On my honor, I have neither given nor received unauthorized aid in doing this assignment.

Print: ______________________________________________________________________

Sign: ______________________________________________________________________

Version A

Q1: theophylline (10)
Q2: Cyclosporine (10)
Q3: vancomycin (5)
Q4: DDI (5)
Q5: Digoxin (10)
Q6: Phenytoin (5)
Q7: procainamide (10)
Q8: phenytoin (10)
Q9: Digoxin (10)
Q10: gentamicin (10)
Q11: Age (5)
Q12: Methotrexate (10)

Total Point: 100
Question 1:
G.H. is a 2-year-old, 10 kg male child in the PICU who is placed on a theophylline drip at 1 mg/kg/hr after first receiving a 5 mg/kg bolus at 1 pm. The resident on duty asks for your advice with the pharmacokinetic monitoring of the patient. You suggest a level at one and seven hours after starting the drip.

• Theophylline conc. at 2:00 pm: 12.3 mg/L
• Theophylline conc. at 8:00 pm: 19.1 mg/L

Please calculate the clearance and half-life of theophylline in G.H.

A) Cl: 0.33L/min; t1/2: 14.2h
B) Cl: 0.15L/h; t1/2: 10.1h
C) Cl: 0.28L/h; t1/2: 12.3h
D) Cl: 4.7mL/min; t1/2: 10.3h
E) Cl: 2.9mL/min; t1/2: 15.5h

\[
Cl = \frac{2 \times R_d}{(C_1 + C_2)} = \frac{2 \times V_d \times (C_1 - C_2)}{(C_1 + C_2) \times (C_2 - C_1)}
\]

\[
= \frac{2 \times 1 \text{ mg} \times 10\text{ kg} \times (12.3 \text{ mg/L} - 19.1 \text{ mg/L})}{(12.3 \text{ mg/L} + 19.1 \text{ mg/L})} = 0.26 \text{ L/h}
\]

\[
t_{1/2} = \frac{0.693}{Cl} \times \frac{0.693}{0.26 \text{ L/h}} = 12.34 \text{ h}
\]
Question 2:

B.D. is a 32 year old 72 kg male. He received a kidney transplant and is to be started on cyclosporine. Design an oral dosing regimen with a Cmax of 400ng/mL and a Cmin of 150ng/mL. Cyclosporine is rapidly absorbed.

A) 125 mg TID
B) 250 mg TID
C) 200 mg BID
D) 200 mg TID
E) 250 mg QD

\[ Cl = 0.5 \text{L/hr/kg} \times 72\text{kg} = 36\text{L/hr} \]

\[ Vd = 4.5 \text{L/kg} \times 72\text{kg} = 324\text{L} \]

\[ Ke = \frac{Cl}{Vd} = \frac{36\text{L/hr}}{324\text{L}} = 0.111\text{hr}^{-1} \]

\[ Tau = \frac{\ln(400/150)}{0.111 \text{hr}^{-1}} = 8.83 \text{hr} \approx 8\text{hours} \]

\[ Dose = Cmax \times (1-e^{-ke \times tau}) \times Vd/F = \frac{400\text{mg/L}}{1000} \times (1-e^{(-0.111 \text{hr}^{-1} \times 8\text{hr})}) \times 324\text{L}/0.3 \]

\[ = 254\text{mg} \approx 250\text{mg} \]

Dosing regimen = 250mg TID

Question 3:

With aminoglycosides usually Cmax and Cmin are calculated using IV infusion equations. However, with vancomycin it is acceptable to use IV bolus equations to calculate Cmax and Cmin instead of IV infusion equations. Why is it justified to use these equations with vancomycin compared to aminoglycosides?

A) Vancomycin has a lower clearance which results in a smaller fluctuation.
B) Vancomycin has a smaller volume of distribution which results in a larger fluctuation.
C) Vancomycin has a higher clearance which results in a larger half-life.
D) Vancomycin has a smaller half-life which results in a smaller fluctuation.
E) Vancomycin has a longer half-life which results in a smaller fluctuation.
Questions 4:

A clinical study was performed to assess the effect of Rifampin on the Tacrolimus pharmacokinetics after oral and intravenous administration. The same doses were used in the two phases. A washout period was between two phases. Rifampin is considered to be a first-line agent for the treatment of tuberculosis, and induces CYP3A metabolism and P-gp-mediated transport. Which of the following statement is FALSE based on the available information?

