<table>
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<tr>
<th></th>
<th>Drug</th>
<th>Points</th>
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<td>Digoxin</td>
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<td>2</td>
<td>Theophylline</td>
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<td>3</td>
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<td>4</td>
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R.J. is a 50-year-old, 70-kg man (non-obese) and has a serum creatinine of 1.2 mg/dL. R.J. is on long-term medication with verapamil. Calculate an oral maintenance dose at that will achieve an average steady state digoxin plasma concentration of 750 ng/L. You may assume a rapid absorption process.

\[
CL_{Cr} = \frac{(140 - \text{age})(\text{weight in kg})}{72(SCR_{ss})} = \frac{(140 - 50)(70)}{72(1.2)} = 72.9 \text{ mL/min}
\]

\[
CL_{\text{min}} = (f_{\text{verapamil}})(0.8(\text{weight in kg}) + (CL_{Cr} \text{ in } \frac{\text{mL}}{\text{min}}))
\]

\[
= 0.75(0.8 \times 70 + 72.9) \approx 97 \text{ mL/min}
\]

\[
97 \text{ mL/min} = 5.8 \frac{L}{h} = 139.2 \frac{L}{\text{day}}
\]

\[
MD = \frac{CL \times C_{ss,avg} \times \tau}{F} = \frac{139.2 \frac{L}{\text{day}} \times 0.75 \frac{\mu g}{L} \times 1 \text{day}}{0.7} \approx 150 \mu g
\]

A 100 mg
B 150 mg
C 100 \mu g
D 150 \mu g
E 200 mg
2) J.D. is a 2-year-old, 9 kg male child in the hospital who is placed on a theophylline drip at 1 mg/kg/hr after first receiving a 5 mg/kg bolus at 1 pm. The infusion is discontinued at 10pm. Plasma concentration samples were obtained at 2pm and 8pm and were 12 mg/L and 18 mg/L, respectively. Estimate his theophylline half-life based on the Chiou-equation?

\[ VD = \left( 0.5 \frac{L}{kg} \right) (9kg) = 4.5L \]

\[ R_0 = 9 \frac{mg}{h} \]

\[ CL = \frac{2R_0}{C_1 + C_2} + \frac{2Vd(C_1 - C_2)}{(C_1 + C_2)(t_2 - t_1)} = \frac{2 \left( 9 \frac{mg}{h} \right)}{(12 + 18) \frac{mg}{L}} + \frac{2(4.5L)(12 - 18) \frac{mg}{L}}{(12 + 18) \frac{mg}{L} (6h)} = \]

\[ 0.6 \frac{L}{h} - 0.3 \frac{L}{h} = 0.3 \frac{L}{h} \]

\[ k_e = \frac{CL}{VD} = \frac{0.3 \frac{L}{h}}{4.5L} = 0.0666 \frac{L}{h} \]

\[ t_{0.5} = 10.4h \]

A 10 h
B 12 h
C 14 h
D 16 h
E Chiou-Equation is not applicable for this situation
R.I., a 39-year-old, 52-kg woman, 5’6” tall, who received a liver transplant, is to be started on oral treatment with cyclosporine. Recommend a dosing regimen (dose and dosing interval) that would achieve total steady state concentrations of 400 and 150 ng/mL. You may assume a rapid absorption process.

\[
CL = \left(0.5 \frac{L}{h(kg)}\right)52kg = 26 \frac{L}{h}
\]

\[
VD = \left(4.5 \frac{L}{kg}\right)52kg = 234L
\]

\[
k_e = \frac{CL}{VD} = \frac{26 \frac{L}{h}}{234L} = 0.111 \frac{1}{h}
\]

\[
\tau = \frac{\ln \left(\frac{C_{max,ss,total}}{C_{min,ss,total}}\right)}{k_e} = \frac{\ln \left(\frac{400 \frac{ng}{mL}}{150 \frac{ng}{mL}}\right)}{0.111 \frac{1}{h}} = 8.84h \approx 8h
\]

\[
C_{max,ss,total} = \frac{F(Dose)}{VD} \frac{1}{(1 - e^{-k_e \tau})}
\]

