

# Cases: Gentamicin & Vancomycin Pharmacokinetics

Ronald A. Herman, Ph.D.

Clinical Pharmacokinetics

## Prior to completing this activity:

You should have:

1. Downloaded the WinPK desktop version to your tablet, laptop or desktop or the PK-App program to your iPhone, iPad, Android phone or MAC.
2. The programs are available at this website: <http://pocapps.net>. Follow the instructions on the download page. They are also available from ICON or from my webpage (<http://rherman.pharmacy.uiowa.edu>).

## Activity Objectives

On completion of the exercise you should be able to:

1. Know how to use the equations and/or programs to perform prospective or retrospective calculations.
2. Specifically, to prospectively calculate an initial dose regimen for these agents given a person's demographic characteristics for both vancomycin and the aminoglycosides.
3. And to retrospectively dose a patient with an aminoglycoside or vancomycin given a person's concentration-time data (peak and/or trough).

## Introduction

Hospital Policy

- It is hospital policy, both at UIHC and the VA hospital, that every order received for an aminoglycoside or vancomycin the pharmacist must prospectively estimate peak and trough concentrations for the dosing regimen the physician has prescribed.
- Whenever predicted values differ significantly from target values the pharmacist contacts the prescriber and recommends a more appropriate dosing regimen.
- As a result, quite often the pharmacist is consulted and asked to recommend an initial dosing regimen before the therapy is initiated.

## Vancomycin Prospective Dosing

Case 1

A 65 Y.O. male with a Sr.Cr. of 1.4 mg/dl develops a cellulitis. The Gram stain shows a Gram + cocci. The physician suspects *Staph. aureus* and wants to start vancomycin. The patient is 5' 4" and weighs 86 Kg. What would be the appropriate dose to use?

Estimate IBW:

$$IBW = 50Kg + 2.3 * (Htin. - 60) = 59.2 Kg \quad \text{Eq. 1}$$

Estimate CrCl-Wt:

$$\begin{aligned} BMI &= 86 Kg / (65 in * 0.0254 m/in)^2 = 32.5 \\ \text{so CrCl-Wt} &= 59.2 Kg + 0.4 * (86 Kg - 59.2 Kg) = 69.9 Kg \quad \text{Eq. 2} \end{aligned}$$

Estimate CrCl:

$$CrCl = \frac{(140 - Age) \cdot CrClWt}{SrCr \cdot 72} = 52.0 \text{ ml/min}$$

$$SrCr = \frac{SrCr + 0.07}{0.987} = 1.49 \quad \text{Corr: } 48.9 \text{ ml/min} \quad \text{Eq. 3}$$

Population PK data for vancomycin estimates the elimination rate constant and half-life:

$$k_e = \frac{44 + (8.3 \cdot CrCl)}{10000} = 0.0476 \text{ Hr}^{-1} \quad \text{Eq. 4}$$

$$t_{1/2} = \frac{\ln 2}{k_e} = 14.6 \text{ Hr} \quad \text{Eq. 5}$$

Estimate the volume of distribution:

$$V_{ss} = V_d \text{ factor} \cdot ActWT \quad V_{ss} = 0.7 \text{ L/Kg} \cdot 86 \text{ Kg} = 60.2 \text{ L} \quad \text{Eq. 6}$$

Estimate Tau (the 5<sup>th</sup> equation in the Sawchuk-Zaske list):

$$\tau = \frac{\ln(C_{\max/\text{desired}}/C_{\min/\text{desired}})}{k_e} + t_{\text{inf}} = \frac{\ln(36/14)}{0.0476 \text{ Hr}^{-1}} + 1.5 \text{ Hr} = 21.3 \text{ Hr} \quad \text{Eq. 7}$$

Select a practical Tau (e.g. Q4H, Q6H, Q8H, Q12H or Q24H) based on this estimate. Here Q24H.