A) Tacrolimus could be a substrate of P-gp or CYP3A.
B) Dose regimen needs to be adjusted for tacrolimus when co-administration of rifampin.
C) Tacrolimus is partially eliminated by kidney.
D) Rifampin has impacts on the pharmacokinetics of tacrolimus.
E) Drug-drug interaction could be an issue for tacrolimus.

As indicated by the decrease of concentration of Tacrolimus when co-administration of rifampin, and Rifampin induces CYP3A metabolism and P-gp-mediated transport.

Renal clearance for Tacrolimus is 0% from class slide.

Rifampin could increase Tacrolimus elimination from body, which could result in no pharmacological/therapeutic effect of Tacrolimus.
Question 5:

Please mark the CORRECT statements about Digoxin.

1) Digoxin is a PGP-substrate.
2) Digoxin follows a one compartment body model.
3) Digoxin levels are increased in patients with hyperthyroid function.
4) Digoxin distributes rapidly into the myocardial tissue.
5) Digoxin is only renally eliminated

A) 1, 3, 4
B) 2, 3, 5
C) 1, 2, 3, 4
D) 1, 2, 4, 5
E) None of the above
Question 6:

Which of following statement is FALSE about phenytoin?

A) The metabolism of phenytoin is capacity–limited which means that the clearances values increase with increasing plasma concentrations (at high concentrations).
B) The bioavailability of phenytoin is difficult to evaluate because of the drug’s capacity–limited metabolism.
C) The clinical usefulness of the phenytoin half-life is limited because the time required to achieve steady state can be much longer than the usual 3 to 5 times the apparent half-life.
D) When the oral loading dose of phenytoin is divided into three separate doses, the possibility of nausea and vomiting decreases. And the time to peak concentration decreases too.
E) All of the above are true
A.S., a 62-year-old, 62 kg female, was admitted to the ER with a diagnosis of tachyarrhythmia. A.S. has a history of mild chronic renal failure, a serum creatinine of 1.7mg/dL. A.S. developed premature ventricular contractions (PVCs) which were unresponsive to lidocaine. Calculate a parenteral loading dose of procainamide designed to achieve a plasma concentration of around 7mg/L and an i.v. maintenance infusion rate that will maintain an average plasma concentration of 5mg/L.

A) Loading Dose = 1200 mg; Maintenance infusion rate = 184 mg/min
B) Loading Dose = 1000 mg; Maintenance infusion rate = 120 mg/min
C) Loading Dose = 1200 mg; Maintenance infusion rate = 3.5 mg/min
D) Loading Dose = 1000 mg; Maintenance infusion rate = 2 mg/min
E) Loading Dose = 1200 mg; Maintenance infusion rate = 150 mg/min

\[ V_d = 2L/kg \times 62kg = 124L \]

\[ LD = \frac{C_p \times V_d}{F \cdot S} = \frac{7 \times 124}{1 \times 0.87} = 997.7mg \approx 1000mg \]

\[ CL_{\text{creat}} = \frac{(140 - \text{age}) \times ABW}{85 \times C_{p_{\text{creat}}}} = \frac{(140 - 62) \times 62kg}{85 \times 1.7mg/dl} = 33.467ml/min = 2L/h \]

\[ CL_{\text{total}} = 3 \times 2L/h + 0.23 \times 62 = 20.26L/h \]

\[ MD = \frac{C_{pss} \times CL}{S \cdot F} = \frac{5mg/L \times 20.26L/h}{0.87 \times 1} = 116.44mg/h = 1.94mg/min \approx 2mg/min \]
Question 8:

An 85 kg patient is to be treated p.o. with sodium phenytoin capsules. Assuming a phenytoin volume of distribution of 0.65 L/kg, Km of 4 mg/L and Vmax of 7 mg/kg/day, calculate the daily maintenance dose to produce an average steady state phenytoin concentration of 15 mg/L.

A) 300 mg  
B) 400 mg  
C) 500 mg  
D) 600 mg  
E) 700 mg

Population value:
Vmax = 7 mg/kg/day * 85 = 595 mg/day  
Km = 4mg/L

R0=(Vmax*C/(Km+C))/S=595mg/day*15mg/L/(4mg/L+15mg/L)/0.92=510~500mg/day
Question 9:

A.H. (55 years old, 58 kg, SrCr = 2.5 mg/dL, female) was admitted to the hospital and was diagnosed with congestive heart failure. She had been taking 0.25 mg digoxin qd for 3 months. The digoxin plasma concentration was determined to be 5 μg/L. How long will it take for the concentration to fall back to 1 μg/L?