Thus,

\[
Dose = \frac{(C_{max,ss,total})(VD)(1 - e^{-k_e \tau})}{F} = \frac{\left(400 \frac{\mu g}{L}\right)(459L)\left(1 - e^{-0.111 \frac{1}{h}8h}\right)}{0.3}
\]

\[
\approx 360mg
\]

A 320 mg  
B 340 mg  
C 360 mg  
D 380 mg  
E 400 mg
Which of the following changes will happen when clearance decreases? (assume volume of
distribution does not change)

A) Shorter half-life, higher average steady state concentration
B) Longer time to steady state, shorter half-life
C) Longer time to steady state, lower average steady state concentration
D) Longer time to steady state, higher average steady state concentration
E) All of them are false

Cl decreases, Vd keeps the same, so ke decreases, t1/2 becomes longer,
The time to steady state becomes longer, Cpss average increases.
Drug A, which is known to be a low-extraction drug, is given as an IV infusion. How would simultaneous administration of drug B that is known to significantly inhibit the main metabolic enzymes of drug A affect the plasma concentration at steady state ($C_{pss}$) of drug A?

A) $C_{pss}$ increases  
B) $C_{pss}$ decreases  
C) $C_{pss}$ no change  
D) Not predictable

$Cl_{int}$ of drug will decrease when its metabolic enzyme is inhibited. So the $C_{pss}$ will increase.
A 100 kg patient is to be treated p.o. with sodium phenytoin capsules. Assuming a phenytoin volume of distribution of 0.65 L/kg, phenytoin Km of 4 mg/L and phenytoin Vmax of 7 mg/kg/day, calculate the following:

a. The loading dose to produce an initial phenytoin concentration of 18 mg/L. How would you administer this dose?

b. The daily maintenance dose to produce an average steady state concentration of 15 mg/L.

A. LD:1000mg, MD:300mg/day
B. LD:1300mg, MD: 900mg/day
C. LD:400mg dose followed by three 300mg doses at two hour intervals, MD: 600 mg/day
D. LD:300mg dose followed by three 200mg doses at two hour intervals, MD: 900 mg/day
E. LD:100mg dose followed by three 400mg doses at two hour intervals, MD: 300 mg/day

Answer: C

a.

\[ V_d = 0.65 \text{L/kg} \times 100 \text{kg} = 65 \text{L} \]

\[ LD = \frac{C_p \times V_d}{(S \times F)} = \frac{18 \text{mg/L} \times 65 \text{L}}{(0.92 \times 1)} = 1271 \text{mg} \approx 1300 \]

The dose is given as a 500mg dose, followed by three 300mg doses at two-hour intervals to decrease the possibility of nausea and vomiting which may be associated with a single large dose.

b. \[ MD = V_m \cdot Cpss \cdot \tau \frac{\tau}{(K_m + C) \cdot S \cdot F} = \frac{7 \text{mg/kg/day} \cdot 100 \text{kg} \cdot 15 \text{mg/L} \cdot 1 \text{day}}{(4 \text{mg/L} + 15) \cdot 0.92 \cdot 1} = 600 \text{mg/day} \]
7) C.S., a 13-year-old, 53.5 kg female, is receiving valproic acid sprinkles 250 mg (2x125mg) po every 8 hr for her seizure disorder. Calculate her valproic acid level at steady state. What dose adjustment would you recommend for this patient?

A. 100mg/L, continue with the current dose regiment
B. 75ug/mL, continue with the current dose regiment
C. 15mg/L, increase the dose to 500mg every 8 hr
D. 45ug/mL, increase the dose to 375mg every 8 hr
E. 75ug/mL, lower the dose to 200mg every 8 hr

Answer: D

Cl=(13mL/kg/hr)(53.5kg)=695.5mL/hr or 0.6955L/hr
Cpss ave=(1)(1)(250mg/8hr)/(0.6955L/hr)=44.9 mg/L=45mg/L=45ug/mL

valproic acid $C_{\text{max}}$ < 100mg/L, $C_{\text{min}}$ > 50mg/L.

