Aminoglycoside Homework Problems 2014

1. TM is a 40 yo female, hospitalized for a ruptured appendicitis. Prior to surgery, you are asked to recommend a tobramycin dose for this patient; she will also be started on piperacillin/tazobactam. Other pertinent data: height 5'2", 55 kg, SrCr 1.3 mg/dL. Desired steady-state peak is 6 mcg/ml; trough 1 mcg/ml.

a) Recommend an initial dose, using conventional dosing for TM.

↗ initial dose - use population parameters

$R_0 = \frac{70\,mg}{0.5\,h} = 140\,mg/h$

1. $CrCl = \frac{(140-40)(55)}{72 \times 1.3} \times 0.85 = 50\,mL/min$

2. $K_e = 0.00293\,(50\,mL/min) + 0.014 = 0.16/h$

3. $V_D = \frac{0.25\,L}{kg} \times 50.1\,kg = 12.5\,L$ ← use IBW! unless obese, then use Adjusted BW

$IBW = 45.5 + 2.3(2) = 50.1\,kg$

4. $LD\,(optional) = C_{max\,desired} \times V_D$

$LD = \frac{6\,mg}{L} \times 12.5\,L$

$LD = 75\,mg \Rightarrow 80\,mg\ IV$

5. $T = \frac{\ln(6\,mg/L \,/\, 1\,mg/L)}{0.16/h} + 0.5\,h = 11.7\,h \Rightarrow 12\,h$

6. $R_0 = (0.16/h)(12.5\,L)(6\,mg/L) \times \frac{(1-e^{-0.16/h \times 12\,h})}{(1-e^{-0.16/h \times 0.5\,h})}$ (12) (0.85339) (0.07688)

$R_0 = \frac{133\,mg}{h} \times 0.5\,h = 66.6\,mg \Rightarrow 70\,mg$ ← round aminoglycoside doses to nearest 10 mg

7. $C_p = \frac{\frac{140\,mg}{h}}{(0.16/h)(12.5\,L)} \times \frac{(1-e^{-0.16/h \times 0.5\,h})}{(1-e^{-0.16/h \times 12\,h})}$

$C_p = 6.3\,mg/L$

8. $C_T = \frac{6.3\,mg}{L} \times e^{-0.16/h\,(12\,h - 0.5\,h)}$

$C_T = 1\,mg/L \rightarrow ok$

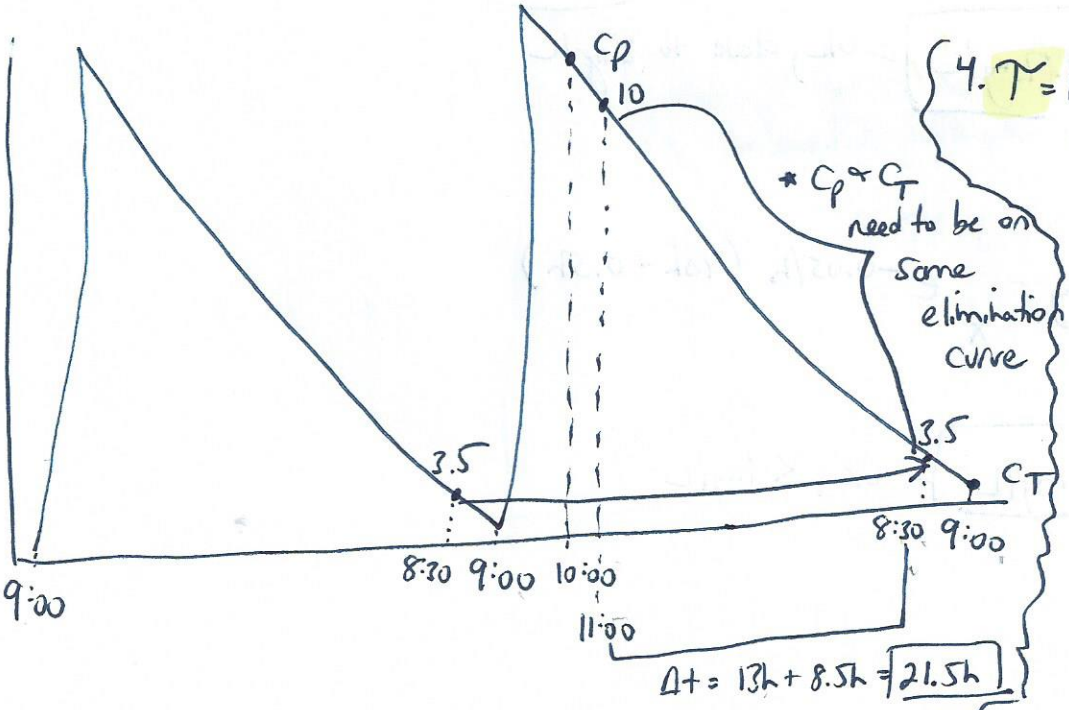
LD = 80 mg IV x 1,
then
70 mg IV q 12h.