- a. 2 days
- b. 4 days
- c. 8 days
- d. 16 days
- e. 31 days

\[ \text{Clcr (female)} = (140-55) \times 58 / (85 \times 2.5) = 23.2 \text{ ml/min} \]

\[ \text{Cl (CHF patients)} = (0.33 \times 58) + (0.9 \times 23.2) = 40.0 \text{ ml/min} \sim 57.6 \text{ L/day} \]

\[ V = (3.8 \times 58) + (3.1 \times 23.2) = 292 \text{ L} \]

\[ k = \text{Cl} / V = 57.6 / 292 = 0.197 \text{ day}^{-1} \]

\[ t = \ln (C1/C2) / k = \ln (5/1) / 0.197 = 8.15 \text{ days} \]

Question 10:

A patient was given 100 mg gentamicin over 30 minutes (i.v.) from 8:30 to 9:00 am. The following two serum levels were measured: 6 μg/ml at 9:30 am and 2 μg/ml at 4:00 pm. Calculate:

a. the peak concentration at 9:00 am, b. the volume of distribution. (assume steady state levels)

- A. a:6.53 ug/ml, b:19.8L
- B. a:12.84ug/ml, b: 39.6L
- C. a:6.53 mg/ml, b:22.2L
- D. a: 12.84ug/ml, b:39.6L

a
\[ k = \frac{\ln \left( \frac{C^*_{\text{max}}}{C^*_{\text{min}}} \right)}{\Delta t} \]

\[ k = \frac{\ln 6}{6.5} = 0.169 \text{ hr}^{-1} \]

\[ t_{1/2} = \frac{0.693}{0.169} = 4.1 \text{ hr} \]

b.

\[ C_{\text{max}} = \frac{C^*_{\text{max}}}{e^{-k \cdot t_{\text{max}}}} \]

\[ C_{\text{max}} = \frac{6}{e^{-0.169 \cdot 0.5}} = 6.53 \mu g / mL \]

c.

\[ C_{\text{min}} = C^*_{\text{min}} \cdot e^{-k \cdot t_{\text{min}}} \]

\[ C_{\text{min}} = 2 \cdot e^{-0.169 \cdot 0.5} = 1.84 \mu g / mL \]

d.

\[ V_d = \frac{D}{k \cdot T} \cdot \left( \frac{1 - e^{-k \cdot T}}{C_{\text{max}} - C_{\text{min}} \cdot e^{-k \cdot T}} \right) \]

\[ V_d = \frac{100}{0.169 \cdot 0.5} \cdot \left( \frac{1 - e^{-0.169 \cdot 0.5}}{6.53 - 1.84 \cdot e^{-0.169 \cdot 0.5}} \right) = 1183.43 \cdot \frac{0.081}{4.84} = 19.8 \text{ L} \]
Question 11:
Which combination of the following pharmacokinetic changes best describes the elderly and neonates? (These groups share similar PK characteristics.)

1. Low renal clearance
2. Longer half-lives
3. Low metabolic clearance
4. Decreased protein binding
5. Relatively less body water

A) 1 & 4

B) 1, 2, 3 & 4

C) 1, 3, 4 & 5

D) 1, 4, & 5

E) all of the above
Questions 12:

T.X. is a 53 kg female patient (47 years) to receive methotrexate therapy. Her serum creatinine is 1.2 mg/dL. She is treated with a loading dose (20 mg) followed by an infusion of 25 mg/h over 36 hours. She will then receive a 10 mg/m² dose of leucovorin q6h (four doses) followed by eight oral doses (q6h) of 20 mg. Calculate the expected MTX concentration at 60hr after the start of the infusion and the expected time that the methotrexate level will fall below 0.1 μM by using the typical half-life parameters? After the drug sampling report [14 μM (24h), 1.74 μM (48 h), and 0.20 μM (75h)], adjust your prediction according to data. (You can assume the plasma concentration already reached steady state after 24 hrs infusion.)