Cpss ave=(1)(1)(375/8hr)/(0.6955L/hr)=67mg/L

or

Cpss ave=(1)(1)(500/8hr)/(0.6955L/hr)=90mg/L

Both 375mg or 500 mg works, but answer C has 15mg/L. so answer should be D
8)

H.P., a 45-year-old, 70kg male, is to be started on Phenobarbital for his seizure disorder. Calculate the maintenance dose of sodium Phenobarbital that will produce a steady-state concentration of 30 mg/L.

A. 201.6 mg/day sodium phenobarbital
B. 448 mg/day sodium phenobarbital
C. 224 mg/day sodium phenobarbital
D. 403.2 mg/day sodium phenobarbital
E. 180 mg/day sodium phenobarbital

Answer: C

\[ S = 0.9 \]
\[ F = 1 \]
\[ CL (adult) = 4 \text{ml/kg/hr} \]
\[ MD = \frac{C_{pss} \cdot Cl \cdot \tau}{S \cdot F} \]
\[ = (30 \text{mg/L}) \cdot (4 \text{ml/kg/hr}) \cdot 70 \text{kg} \cdot 24 \text{hr} / 0.9 \cdot 1 \cdot 1 \text{day} \cdot 1000 \text{ml} = 224 \text{mg/day} \]
V.A., a 25-year-old, 61-kg woman (non-obese, SCr = 1.2 mg/dL) is to receive a course of methotrexate (MTX) therapy for acute lymphoblastic leukemia. Her regimen will consist of an IV infusion of 40 mg/h for 36 hours. Calculate her anticipated MTX plasma level (in μM) 60h after the beginning of the infusion. You may assume that steady state has been achieved after 24h.

\[
CL_{Cr} = \frac{(140 - age)(weight \ in \ kg)}{72(SCr_{ss})} = \frac{(140 - 25)(61)}{85(1.2)} = 68.8 \frac{mL}{min}
\]

\[
68.8 \frac{mL}{min} = 4.1 \frac{L}{h}
\]

\[
CL_{MTX} = (1.6)CL_{Cr} = (1.6)4.1 \frac{L}{h} = 6.6 \frac{L}{h}
\]

\[
C_{36} = C_{ss,avg} = \frac{Dose}{\tau * CL} = \frac{40mg}{(1h)(6.6 \frac{L}{h})} = 6.1 \frac{mg}{L}
\]

\[
6.1 \frac{mg}{L} = 13.4 \mu M
\]

Let \( t^* \) be the time (after stop of the infusion) that is required to for MTX concentration to fall to 0.5 μM.

\[
t^* = \frac{ln\left(\frac{13.4 \mu M}{0.5 \mu M}\right)}{0.231 \frac{1}{h}} = 14.2h
\]

\[
60h - 36h - 14.2h = 9.8h
\]

\[
k_e(< 0.5\mu M) = \frac{ln(2)}{10h} = 0.0693 \frac{1}{h}
\]

\[
C_{60} = C_{50.2}(e^{-0.0693 \cdot 9.8h}) = 0.5\mu M(e^{-0.0693 \cdot 7.9h}) = 0.25\mu M
\]

A 0.15 μM
B 0.25 μM
C 0.35 μM
D 0.45 μM
E 0.55 μM
Determinate a regimen (dose and dosing interval) for Amikacin to treat a male patient (50-year-old, 60 kg, 160 cm, $C_{p,creat}=1.2\text{mg/dL}$,) that suffers from a pulmonary infection if the “true” peak and trough concentrations at steady state are supposed to be 30 mg/L and 5 mg/L, respectively. (Assume a short-term infusion over 30 minutes, $Cl=Cl_{creat}$ and $V_d=0.25\text{L/kg}$). Calculate $ke$ via $ke=Cl/V_d$

A) 600 mg, Q 8h  
B) 400 mg, Q12h  
C) 500 mg, Q 8h  
D) **400 mg, Q 8h**  
E) 500 mg, Q12h

$V_d= 0.25*60=15(\text{L})$

For male: IBW (kg) = 50 + 0.9*(height in cm - 150) = 50+0.9*(160-150) = 59 (kg)