Using the practical interval, estimate the new dose (the 6<sup>th</sup> equation in the Sawchuk-Zaske list):

$$R_0 = C_{\max, \text{desired}} \cdot V_{ss} \cdot k_e \left[ \frac{1 - e^{-k_e \tau}}{1 - e^{-k_e t_{\text{inf}}}} \right] \quad \text{Eq. 8}$$

$$= 36 \text{ mg/L} \cdot 60.2 \text{ L} \cdot 0.0476 \text{ Hr}^{-1} \left[ \frac{1 - e^{-0.0476 \text{ Hr}^{-1} \cdot 24 \text{ Hr}}}{1 - e^{-0.0476 \text{ Hr}^{-1} \cdot 1.5 \text{ Hr}}} \right] = 1019.4 \text{ mg/Hr}$$

$$Dose = R_0 \cdot t_{\text{inf}} = 1019.4 \text{ mg/Hr} \cdot 1.5 \text{ Hr} = 1529 \text{ mg} \approx 1500 \text{ mg} \quad \text{Eq. 2}$$

Make a practical recommendation (Vancomycin is usually dose in 250 mg increments):

**1500 mg Q24H**

Verify that this will give you desirable steady state peak and trough concentrations:

$$C_{ss, pk} = \frac{R_0}{V_{ss} \cdot k_e} \cdot \frac{(1 - e^{-k_e t_{\text{inf}}})}{(1 - e^{-k_e \tau})} \quad \text{Eq. 3}$$

$$C_{ss, pk} = \frac{1500 \text{ mg} / 2 \text{ Hr.}}{60.2 \text{ L} \cdot 0.0476 \text{ Hr}^{-1}} \cdot \frac{(1 - e^{-0.0476 \cdot 2})}{(1 - e^{-0.0476 \cdot 24})} = 34.9 \text{ mg/L}$$

$$C_{ss, tr} = C_{ss, pk} \cdot e^{-k_e(\tau - t_{\text{inf}})} = 34.9 \text{ mg/L} \cdot e^{-0.0476(24-2)} = 12.25 \text{ mg/L} \quad \text{Eq. 4}$$

## Steps to use the Desktop Dosing Calculator:

1. Start the desktop version: WinPK.
2. You see the input screen. To calculate the patients IBW you will need to input the patients age, weight, height and serum creatinine. The desktop input starts with a default value and you can type a new number or use the up/down arrows to change your value. Once you have entered a valid number you can use the round button to switch back and forth between metric and English measurements. You also will use the round buttons to select the sex of the patient, and if you know that the patient is de-hydrated or over-hydrated you will want to change their hydration status. So in this case enter 65 for the age, 86 for the weight, 64 for the height and 1.4 for the SrCr. Select male if it is not already selected. Once all the values have been entered, the program will calculate and display IBW, AdjWT and CrClWt (59.2, 69.9 and 69.9).
3. The program has already displayed the patient's estimated creatinine clearance (52.0) and their normalized CrCl (44.9ml/min/1.73 m<sup>2</sup>). (Note the original C-G CrCl estimate does not use the corrected SrCr but the corrected value is also shown on the screen (48.9 ml/min))
4. If you select File on the top of WinPK, you will be given several options. The first is Patient Data (Input) the screen that you are at. From other screens you can select that to come back to this starting point.
5. If you choose Prospective PK, it will take you to a screen where you can determine a dosing regimen prospectively.
  - a. The first thing you will do is use one of the four arrows on the bottom right to select one of the drug options (Amikacin, Gentamicin-MDD, Gentamicin-EID, Tobramycin, Vancomycin P/T or Vancomycin TR only). Press the right arrow until you come to Vancomycin P/T.
  - b. Once a drug has been selected it uses the ActWT to calculate a Vd (60.2 L) and CrCl to calculate Ke (0.0476 Hr<sup>-1</sup>) and half-life (14.6 Hr.). It also goes on to select an infusion time (1.5 hr), suggested dose (1500 mg) and suggested dosing interval (24 hrs). It also gives you the predicted peak (35.3) and trough (12.1) for this suggested regimen. It doesn't always make the best choice, so you are given the option to make changes.
  - c. To do that select Change from the menu bar (*top of the desktop*). Now choose which parameter you want to change, the drug, the target peak, the target trough, the dose, the dosing interval or the infusion time. Sometimes it will suggest an impractical interval, for example Q30H and this is how you would change it.
  - d. Here you want to change the infusion time because it is suggesting 1.5 g, which should be infused over 2.0 hrs, so select infusion on the Change menu. Now the arrows on the bottom have changed and the inner arrows go up or down by a small increment, while the outer ones go up and down by a larger increment. The values of those increments change by whether or not it is a dose or time that you are changing. Increase the infusion to 2.0 Hr.
6. You should now be able to make that recommendation for initiation of the vancomycin.