A) Expected: $C_{60h}=0.24uM$, $t_{0.1uM}=73$ hr; Adjusted: $C_{60h}=0.40uM$, $t_{0.1uM}=90$ hr
B) Expected: $C_{60h}=0.40uM$, $t_{0.1uM}=80$ hr; Adjusted: $C_{60h}=0.45uM$, $t_{0.1uM}=85$ hr
C) Expected: $C_{60h}=0.75uM$, $t_{0.1uM}=88$ hr; Adjusted: $C_{60h}=0.55uM$, $t_{0.1uM}=82$ hr
D) Expected: $C_{60h}=0.40uM$, $t_{0.1uM}=80$ hr; Adjusted: $C_{60h}=0.65uM$, $t_{0.1uM}=88$ hr
E) Expected: $C_{60h}=0.15uM$, $t_{0.1uM}=68$ hr; Adjusted: $C_{60h}=0.32uM$, $t_{0.1uM}=108$ hr

Calculate the expected MTX steady-state concentration (in μM).

$$CL_{Cr} = \frac{(140 - 47) \cdot 53}{85 \cdot 1.2} = 48.3 mL/min \approx 2.9 L/h$$

$$CL_{MTX} = CL_{Cr} \cdot 1.6 = 2.9 L/h \cdot 1.6 = 4.64 L/h$$

$$C_{ss} = \frac{R_{u}}{CL} = \frac{25mg/h}{4.64L/h} = \frac{5.39mg/L}{0.454} = 11.87uM$$

Calculate the predicted concentrations at 24, 48 and 60 h after the start of the MTX infusion.

36 h: $11.87 \mu M$

$$t_{0.5\mu M} = \frac{\ln \left( \frac{11.87}{0.5} \right)}{0.231} + 36 = 13.7 + 36 = 49.7 h$$
60 h: \[ Cp = 0.5 \mu M \cdot e^{-0.0693(60 - 49.7)} = 0.24 \mu M \]

\[ t_{0.1 \mu M} = \frac{\ln\left(\frac{0.5}{0.1}\right)}{0.0693} + 49.7 = 72.9 h \]

The reported levels were 14 \( \mu \)M (24h), 1.74 \( \mu \)M (48 h), and 0.20 \( \mu \)M (75h)

\[ k_\alpha = \frac{\ln\left(\frac{14}{1.74}\right)}{12} = 0.174 h^{-1} \]

\[ t_{0.5 \mu M} = 36 + \frac{\ln\left(\frac{14}{0.5}\right)}{0.174} = 55.2 h \]

\[ k_\beta = \frac{\ln\left(\frac{0.5}{0.2}\right)}{75 - 55.2} = 0.0463 h^{-1} \]

\[ T_{1/2 \beta} = 15 h \Rightarrow Cp60 = 0.4 \mu M \text{ and } t_{0.1 \mu M} = 90 h \]
Once-a-day Aminoglycosides

Aminoglycosides

\[ V_d \text{ [L/kg]} = 0.25 \]

\[ CL \text{ [L/h/kg]} = CL_{Cr} \]

\[ t_{1/2} \text{ [h]} = 2-3 \]

\[ \% \text{ renal} = 100 \]

\[ F = - \]

\[ S = - \]

\[ C_{max} \text{ [mg/L]} > 8-10 \cdot \text{MIC} \]

\[ C_{min} \text{ [mg/L]} < 2 \text{ (G, T)} \]

\[ < 10 \text{ (A)} \]

Dosing Weight

- if TBW > 1.2 IBW: IBW + 0.4 (TBW - IBW)
- Third Space Fluids: Add to \( V_d \) (1L/kg)

Dettli Equation:

\[ k = 0.00293 \cdot CL_{Cr} \text{[ml/min]} / 0.014 \text{ [h}^{-1}] \]
Cyclosporine

Vd [L/kg] 4.5 L/kg
CL [L/h/kg] 0.5
$ t_{1/2}$ [h] 7
% renal -
F 0.3
S -
$f_u$ 0.1
$C_{max}$ [ng/mL] <400
$C_{min}$ [ng/mL] >150

Tacrolimus

Vd [L/kg] 1
CL [L/h/kg] 0.04-0.08
$ t_{1/2}$ [h] 10
% renal -
F 0.25 (highly variable)
S -
$f_u$ 0.01
$C_{max}$ [ng/mL] <20
$C_{min}$ [ng/mL] >5
### Methotrexate

