

DB is a 59 year old female who presents to the emergency room with chills, fever, anorexia, and cough. Her past medical history is significant for COPD, diabetes, and hypertension. She was hospitalized for pneumonia two months ago.

She states that she has had increased shortness of breath over the past few weeks. She visited her doctor and received a course of moxifloxacin two weeks prior. However, she only took three days of her antibiotic course because she sold the rest to a friend who didn't have enough money to see the doctor but had a similar cough to DB's.

Ht 62 inches **Wt** 246 lbs **B/P** 150/90 **RR** 25 **Temp** 38°C

Allergies: Penicillins (reaction – anaphylaxis)

Labs

WBC 18.2 (76% segs) **SCr** 2.6 mg/dL **BUN** 37 mg/dL

Gram stain of sputum and bronchoalveolar lavage reveals gram-negative rods

The medical resident is concerned that DB is at risk for multi-drug resistant pneumonia and wishes to start a broad spectrum regimen. As the clinical pharmacist, you suggest tobramycin to cover possible gram-negative organisms due to her penicillin allergy. The team agrees, planning to give one dose in the ER and transferring the patient to the ICU.

- 1) **What is the anticipated half-life of tobramycin?**
- a. 5.5 h
 - b. 6.4 h
 - c. 11.3 h
 - d. **12.9 h**
 - e. None of the above

How to solve for answer

Since we only have data regarding DB's height, weight, and serum creatinine, we must use population kinetics to estimate her half-life, i.e. the Dettli equation.

Step 1 – Determine DB's ideal body weight

Height – 62 inches
 $IBW_{female} = 45 + 2.3(2) = 45 + 4.6 = 49.6 \text{ kg}$

Step 2 – Determine DB's creatinine clearance

$$CrCl = \frac{(140-59)(49.6)}{(72)(2.6)} (0.85) = 18.24 \text{ mL/min}$$

Step 3 – Determine DB's elimination constant using the Dettli equation

$$k_d = 0.0024(CrCl) + 0.01 = (0.0024 \cdot 18.24) + 0.01 = 0.0538$$

Step 4 – Determine DB's anticipated half-life of tobramycin

$$t_{1/2} = \frac{\ln 2}{k_d} = \frac{0.693}{0.0538} = 12.881 \text{ h} \qquad \text{Round to 12.8 h}$$

2) What dose of tobramycin do you recommend based on a 2 mg/kg/dose? (Round to the nearest 20 mg)

- a. 100 mg
- b. **140 mg**
- c. 220 mg
- d. 500 mg
- e. None of the above

How to solve for the answer

Since we know that DB's actual body weight is greater than her ideal body weight, we need to determine if we should use an adjusted dosing weight.

Step 1 – Determine if ABW > 30% of IBW

$$ABW = 246 \text{ lbs} / 2.2 = 111.8 \text{ kg}$$

$$IBW = 49.6 \text{ kg}$$

$$111.8 / 49.6 = 2.25 \rightarrow \text{greater than 30\% (225\% greater)}$$

Step 2 – Determine dosing weight

$$DW = LBW + 0.4(ABW - LBW)$$

$$= 49.6 + 0.4(111.8 - 49.6) = 49.6 + 0.4(62.2) = 49.6 + 24.88 = 74.48 \text{ kg}$$

Step 3 – Determine 2 mg/kg dose

$$\text{Dose} = (2)(74.48) = 148.96 \rightarrow$$

Rounded to 140 mg

Two days later, you review DB's progress. You see that she has been receiving a tobramycin dose of 120 mg q12h. She has been showing improvement in treatment and her serum creatinine has slightly improved. You request tobramycin levels with the next dose to ensure adequate dosing.

Tobramycin 2.9 mg/L @ 0730
Tobramycin 7.6 mg/L @ 1030

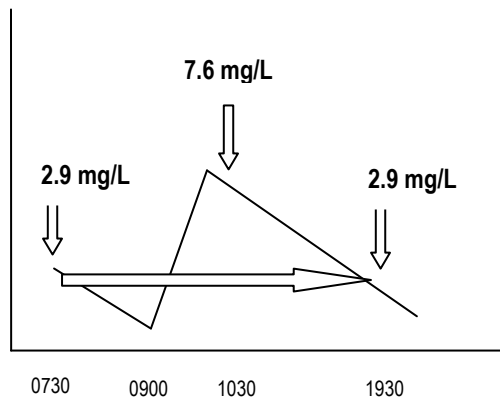
After checking the medical administration record, you see that tobramycin doses are given around 0900 and 2100. Per hospital policy all aminoglycosides are infused over 1 hour.