### Steps to use the iPhone, iPad, Android or MAC Dosing Calculator:

1. If you downloaded the PK-App and saved it to your home screen you can select the App icon and start it without being connected to the internet. If not, you need to access the App from the appropriate webpage.
2. You see the input screen. To calculate the patient CrCl you will need to input the patients age, weight, height and serum creatinine. Default values are displayed. Press the black button (e.g. Age) and you will the pictures at the bottom replaced by a white input box and a slider. You can click in the box and type a new number or use the slider to change your value. Once you have entered a valid number press the round save button to register the value in the table. Do this for all four then select the correct gender, units, and race. So in this case enter 65 for the age, 86 for the weight, 64 for the height and 1.4 for the SrCr. Select male if it is not already selected. Select the bottom center button "Input Pt. Info".
3. The program displays the patient specifics, various body mass calculations and renal function estimations.
4. Next select the bottom right button, "Select Drug".
5. From this screen select the proper drug and whether or not you want to do a prospective or retrospective calculation.
  - a. In this case choose prospective, Vancomycin P/T and then choose the upper right button "Results".
  - b. The first grid displays patient information. The second grid displays the estimates of distribution and elimination that come prospective.
  - c. You see that it displays default target values that were used in the calculation. You can press the black PK or TR button to change to a different default target value.
  - d. The recommended dose, interval and infusion time are suggested. Then SS Pk and Tr are also displayed from the calculation.
  - e. You can press the black button dose, tau or T inf to change any of those to see how they would change the predicted value.
  - f. Sometimes the program will suggest an impractical interval, for example Q30H and this is how you would change it.
6. You should now be able to make that recommendation for initiation of the vancomycin

### Vancomycin Trough Only - Retrospective

#### Case 2

The above patient was given 1000 mg Q24H and the trough right before the fifth dose was 11.4 mg/dL. What new dose would you recommend?

Vancomycin routine monitoring should be a single trough level at steady state. The patient should be at steady just before the fifth dose. So for a single level dosage adjustments are proportional. Use the following equation and let's target 15 mg/L in this case:

$$\left(\frac{\text{Dose}}{\text{Tau}}\right)_{\text{new}} = \left(\frac{\text{Dose}}{\text{Tau}}\right)_{\text{current}} * \frac{C_{\text{desired}}}{C_{\text{ss, measured}}}$$

$$\text{New Dose} = (1000 \text{ mg}/24 \text{ hr}) * 15 \text{ mg}/\text{dL} / 11.4 \text{ mg}/\text{dL} = 54.8 \text{ mg}/\text{hr}$$

Generally, if the ratio of  $C_{\text{desired}} / C_{\text{measured}}$  is 1.5 or more then decrease the dosing interval ( $\tau$ ) from 12 hours to 8 hours (or 24 hours to 12 hours). If the ratio is less than 0.67 then increase the dosing interval from 12 hours to 24 hours or 24 hours to 36 hours. If the ratio is between 0.67 and 1.5, then do not change the dosing interval, only alter the dose.