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{Vd} [\text{L/kg}]$</td>
<td>$0.2 ,(V_o)$, $0.7 ,(V_d)$</td>
</tr>
<tr>
<td>$\text{CL} [\text{L/h/kg}]$</td>
<td>$1.6 \cdot \text{CL}_{\text{Cr}}$</td>
</tr>
<tr>
<td>$t_{1/2} [\text{h}]$</td>
<td>$3 &gt; 0.5 ,\mu\text{M}$, $10 &lt; 0.5 ,\mu\text{M}$</td>
</tr>
<tr>
<td>% renal</td>
<td>80</td>
</tr>
<tr>
<td>$F$</td>
<td>1 (&lt;30mg/m$^2$)</td>
</tr>
<tr>
<td>$S$</td>
<td>1</td>
</tr>
<tr>
<td>$f_u$</td>
<td>0.5</td>
</tr>
<tr>
<td>$\mu\text{M} = \text{mg/L}/0.454$</td>
<td></td>
</tr>
<tr>
<td>MTX</td>
<td>LD and 36h-Infusion</td>
</tr>
<tr>
<td>% Leucovorin-Rescue</td>
<td>10 mg/m$^2$ Q6h for 72h or MTX&lt;0.1 \mu M</td>
</tr>
<tr>
<td>if MTX &gt; 1 \mu M at 48h, increase</td>
<td>Leucovorin to 50-100 mg/m$^2$ Q6h</td>
</tr>
</tbody>
</table>

**Body Surface Area**

$$BSA = \left( \frac{TBW}{70} \right)^{0.73} \cdot 1.73 \,m^2$$
### Lidocaine

<table>
<thead>
<tr>
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<th>Value</th>
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<tbody>
<tr>
<td>$V_c$, $V_d$ [L/kg]</td>
<td>0.5, 1.3 TBW 0.3, 0.9 (CHF) 0.6, 2.3 (Cir.)</td>
</tr>
<tr>
<td>$CL$ [L/h/kg]</td>
<td>0.6 IBW 0.36 (CHF) 0.36 (Cir.)</td>
</tr>
<tr>
<td>$t_{1/2}$ [h]</td>
<td>0.1 ($\alpha$) 1.7 ($\beta$)</td>
</tr>
<tr>
<td>% renal</td>
<td>2</td>
</tr>
<tr>
<td>$F$</td>
<td>0.4</td>
</tr>
<tr>
<td>$S$</td>
<td>0.87</td>
</tr>
<tr>
<td>$C_{max}$ [mg/L]</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>$C_{min}$ [mg/L]</td>
<td>&gt; 1</td>
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</table>

### Procainamide

<table>
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<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>$V_d$ [L/kg]</td>
<td>2</td>
</tr>
<tr>
<td>$CL$ [L/h]</td>
<td>$3 \cdot CL_{Cr} + 0.23 \cdot BW$ ↓ (0.5) in CHF $1.6 \cdot CL_{Cr} + 0.025 \cdot BW$</td>
</tr>
<tr>
<td>$t_{1/2}$ [h]</td>
<td>0.1 ($\alpha$) 3 ($\beta$) 6</td>
</tr>
<tr>
<td>% renal</td>
<td>70</td>
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<tr>
<td>$F$</td>
<td>0.85</td>
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<tr>
<td>$S$</td>
<td>0.87</td>
</tr>
<tr>
<td>$C_{max}$ [mg/L]</td>
<td>&lt; 8</td>
</tr>
<tr>
<td>$C_{min}$ [mg/L]</td>
<td>&gt; 4</td>
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### Phenobarbital

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<thead>
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<tbody>
<tr>
<td>Vd [L/kg]</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>CL [L/h/kg]</td>
<td>0.004 (ad.)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.008 (ch.)</td>
<td></td>
</tr>
<tr>
<td>t₁/₂ [h]</td>
<td>120 (ad.)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>60 (ch.)</td>
<td></td>
</tr>
<tr>
<td>% renal</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>0.9 (sodium)</td>
<td></td>
</tr>
<tr>
<td>Cₘₐₓ [mg/L]</td>
<td>&lt;40</td>
<td></td>
</tr>
<tr>
<td>Cₘᵢₙ [mg/L]</td>
<td>&gt;15</td>
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### Carbamazepine