$R_0 = \frac{120mg}{0.5h} = 240mg/h$

2. GF is a 50 yo, 75 kg, 178 cm man with gram-negative pneumonia. His Srcr is 3.5mg/dL and has been stable. Gentamicin 120mg Q24H was prescribed **(conventional dose).** He receives his gentamicin at 09:00 daily. Levels obtained on the 3rd day of therapy were reported as: 10 mcg/ml at 11:00, and 3.5 mcg/ml at 08:30. Desired peak is 8 mcg/ml and trough is 0.5 mcg/ml.

* Use pt-specific PK equations since you have measured levels *

a) Assess these concentrations and recommend dosing changes if necessary.



* Cp & CT need to be on same elimination curve

$\Delta t = 13h + 8.5h = 21.5h$

4. $T = \frac{\ln(8mg/L / 0.5mg/L)}{0.05/h} + 0.5h$

55.6h → try 48h

1. $k_e = \frac{\ln(C_1/C_2)}{t} = \frac{\ln(10mg/L / 3.5mg/L)}{21.5h} = 0.05/h$

5. $R_0 = (0.05/h)(16.9L)(8mg/L)\frac{(1-e^{-0.05/h \times 48h})}{(1-e^{-0.05/h \times 0.5h})}$

(0.90928; 0.02469)

$R_0 = \frac{249mg}{h} \times 0.5h = 124mg \Rightarrow$ 120mg

2. Ext peak

$C_2 = C_1 \times e^{-k_e x t}$

$10mg/L = C_p \times e^{-0.05/h \times 1h}$

$C_p = 10.5mg/L$

Ext trough

No need to ext. trough w/in 30 minutes

$C_T = 3.5mg/L$ too high!

3. $V_0 = \frac{\frac{240mg}{h}}{0.05/h} \times \frac{(1-e^{-0.05/h \times 0.5h})}{(10.5mg/L - 3.5mg/L)} = 16.9L$

120mg IV q 48h

$C_p = 7.7mg/L$; $C_T = 0.7mg/L$

6. $C_p = \dfrac{\dfrac{240\,mg}{h}}{(0.05/h)(16.9L)} \times \dfrac{(1-e^{-0.05/h \times 0.5h})}{(1-e^{-0.05/h \times 48h})}$

284.02 — 0.02469 — 0.90928

$C_p = 7.7\,mg/L$ — ok, close to 8 mg/L

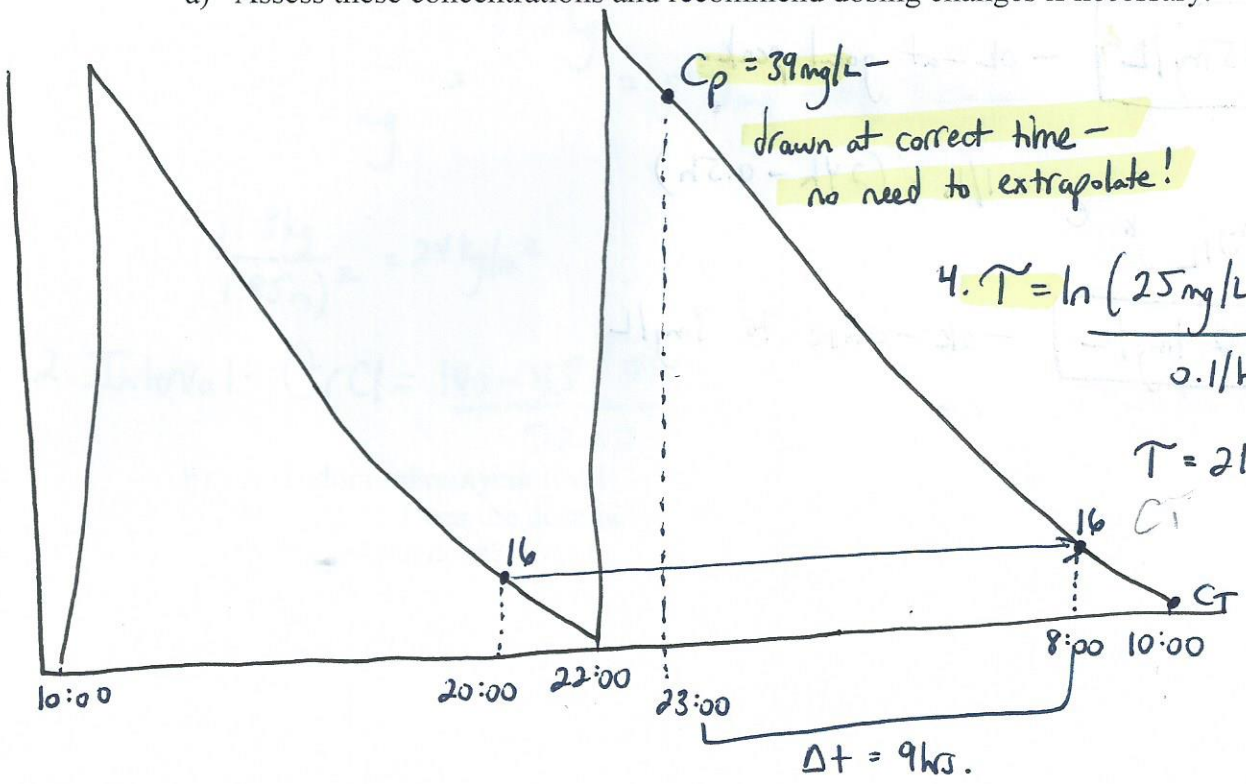
7. $C_T = \dfrac{7.7\,mg}{L} \times e^{-0.05/h\,(48h - 0.5h)}$