Here the ratio is  $15 \text{ mg}/\text{dL} / 11.4 \text{ mg}/\text{dL} = 1.30$  so change only the dose:

$$54.8 \text{ mg}/\text{hr} * 24 \text{ hr} = 1315 \text{ mg} \text{ (Round to the nearest 250 mg increment)}$$

**1250 mg Q24H**

### Dosing Calculator Instructions

1. Start the program and input patient information.
  - a. Age 65, Wt is 86 and Ht is 65"
  - b. Check Male
  - c. Enter 1.4 for SrCr
2. For WinPK
  - a. Now choose File then Retrospective PK
  - b. Select the drug: Vancomycin-TR Only
3. For the PK-App
  - a. Choose button "Select Drug" at the bottom
  - b. Select the Vancomycin-TR Only and Retrospective
  - c. Then select "Results"
4. Enter the level information:
  - a. Dose given: 1000 mg
  - b.  $\tau$ : 24
  - c.  $T_{\text{inf}}$ : 1.5 Hr.
  - d. TR measured: 11.4
  - e. TR desired: leave at 15
5. Press Enter button in the middle of the screen for WinPK to show the results. They are automatically displayed in the PK-App
  - a. It changed only the dose because the TR ratio was = 1.30
  - b. It also indicates the predicted new TR with that suggested recommendation of 1250 mg Q24H

### Vancomycin Trough Only - Retrospective

#### Case 3

A 52 year old black female patient, 5'7" and 79 Kg and with a SrCr = 1.3 mg/dL was given 1000 mg Q12H and the trough right before the fifth dose was 17.3 mg/dL. What new dose would you recommend?

$$\left(\frac{\text{Dose}}{\tau}\right)_{\text{new}} = \left(\frac{\text{Dose}}{\tau}\right)_{\text{current}} * \frac{C_{\text{desired}}}{C_{\text{ss,measured}}} \quad \text{Eq. 12}$$

$$\text{New Dose} = (1000 \text{ mg}/12 \text{ hr}) * 15 \text{ mg}/\text{dL} / 17.3 \text{ mg}/\text{dL} = 72.3 \text{ mg}/\text{hr}$$

Generally, if the ratio of  $C_{\text{desired}} / C_{\text{measured}}$  is 1.5 or more then decrease the dosing interval (Tau) from 12 hours to 8 hours (or 24 hours to 12 hours). If the ratio is less than 0.67 then increase the dosing interval from 12 hours to 24 hours or 24 hours to 36 hours. If the ratio is between 0.67 and 1.5, then do not change the dosing interval, only alter the dose.

Here the ratio is  $15 \text{ mg}/\text{dL} / 17.3 \text{ mg}/\text{dL} = 0.87$  so change only the dose:

$$72.3 \text{ mg}/\text{hr} * 12 \text{ hr} = 867 \text{ mg} \text{ (Round to the nearest 250 mg increment)}$$

**750 mg Q12H**

### Dosing Calculator Instructions

1. Start the program and input patient information.
  - a. Age 52, Wt is 79 and Ht is 67"
  - b. Check Black and Female
  - c. We do not need a SrCr for a retrospective calculation. I would enter 1.0 if you don't know it.
2. WinPK
  - a. Now choose File then Retrospective PK
  - b. Select the drug: Vancomycin-TR Only
3. PK-App
  - c. Choose the button "Select Drug"
  - d. Select Retrospective, Vancomycin-TR Only and then press Results
4. Enter the level information:
  - a. Dose given: 1000 mg
  - b. Tau: 12
  - c. TR measured: 17.3
  - d. TR desired: leave at 15
5. Press Enter button in the middle of the screen.
  - a. It changed only the dose because the TR ratio was  $> 0.67$
  - b. It also indicates the predicted new TR with that suggested recommendation of 750 mg Q12H

### Vancomycin Trough Only - Prospective

#### Case 4

A 5' 5" 88 Kg. 72 Y.O. Hispanic female patient has been on vancomycin 750 mg Q12H for 3 days. A single trough level came back at 6.6 mg/dl. What new dose would you recommend?

$$\left(\frac{\text{Dose}}{\text{Tau}}\right)_{\text{new}} = \left(\frac{\text{Dose}}{\text{Tau}}\right)_{\text{current}} * \frac{C_{\text{desired}}}{C_{\text{ss,measured}}} \quad \text{Eq. 12}$$

$$\text{New Dose} = (750 \text{ mg}/12 \text{ hr}) * 15 \text{ mg}/\text{dL} / 6.6 \text{ mg}/\text{dL} = 142 \text{ mg}/\text{hr}$$

Here the ratio is 2.3 so let's change the Tau to every 8 hours and adjust the dose.