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Unit</th>
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<tbody>
<tr>
<td>Vd [L/kg]</td>
<td>1.4 (variable)</td>
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</tr>
<tr>
<td>CL [L/h/kg]</td>
<td>0.064 (mono)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.1 (poly)</td>
<td></td>
</tr>
<tr>
<td>t₁/₂ [h]</td>
<td>30 (first dose)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>15 (mono)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 (poly)</td>
<td></td>
</tr>
<tr>
<td>% renal</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>0.8 IR (0.7 XR)</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Cₘₐₓ [mg/L]</td>
<td>&lt;12</td>
<td></td>
</tr>
<tr>
<td>Cₘᵢₙ [mg/L]</td>
<td>&gt;4</td>
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</table>
Valproic Acid

- **Vd [L/kg]**: 0.14 (variable)
- **CL [L/h/kg]**:
  - Adults: 0.008
  - Children: 0.013
- **t_{1/2} [h]**:
  - Adults: 11
  - Children: 7
- **% renal**: 2
- **F**: 1
- **S**: 1
- **C_{max} [mg/L]**: < 100
- **C_{min} [mg/L]**: > 50

Theophylline

- **Vd [L/kg]**: 0.5
- **CL [L/h/kg]**:
  - Adults: 0.04
  - Children: 0.08
- **t_{1/2} [h]**:
  - Adults: 8
  - Children: 4
- **% renal**: 18
- **F**: 1
- **S**: 0.8 (A)
- **C_{max} [mg/L]**: < 20
- **C_{min} [mg/L]**: > 10

Clearance-Factor:
- Smoking: 1.6
- CHF: 0.4
- Cystic Fibrosis: 1.5
- Cirrhosis: 0.5
- Pulmonary Edema: 0.5
- Viral Illness: 0.5
- Erythromycin: 0.75
- Ciprofloxacin: 0.7
- Cimetidine: 0.6
- Influenza vaccine: 0.5
- Phenobarbital: 1.3
- Rifampin: 1.3
- Phenytoin: 1.6
Vancomycin

Loading Dose
Maintenace Dose
25 mg/kg
19 mg/kg

CL<sub>Cr</sub> [mL/min]

Dosing Interval [days]

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Figure 1: Detroit Receiving Hospital and University Health Center vancomycin dosing nomogram. (Updated 5/06)
Vancomycin

\[ V_d [L] = 0.17 \cdot \text{age} + 0.22 \cdot \text{TBW} + 15 \]

CL \[ CL_{Cr} \]

\[ t_{1/2} [h] = 7 \]

% renal \[ 80-90 \]

F \[ - \]

S \[ - \]

\[ C_{\text{max}} [\text{mg/L}] < 40-50 \]

\[ C_{\text{min}} [\text{mg/L}] \sim 10 \]

Phenytoin

\[ V_d [L/kg] = 0.65 \]

\[ V_{\text{max}} [\text{mg/kg/day}] = 7 \]

\[ K_M [\text{mg/L}] = 4 \]

% renal \[ 2 \]

F \[ 1 \]

S \[ 0.92 \]

\[ C_{\text{max}} [\text{mg/L}] < 20 \]

\[ C_{\text{min}} [\text{mg/L}] > 10 \]

Oral Products: 30, 50, 100, 200, 300

Bid or qd (Sustained Release)

\[ C = \frac{K_M \cdot R_0}{V_{\text{max}} - R_0} \]

\[ R_0 = \frac{V_{\text{max}} \cdot C}{K_M + C} \]

\[ R_0 = \frac{S \cdot F \cdot D}{\tau} \]

\[ V_{\text{max}} = \frac{D_1 \cdot D_2 \cdot (C_2 - C_1)}{C_2 \cdot D_1 - C_1 \cdot D_2} \]

\[ C_{\text{normed}} = \frac{C'}{(1 - 0.1) \cdot \frac{\text{Album}}{4.4} + 0.1} \]
## Digoxin

**Vd [L]**  
\[3.8 \cdot \text{IBW [kg]} + 3.1 \cdot \text{CL}_{\text{Cr}} [\text{mL/min}]\]

**CL [mL/min]**  
\[0.8 \cdot \text{IBW} + \text{CL}_{\text{Cr}} [\text{mL/min}]\]  
\[(\text{CHF}) \quad 0.33 \cdot \text{IBW} + 0.9 \cdot \text{CL}_{\text{Cr}} [\text{mL/min}]\]

**t\(_{1/2}\) [h]**  
40

**% renal**  
60

**F**  
0.7 (T), 0.8 (E), 1.0 (C)

**S**  
1

**\(C_{\text{max}} \text{ [ng/mL]}\)**  
< 2

**\(C_{\text{min}} \text{ [ng/mL]}\)**  
> 0.8