- 3) Calculate DB's V_d .
- 19.6 L
 - 13.5 L
 - 22.8 L
 - 17.3 L
 - None of the above

How to solve for the answer

Since we have actual levels for DB, we can use the patient specific trough and peak data to tailor DB's dosing regimen.

Step 1 – Determine DB's k_d from actual data



Since DB is at steady state, we can extrapolate the level taken at 0730 to 1930 to use that to determine k_d

Time between 1030 and 1930 = 9 h

$$2.9 = 7.6e^{-(k_d \times 9)}$$

$$k_d = \frac{(\ln \frac{2.9}{7.6})}{-9} = 0.107048612$$

Step 2 – Determine actual peak

- Dose given at 0900
- Infusion time = 1h
- Level at 1030 = 7.6 mg/dL

Since dose given at 0900 and infusion time is 1h, true peak at 1000

Time between peak and level = 0.5h

$$7.6 = C_{\max} e^{(-0.107 \times 0.5)}$$

$$C_{\max} = \frac{7.6}{e^{(-.107 \times 0.5)}} = 8.017673137$$

Step 3 – Determine actual trough

- Time of 2.9 mg/L level = 0730
- Time of true trough = 0900

Time between 0730 and 0900 = 1.5h

$$C_{\min} = 2.9 e^{(-0.107 \times 1.5)} = 2.469981688$$

Step 4 – V_d equation

$$V_d = \frac{\frac{Dose}{t_{inf}} (1 - e^{(-kt_{inf})})}{k_d (C_{max} - C_{min} e^{(-kt_{inf})})}$$

Knowns

- Dose = 120
- $t_{inf} = t' = 1h$
- $k_d = 0.107$
- $C_{max} = 8.02$
- $C_{min} = 2.47$

$$V_d = \frac{\frac{120}{1} (1 - e^{(-0.107 \times 1)})}{0.107 (8.02 - 2.47 e^{(-0.107 \times 1)})} = \frac{120 (0.101474327)}{0.107 (5.800641588)} = \frac{12.17691924}{0.620668649} = 19.61903386$$

- 4) What is DB's new half-life?
- 2.2h
 - 5.3 h
 - 6.5h**
 - 7.9 h
 - None of the above

How to solve for the answer

Since we have actual levels for DB, we can use the patient specific trough and peak data to determine DB's half-life

Step 1- Determine half-life

In the previous problem, we determined the k_d to 0.107

$$t_{\frac{1}{2}} = \frac{\ln 2}{k_d} = \frac{0.693}{0.107} = 6.478$$

Round to 6.5 h

After consulting with the team, you decide to adjust DB's dose. You calculate your dose and round it to the nearest 20 mg; your suggestion to the team is a dose of 260 mg q24h, resulting in a peak of 13.6 mg/L and trough of 1 mg/L. The attending, however, disagrees with you and wishes to target a higher peak, per his experience with higher peaks in cystic fibrosis patients. By his calculations, he says the patient should receive 340 mg q24h.

- 5) **Using the physician's new dosing regimen, what will DB's new peak and trough be?**
- a. 15.3 mg/L; 1.2 mg/L
 - b. 16.8 mg/L; 0 mg/L
 - c. **17.8 mg/L; 1.3 mg/L**
 - d. 21.5 mg/L; 0 mg/L
 - e. None of the above

Step 1 – Determine the ratio of the physician's dose to your dose

Your dose = 260 mg

Physician's dose = 340 mg

$$\text{Ratio} = 340/260 = 1.307692308$$

The levels should increase by a factor of 1.3

Step 2 – Determine new peak

$$(13.6) \times (1.3) = 17.78 \rightarrow \text{round to } \mathbf{17.8 \text{ mg/L}}$$

Step 3 – Determine new trough

$$(1) \times (1.3) = 1.3 \rightarrow \text{round to } \mathbf{1.3 \text{ mg/L}}$$