

XZ is a 39 year old female who presents to the ER accompanied by her daughter with fever, lethargy, and hypotension. Her daughter provides the history as XZ is incoherent and not very lucid. During the admission interview, her daughter states that XZ was recently discharged from a local community hospital after treatment of a complicated urinary tract infection. Her daughter doesn't remember what drug she was treated with but does remember the nurse telling her it was "some kind of fancy penicillin." XZ did receive a prescription to continue as an outpatient but could not afford it so she did not bother to even try to fill it. A basic metabolic profile (BMP), complete blood count (CBC), urinalysis (UA), urine culture, and blood culture x 2 are ordered. She is started on IV fluids and a pressor.

Physical Exam: T_{max} 102°F, BP 80/50 mmHg, P 100 BPM, R 15/min, Ht 65 inches, Wt 80 kg

Labs: WBC 19.8, Plt 140, BUN 45 mg/dL, SCr 1.6 mg/dL

UA: Nitrate -, Leukocyte esterase +, WBC 50

Gram stains of blood cultures show gram negative bacilli in both bottles.

Because of her PMH, the ER physician is afraid the bacteria causing XZ's urinary tract infection have caused bacteremia. He is also worried that it may have some drug resistance associated with it and asks you, the pharmacist, to recommend a dose of tobramycin and send the drug STAT.

- 1) What is the anticipated half-life of tobramycin in XZ?
 - a. 3.89 h
 - b. 4.53 h
 - c. 4.67 h
 - d. 5.38 h
 - e. 6.24 h**

How to solve for the answer

Step 1: Calculate IBW

$$\begin{aligned} IBW_{female} &= 45 + 2.3 \text{ (inches greater than 60)} \\ &= 45 + 2.3 (5) = 45 + 11.5 = \mathbf{56.5 \text{ kg}} \end{aligned}$$

Step 2: Calculate CrCl

ABW > IBW, so use IBW in CrCl equation

$$\begin{aligned} CrCl_{female} &= \{[(140 - \text{age})(IBW)] / [(72)(SCr)]\} * 0.85 \\ &= \{[(140 - 39)(56.5)] / [(72)(1.6)]\} * 0.85 = \mathbf{42.10 \text{ mL/min}} \end{aligned}$$

Step 3: Determine k_d using the Dettli equation

$$\begin{aligned} K_d &= 0.0024 (CrCl) + 0.01 \\ &= 0.0024 (42.10) + 0.01 = \mathbf{0.11104} \end{aligned}$$

Step 4: Determine $t_{1/2}$ from k_d .

$$\begin{aligned} t_{1/2} &= \ln 2 / k_d \\ &= 0.693 / 0.11104 = \mathbf{6.24 \text{ h}} \end{aligned}$$

- 2) What dose of tobramycin do you recommend based on a 2 mg/kg/dose? (The pharmacy policy is to round the dose to the nearest 20 mg.)
- a. 100 mg
 - b. 120 mg
 - c. 140 mg**
 - d. 160 mg
 - e. 180 mg

How to solve for the answer

Step 1: Is ABW > IBW by 30% or greater?

$$80 \text{ kg} / 56.5 \text{ kg} = 1.415$$

Yes, so we must determine the dosing weight

Step 2: Calculate dosing weight (DW)

$$\begin{aligned} \text{DW} &= \text{IBW} + 0.4 (\text{ABW} - \text{IBW}) \\ &= 56.5 + 0.4 (80 - 56.5) = 56.5 + 9.4 = \mathbf{65.9} \end{aligned}$$

Step 3: Calculate dose.

$$\begin{aligned} \text{Dose} &= 2 \text{ mg/kg} * \text{DW} \\ &= 2 \text{ mg/kg} (65.9 \text{ kg}) = 131.8 \rightarrow \text{rounding to the nearest 20, we get } \mathbf{140 \text{ mg}} \end{aligned}$$

XZ is transferred to the ICU, and, after three days, she has some improvement. She no longer requires pressor support and is able to answer questions now. Her renal function has also improved as demonstrated by increased urine output and a SCr of 1.2 mg/dL. After being moved to the ICU and receiving an initial dose of tobramycin, she was continued on a regimen of 120 mg q 12 h. To ensure that her renal function continues to improve and to make sure the bacteremia is being treated appropriately, you order tobramycin levels to ensure they are in the appropriate therapeutic range. (She has received 5 doses so far; assume she is at steady state). The lab reports the following data:

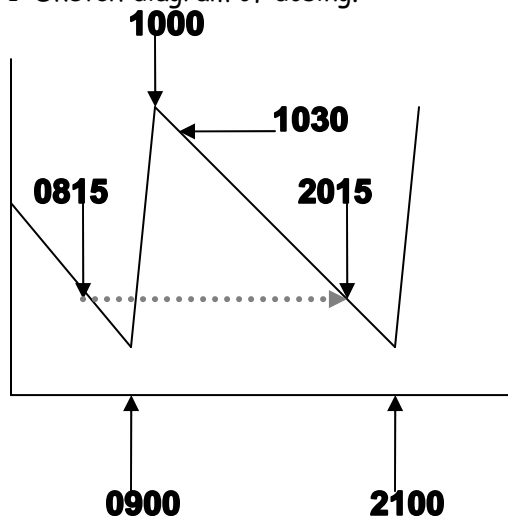
Tobramycin trough at 0815: **1.3 mg/L**
 Tobramycin peak at 1030: **9.9 mg/L**

After talking to the nurse, you find out that the next dose was given at 0900 and infused over one hour, per hospital aminoglycoside policy.