$C_T = 0.7\,mg/L$ — ok, < 1 mg/L

$R_0 = \frac{800\,mg}{0.5\,h} = 1600\,mg/h$

3. RT is a 5'10", 190 lb, 60 yo M admitted with gram-negative sepsis resistant to gentamicin and tobramycin. His SrCr is 1.8 mg/dL and has been stable. He is receiving amikacin 800mg IV q12h at 10:00 and 22:00. After the third dose, obtained levels are as follows: 16mcg/mL at 20:00 and 39 mcg/mL at 23:00. Desired amikacin peak is 25 mcg/ml and desired trough is 3 mcg/ml. ? = mg/L

a) Assess these concentrations and recommend dosing changes if necessary.



drawn at correct time – no need to extrapolate!

4. $T = \frac{\ln(25\,mg/L / 3\,mg/L)}{0.1/h} + 0.5h$

$T = 21.7h \Rightarrow \boxed{24h}$

1. $k_e = \frac{\ln(39\,mg/L / 16\,mg/L)}{9h} = \boxed{0.1/h}$

2. Ext trough

$C_2 = C_1 \times e^{-ke \times t}$

$C_T = 16\,mg/L \times e^{-0.1/h \times 2h}$

$\boxed{C_T = 13\,mg/L}$ too high!

Ext peak

No need to ext peak – drawn at right time.

$\boxed{C_p = 39\,mg/L}$

3. $V_0 = \frac{1600\,mg/h}{0.1/h} \times \frac{(1 - e^{-0.1/h \times 0.5h})}{(39\,mg/L - 13\,mg/L)} = \boxed{30\,L}$

5. $R_0 = (0.1/h)(30L)(25\,mg/L) \times \frac{(1 - e^{-0.1/h \times 24h})}{(1 - e^{-0.1/h \times 0.5h})}$

$R_0 = 1398\,mg/h \times 0.5h = \boxed{700\,mg}$

→

700 mg IV q 24h

$C_p = 25\,mg/L$; $C_T = 2.4\,mg/L$

6. $C_p = \dfrac{\dfrac{1400\,mg}{h}}{(0.1/h)(30\,L)} \times \dfrac{(1-e^{-0.1/h \times 0.5h})}{(1-e^{-0.1/h \times 24h})}$

$\boxed{C_p = 25\,mg/L}$ – ok – at goal peak

7. $C_T = 25\,mg/L \times e^{-0.1/h \times (24h - 0.5h)}$

$\boxed{C_T = 2.4\,mg/L}$ – ok – close to 3 mg/L

4. EM is a 45 yo, 180 lb, 6'1" man with *Pseudomonas aeruginosa* sepsis. His SrCr is 2.1 mg/dL and has been stable.

a) Recommend a tobramycin dose for this patient using extended-interval aminoglycoside dosing.

1. Dose = $\frac{7\text{ mg}}{\text{kg}} \times 81.8\text{ kg}$ → Use actual body wt $= 572\text{ mg} \Rightarrow$ **570 mg**

BMI = $\frac{81.8\text{ kg}}{(1.85\text{ m})^2} = 24\text{ kg/m}^2$

570 mg IV q36h

2. Interval: $CrCl = \frac{140 - 45(81.8\text{ kg})}{72 \times 2.1} =$ **51 mL/min** $\Rightarrow$ **Q36h**

b) A random tobramycin level drawn 7 hours after the dose (recommended above) is 11 mg/L. Does the dose need to be altered? If so, what is the new recommended dose?