TBW is smaller than 120\% IBW (60<59\% 120\%) so we can use TBW to calculate $Cl_{cr}$

$$CL_{cr}= \frac{(140-\text{age}) \cdot BW}{C_{p,cr} \cdot 72}\text{ min} \approx 3.75(\text{L/h})$$  

$$Ke=\frac{Cl_c}{V_d} =3.75/15=0.25$$

$$\tau = \frac{ln(\frac{C_{max}}{C_{min}})}{k} + T = \frac{ln\left(\frac{30}{5}\right)}{0.25} + 0.5=7.6\text{ (h)} \approx 8(\text{h})$$  

$$D=C_{max(\text{desired})} \cdot k \cdot V_d \cdot T \cdot \frac{(1-e^{-k \cdot \tau})}{(1-e^{-k \cdot T})}$$

$$= 30*0.25*15*0.5*\frac{(1-e^{-0.25*8})}{(1-e^{-0.25*0.5})}$$

$$=30*0.25*15*0.5*7.17= 403.3(\text{mg}) \approx 400(\text{mg})$$

So the regimen is 400 mg, Q 8h.
Which of the following statement is TRUE of triazolam metabolism based on the graph below:

A. 1, 2, 3 and 4
B. 3, 4 and 5
C. 2, 3 and 4
D. 1, 3 and 4
E. 2 and 5

Answer: A
12) An antibiotic pharmacokinetic behavior is best characterized by a 2-compartment model. The drug is administered once daily as an intravenous bolus and the following equation best characterizes its behavior: 

\[ C(t) = 18\exp(-0.415t) + 36\exp(-0.062t) \]

where the concentration is in mg/L and time is in hour. Estimate the steady-state area under the curve (AUC) and determine whether the 24-hr AUC/MIC ratio is greater than 400 if the MIC against a specific infection is 1.5 mg/L.

A. AUC = 624 mg.h/L; AUC/MIC ratio is greater than 400  
B. AUC = 580 mg.h/L; AUC/MIC ratio is greater than 400  
C. AUC = 580 mg.h/L; AUC/MIC ratio is less than 400  
D. AUC = 624 mg.h/L; AUC/MIC ratio is less than 400  
E. AUC = 1248 mg.h/L; AUC/MIC ratio is greater than 400

Answer: A

\[
AUC = 18/0.415 + 36/0.062 = 624
\]

\[
AUC/MIC\ ratio = 624/1.5 > 400
\]
P.M., a 45-year-old, 70-kg man, 5’2”, was admitted to the coronary care unit with a diagnosis of heart failure, probable myocardial infarction. Calculate a bolus dose that achieves lidocaine plasma level of 2.8 mg/L which should achieve an immediate response and calculate a maintenance infusion rate of that will achieve a steady-state lidocaine concentration of 2.5 mg/L. (Note: Lidocaine is available as lidocaine hydrochloride). Round appropriately.

\[ IBW_{male} = 50\text{kg} \times 2.3\text{kg}(2) = 54.6\text{kg} \]

\[ IBW \times 1.2 = 65.5\text{kg} \]

Thus, the patient is obese. Use TBW for \( V_c \) and IBW for \( CL \).

\[ V_c = \left( 0.3 \frac{L}{kg} \right) 70\text{kg} = 21L \]

\[ LD = \frac{(V_c)(C_{\text{max.desired}})}{S} = \frac{(21L)(2.8\text{mg/L})}{0.87} = 67.6\text{mg} \]

\[ MD = \frac{(CL)(C_{\text{avg}})}{S} = \frac{(0.36 \frac{L}{h\text{kg}} \times 54.6\text{kg})(2.5\text{mg/L})}{0.87} = 56.5\frac{mg}{h} \]

A. LD = 70 mg, MD = 55 mg/h
B. LD = 80 mg/h, MD = 55 mg
C. LD = 90 mg, MD = 65 mg/h
D. LD = 90 mg/h, MD = 65 mg
E. LD = 100 mg, MD = 65 mg/h
14) Which statement is **wrong**?

   A) Kidney function can be evaluated by creatinine clearance  
   B) Bioavailability of high extraction drugs is dependent on plasma protein binding.  
   C) A multi-compartment-body model has only one volume of distribution.  
   D) Clearance and volume of distribution determine the half-life of a drug.  
   E) Clearance will affect steady-state plasma levels