
Use the information below for questions 7 and 8. Show ALL work and include proper units.

GD is a 50 year old female who will be started on digoxin for rate control in atrial fibrillation. She weighs 52 kg, is 5'4" tall, with a serum creatinine of 1.1 mg/dL.

Digoxin PK: \( V_{\text{normal}} = 6.7 \text{ L/kg} \), \( V_{\text{renal failure}} = 4.7 \text{ L/kg} \).

Dosage forms available are 0.5 mg, 0.25 mg, and 0.125 mg tablets (\( F = 0.8 \)).

\[ \frac{2 \times 52 \text{ kg}}{51.71 \text{ L}} = 0.95 \text{ ml ABW} \]

7. Calculate an oral loading dose to target a serum concentration of 0.9 ng/mL and recommend a dosing regimen. (4 points).

\[
LD = C_{ss} \times V_d = \left( \frac{0.9 \text{ mg/L}}{6.7 \text{ L/kg} \times 52 \text{ kg}} \right) \times 0.8 = 39.195 \text{ mg} \quad \text{or} \quad 0.392 \text{ mg}
\]

Give 0.25 mg STAT, then 0.125 mg/dose x 2 doses @ 4-6 hr intervals.

8. Calculate the digoxin clearance. (5 points).

\[ ABW = 45.5 + 2.3(4) = 54.72 \text{ kg} \quad \text{ABW} < \text{IBW} \]

\[
C_{cl} = \left( \frac{140 - 50}{52 \text{ kg}} \right) \frac{0.85}{72 (1.1 \text{ mg/dL})} = 50.23 \text{ ml/min}
\]

\[
CL_{dig} = 1.303 \left( 50.23 \text{ ml/min} \right) + 40 \text{ ml/min}
\]

\[
CL_{dig} = 105.45 \text{ ml/min} \quad \text{or} \quad \frac{105.45 \text{ ml}}{\text{min}} \times \frac{1 \text{ hr}}{60 \text{ min}} \times \frac{1000 \text{ ml}}{1 \text{ L}} = 6.3274 \text{ hr}
\]