- 3) What is XZ's tobramycin elimination rate constant?
- 0.111
 - 0.144
 - 0.168
 - **0.208**
 - 0.902

How to solve for the answer

Step 1: Sketch diagram of dosing.



Step 2: Determine time period between peak and trough.

The 0815 trough can be mirrored to be the trough at 45 minutes before the 2100 dose.
 So, trough at 2015 = 1.3 mg/dL
 Time between 2015 and 1030 = 9 hours 45 minutes = **9.75 h**

Step 3: Determine k_d using $C_{min} = C_{max}e^{-k_d t}$

$$-k_d = [\ln(C_{min}/C_{max})] / t$$

$$= [\ln(1.3/9.9)] / 9.75 = -0.208, \text{ remember } k_d \text{ is negative by nature}$$

A discussion with the physician yields that she wishes to target a peak of 9 mg/L and a trough of 1 mg/L, and you agree that this is appropriate.

- 4) What is XZ's volume of distribution?
- a. 10.18 L
 - b. 10.75 L**
 - c. 11.61 L
 - d. 12.25 L
 - e. 12.54 L

How to solve for the answer

Step 1: Determine true (back-extrapolated) peak.

Peak drawn at 1030

True peak at 1000

$t = 0.5 \text{ h}$

$$C = C_0 e^{-(k_d t)}$$

$$9.9 = C_0 e^{-(0.208 * 0.5)}$$

$$C_0 = 9.9 / [e^{-(0.208 * 0.5)}] = \mathbf{10.98}$$

Step 2: Determine true trough

Trough drawn at 0815

True trough at 0900

$t = 0.75 \text{ h}$

$$C = C_0 e^{-(k_d t)}$$

$$C = 1.3 e^{-(0.208 * 0.75)}$$

$$C = \mathbf{1.11}$$

Step 3: Determine V_d

$$C_{\max} = 10.98, C_{\min} = 1.11, k_d = -0.208, t' = 1 \text{ h}, K_0 = 120 \text{ mg/h}$$

$$V_d = [K_0 (1 - e^{-k_d t'})] / [k_d (C_{\max} - (C_{\min} * e^{-k_d t'}))]$$

$$= [120 (1 - e^{-0.208 * 1})] / [0.208 (10.98 - (1.11 * e^{-0.208 * 1}))]$$

$$= 22.53515559 / 2.096317639 = 10.74987643, \text{ round to } \mathbf{10.75 \text{ L}}$$

5) What dose and dosing interval should you recommend to achieve these levels in XZ?

- a. 80 mg q8h
- b. 100 mg q12h**
- c. 120 mg q12h
- d. 120 mg q18h
- e. 200 mg q24h

How to solve for the answer

Step 1: Determine dosing interval

$$k_d = -0.208, C_{\min} = 1 \text{ mg/L}, C_{\max} = 9 \text{ mg/L}, t' = 1 \text{ h}$$

$$t = (-1/k_d) * \ln(C_{\min}/C_{\max}) + t'$$

$$= (-1/-0.208) * \ln(1/9) + 1 = 11.5635797, \text{ round to } \mathbf{12 \text{ h}}$$

Step 2: Determine K_0

$$k_d = -0.208, C_{\max} = 9 \text{ mg/L}, t' = 1 \text{ h}, \tau = 12 \text{ h}, V_d = 10.75$$

$$K_0 = [k_d * V_d * C_{\max} (1 - e^{-k_d t'})] / (1 - e^{-k_d \tau})$$

$$= [0.208 * 10.75 * 9 (1 - e^{-0.208 * 1})] / (1 - e^{-0.208 * 12})$$

$$= 18.46550074 / 0.187792963 = 98.32903436, \text{ rounded to the nearest 20 mg, } \mathbf{100 \text{ mg/h}}$$

Step 3: Determine dose

$$K_0 = \text{dose} / t'$$

$$\text{Dose} = K_0 / t' = (100 \text{ mg/h}) / 1 \text{ h} = \mathbf{100 \text{ mg}}$$

Step 4: Double-check peak and trough

C_{\max}

$$K_0 = 100 \text{ mg/h}, k_d = -0.208, t' = 1 \text{ h}, \tau = 12 \text{ h}, V_d = 10.75$$

$$C_{\max} = [K_0 (1 - e^{-k_d t'})] / (k_d * V_d * (1 - e^{-k_d \tau}))$$

$$= [100 (1 - e^{-0.208 * 1})] / (0.208 * 10.75 * (1 - e^{-0.208 * 12}))$$

$$= 18.77929633 / 2.051722305 = 9.152642525, \text{ peak is about } \mathbf{9 \text{ mg/L}}, \text{ so dosing is okay}$$

C_{\min}

$$C_{\min} = C_{\max} e^{-k_d \tau}$$

$$= 9.15 e^{-0.208 * 12}$$

$$= 0.7540088065, \text{ trough is near } \mathbf{1 \text{ mg/L}}, \text{ so dosing is okay}$$