$$142 \text{ mg/hr} * 8 \text{ hr} = 1136 \text{ mg (Round to the nearest 250 mg)}$$

**1250 mg Q8H**

### Dosing Calculator Instructions

1. Start the program and input patient information.
  - a. Age 72, Wt is 88 and Ht is 65"
  - b. Check Hispanic and Female
  - c. We do not need a SrCr for a retrospective calculation. I would enter 1.0 if you don't know it.
2. WinPK
  - a. Now choose File then Retrospective PK
  - b. Select the drug: Vancomycin-TR Only
3. PK-App
  - a. Choose the button "Select Drug"
  - b. Select Retrospective, Vancomycin-TR Only and then press Results
4. Enter the level information:
  - a. Dose given: 750 mg
  - b. Tau: 12
  - c. TR measured: 6.6
  - d. TR desired: leave at 15
5. Press Enter button in the middle of the screen.
  - a. Notice it changed both the dose and the interval because the TR ratio was > 1.5.
  - b. It also indicates the predicted new TR with that suggested recommendation of 1250 mg Q8H
  - c. If you feel the TR of 16.2 mg/L might be too high, then you can adjust the dose or interval.

## Vancomycin Retrospective Dosing

### Case 5

A 5' 6" 68 Kg. 19 Y.O. female burn victim has been on vancomycin 1 Gm Q12H for 5 days. Levels are done and come back with a Pk/Tr = 17/4.1 mg/dl. The skin grafts still show signs of cellulitis and the physician wants to increase the dose. What would you recommend? (The Pk was 60 minutes after a 90 minute infusion.)

Calculate the elimination rate constant:

$$k_e = \frac{\ln\left(\frac{C_{pk}}{C_{tr}}\right)}{t_{tr} - t_{pk}} = \frac{\ln\left(\frac{17}{4.1}\right)}{12 - 2.5} = \frac{\ln\left(\frac{17}{4.1}\right)}{9.5 \text{ Hr.}} = 0.15 \text{ Hr}^{-1} \quad \text{Eq. 1}$$

(In terms of the dosing interval the infusion was started at  $t = 0$ , it stopped at 1.5 hr, and the pk was measured at 2.5 hr and the trough (extrapolated) was at 12 hours, therefore  $t_2 - t_1$  is  $12 - 2.5 = 9.5$ . This is where most errors in calculations are made.)

$$t_{1/2} = \frac{\ln 2}{k_e} = 4.6 \text{ Hr} \quad \text{Eq. 2}$$

Calculate the maximum concentration:

$$C_0 = \frac{C_{pk}}{e^{-k_e(t_{pk}-t_{inf})}} = \frac{17 \text{ mg/L}}{e^{-0.15 \text{ Hr}^{-1}(2.5 \text{ Hr}-1.5 \text{ Hr})}} = 19.75 \text{ mg/L} \quad \text{Eq. 5}$$

Calculate the volume of distribution:

$$V_{ss} = \frac{R_0}{k_e} \cdot \frac{1 - e^{-k_e t_{inf}}}{(C_0 - C_{tr} \cdot e^{-k_e t_{inf}})} \quad \text{Eq. 6}$$

$$= \frac{1000 \text{ mg} / 1.5 \text{ Hr}}{0.15 \text{ Hr}^{-1}} \cdot \frac{1 - e^{-0.15 \text{ Hr}^{-1} \cdot 1.5 \text{ Hr}}}{(19.75 \text{ mg/L} - 4.1 \text{ mg/L} \cdot e^{-0.15 \text{ Hr}^{-1} \cdot 1.5 \text{ Hr}})} = 54.4 \text{ L}$$

Using  $C_0$ ,  $k_e$  and  $V_{ss}$  estimate a dosing interval, a dose and predict the steady state peak and trough using a practical regimen using Eq. 1, Eq. 1, Eq. 2, Eq. 10 and Eq. 11.