- Plot concentration on the Hartford nomogram → falls within Q48h interval.

570 mg IV q 48h.

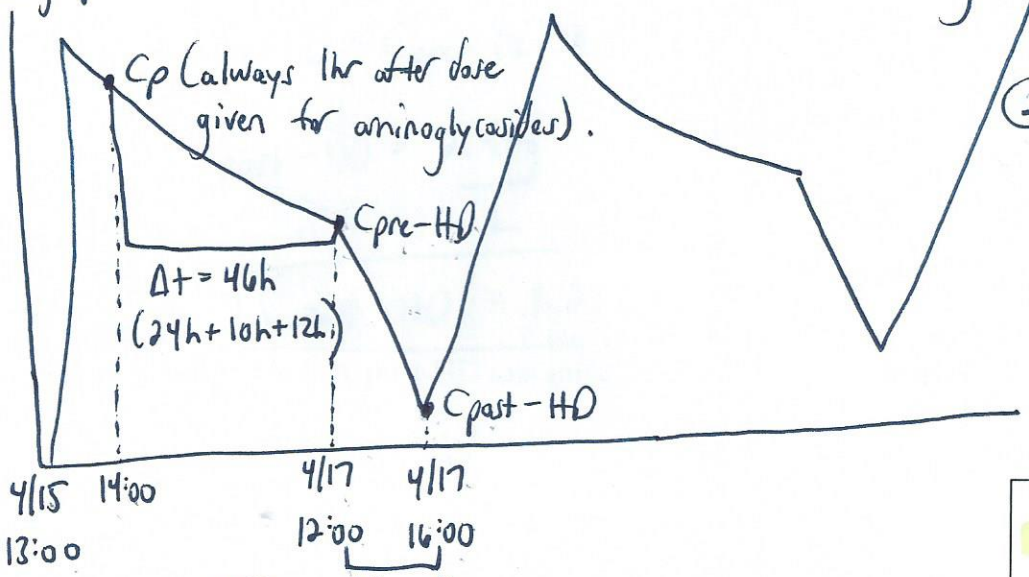
- Extend interval to Q48h

- Continue same dose: 570 mg – (dose always remains the same, but the interval may change).

mcg/mL = mg/L

5. AF is a 55yo, 80kg, 66-inch male with ESRD being admitted with suspected urosepsis. Ceftazidime and tobramycin are to be started. Desired tobramycin peak concentration is 6 mcg/ml. He is to receive his first dose 4/15/14 at 1300. Next scheduled hemodialysis session is 4/17/14 from 1200-1600. You are asked to recommend a dosing regimen for tobramycin.

* plot the graph 1st a) Recommend his first dose (4/15/14 at 1300). – asking for a "LD" - first dose



② $LD = C_{max\ desired} \times V_D$

$LD = \frac{6\ mg}{L} \times 16\ L = 96\ mg$

100 mg

① $V_D = \frac{0.25\ L}{kg} \times 63.8\ kg = 16\ L$ (IBW)

IBW = 50 + 2.3 (6) = 63.8 kg

100 mg IV tobramycin.

b) Estimate pre-HD concentration.

$C_2 = C_1 \times e^{-ke \times t}$

$C_{pre\text{-}HD} = C_{peak} \times e^{-ke_{off} \times t}$

↘ solve for C_{peak} 1st:

$C_{peak} = \frac{LD}{V_D} = \frac{100\ mg}{16\ L} = 6.25\ mg/L$

$C_{pre\text{-}HD} = \frac{6.25\ mg}{L} \times e^{-0.021/h \times 46h}$

$C_{pre\text{-}HD} = 2.4\ mg/L$

$C_{pre\text{-}HD} = 2.4\ mg/L$

c) Estimate post-HD concentration.

$$C_2 = C_1 \times e^{-ke \times t}$$

$$C_{post\text{-}HD} = C_{pre\text{-}HD} \times e^{-ke \times t}$$

$$C_{post\text{-}HD} = \frac{2.4\ mg}{L} \times e^{-0.178/h \times 4h}$$

$$\boxed{C_{post\text{-}HD} = 1.2\ mg/L}$$

$C_{post\text{-}HD} = 1.2\ mg/L$

d) Calculate post-HD tobramycin dose to be given on 4/17/14 at 1600.

$$LD = V_D \times C_{desired}$$

$$\text{Supplemental Dose} = V_D \times (C_{desired} - C_{post\text{-}HD})$$

$$= 16L \times (6\ mg/L - 1.2\ mg/L)$$

$$= 76.8\ mg \Rightarrow \boxed{80\ mg}$$

80 mg IV tobramycin