$$\tau = \frac{\ln(36/14)}{0.15 \text{ Hr}^{-1}} + 1.5 \text{ Hr} = 7.13 \text{ Hr} \approx 8 \text{ Hr}$$

$$R_0 = 36 \text{ mg/L} \cdot 54.4 \text{ L} \cdot 0.15 \text{ Hr}^{-1} \left[ \frac{1 - e^{-0.15 \text{ Hr}^{-1} \cdot 8 \text{ Hr}}}{1 - e^{-0.15 \text{ Hr}^{-1} \cdot 1.5 \text{ Hr}}} \right] = 1018.8 \text{ mg/Hr}$$

$$\text{Dose} = 1018.8 \text{ mg/Hr} \cdot 1.5 \text{ Hr} = 1528 \text{ mg} \approx 1500 \text{ mg}$$

Make a practical recommendation and then verify:

**1500 mg Q8H**

$$C_{ss, pk} = \frac{1500 \text{ mg} / 2 \text{ Hr}}{54.4 \text{ L} \cdot 0.15 \text{ Hr}^{-1}} \cdot \left( \frac{1 - e^{-0.15 \cdot 2}}{1 - e^{-0.15 \cdot 8}} \right) = 34.1 \text{ mg/L}$$

$$C_{ss, tr} = 34.1 \text{ mg/L} \cdot e^{-0.15(8-2)} = 13.9 \text{ mg/L}$$

Steps to use your Dosing Calculator:

1. Start the WinPK program or the PK-App. You will see the input screen.
2. It is not essential to complete this input screen, but I would encourage you to always do it. The only information that the retrospective calculation needs is the patient's DWT when it calculates the steady state Vd on a weight basis. If you did not use this input screen it will use whatever weight is in memory from a previous calculation. Therefore, it will display an invalid Vd (L/Kg) for your patient. Let's enter the patient's age (19), weight (68) and height (66) and make sure female is selected. That will compute a correct dosing weight. Since we don't know serum creatinine enter any value, e.g. 1.0 is normal. (The estimate of CrCl is only used if we are doing a prospective calculation.) The screen displays the ActWT (68 Kg) which will be used as the dosing weight.



3. Select File at the top of WinPK, and then select Retrospective PK or select “Select Drug” on the PK-App.
4. Now in the upper left select the drug in WinPK (use the left or right arrow until you come to Vancomycin –P/T) or select Retrospective on the Select screen and the then Vancomycin P/T and then Results in the PK-App.
5. Now you must enter the peak and trough level information. First enter the dose of vancomycin given (1000). You can click in the box and then type in the number from the keyboard, or use the up/down arrows. Note the dose must be in mg, not in Gm. Then enter the dosing interval (Tau = 12). Then put in the PK (17) and the TR (4.1). Now enter the infusion time (in hours not minutes – 1.5) and then the time from when the infusion stopped to when the peak was measured (T pinf), again in hours (1.0). If the TR was drawn more than 30 minutes before the next dose was started, enter the T early (in hours) – in this case just leave the 0 there.
6. When you press “Enter” in the middle section (in WinPK), then the program will display Ke (0.15 Hr-1), half-life (4.6 hr), C(0) (19.7 mg/L), Vss (54.4 L) and Vd (L/Kg) 0.8 in the bottom section. The results are automatically displayed in PK-App.
7. The middle section will now display a recommended dose, interval and infusion time and then show the predicted P/T for that regimen.
8. The recommended dose of 1.5 g Q8H will give you a P/T of 35.4/13.4 mg/L in WinPK, but you must adjust the infusion time to 2.0 because it is a 1.5 g dose. When you do you will get a P/T of 34.1/13.9 for bot applications.
9. You have the option to change your dose, your interval or your length of infusion if you want to try alternative regimens
10. At this point, you should now be ready to make your recommendation for how to adjust vancomycin dosage based on the drug levels that were measured.

The program does not always make practical suggestions. You have the opportunity to change any of the values. In the menu bar (top of the Windows Desktop) select Changes. You can change the dose, the infusion time or the interval. Up/Down arrows will appear and you can increase or decrease the corresponding parameter. In the PKApp choose one of the black buttons.

### Case 6 – Gentamicin Prospective MDD

SW is a 45 YO 180cm male with a *Pseudomonas* pneumonia. His weight is 196 lb. and his serum creatinine is 0.9 mg/dl. Blood pressure, heart rate, skin turgor and vascular filling of neck veins indicate that SW is normally hydrated. The physician wants to use MDD. What dose (mg) of gentamicin would you recommend for initiation of therapy and what dosing interval would you recommend?

\_\_\_\_\_ mg Gentamicin Q\_\_\_H

#### Case 6 - Prospective

1. Start the program and input patient information.
  - a. For Wt and Ht you must change the unit before clicking in the box or pressing the black button.
  - b. Remember with aminoglycosides the hydration status of the patient is important.
  - c. When you enter SrCr, use 0.9 mg/dl.
  - d. It will use an adjusted (CrClWt).
  - e. CrCl = 118.2 ml/min

2. WinPK
  - a. Now choose File then Prospective PK
  - b. Select the drug: Gentamicin-MDD, not Gentamicin-EID
3. PK-App
  - a. Select the bottom button “Select Drug”
  - b. Choose Gentamicin-MDD
  - c. Hydration status is normal, so leave unchanged.
  - d. Choose Prospective, then Results
4. Notice the calculated parameters:
  - a.  $K_e = 0.352 \text{ Hr}^{-1}$
  - b.  $V_{ss} = 20.0 \text{ L}$
  - c. Half-life = 2.0 hours
5. Make Changes
  - a. The target concentration is based upon the type of infection. Pneumonia is a serious infection so you want your PK 6-8, so a target of 7 is OK, so we don't need to change. If we were treating a UTI, we would want to select a lower target PK.
  - b. If your institution always infuses aminoglycosides over 60 minutes, you could change your infusion time to 1.0 hr.
6. Make Your Recommendation
  - a. The 140 mg Q8H to give a P/T of 6.8/0.5 seems reasonable.

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### Case 7 – Gentamicin Retrospective MDD

If we went with the 140 mg Q8H and the levels came back at 3.3 mg/L at 9:15 am and 0.4 mg/L at 07:50 am and the dose was scheduled to be given at 8:00 am, what recommendation would you make?

#### Case 7 - Retrospective

1. WinPK - Now choose File then Retrospective PK
  - a. Use the arrows in the upper left to select the drug Gentamicin-MDD.
2. PK-App – Choose the bottom button “Select Drug”
  - a. Then change Prospective to Retrospective and press Results
3. Enter the drug level information:
  - a. Dose (mg): 140
  - b. Tau (Hr): 8
  - c. PK: 3.3
  - d. TR: 0.4
  - e. Tinf: (assume 0.5 hour because most antibiotics are given by a programmed infusion device)
  - f. The time post infusion (assume 0.75 hours) – The peak was measured at 9:15 am (dose started 8 am)
  - g. The trough was within 30 minutes so you can enter 0 (or 10/60 if you really want to be precise for T early)

4. WinPK - When you press Enter, C(0), Ke, half-life and Vss are displayed in the lower section. In PK-App they are automatically displayed.
  - a. C(0) is 4.2 mg/L – which is too low for treating pneumonia.
  - b. The Ke and half-life are about what the prospective dosing predicted.
  - c. Vd (L/Kg) is 0.38 which is a little high. The patient may be slightly fluid overloaded. If you make a dosing adjustment you will need to monitor closely because there may be a fluid shift back towards normal hydration which would result in higher levels.
5. The middle section recommends 230 mg Q8H to give a P/T of 6.9/0.7 mg/L.
6. This is probably acceptable and should be the recommendation that you make, although you must monitor closely because fluid shifts out of the body could result in higher concentrations.
7. If you wanted to make changes, you could choose changes from the menu bar and then change the Dose, Dosing Interval or the Infusion Time or use the black buttons in the PK-App. If you had gone with a Tau of 6 you would have come up with a dose of 220 mg Q6H that would have given a P/T = 7.1/1.3 mg/L. It takes more nursing time to administer 4 times a day, and hence is more costly to give the drug every 6 hours instead of every 8, so I tried the Q8H first.

## Case 8 Gentamicin Prospective and Retrospective - EID

### Case 8

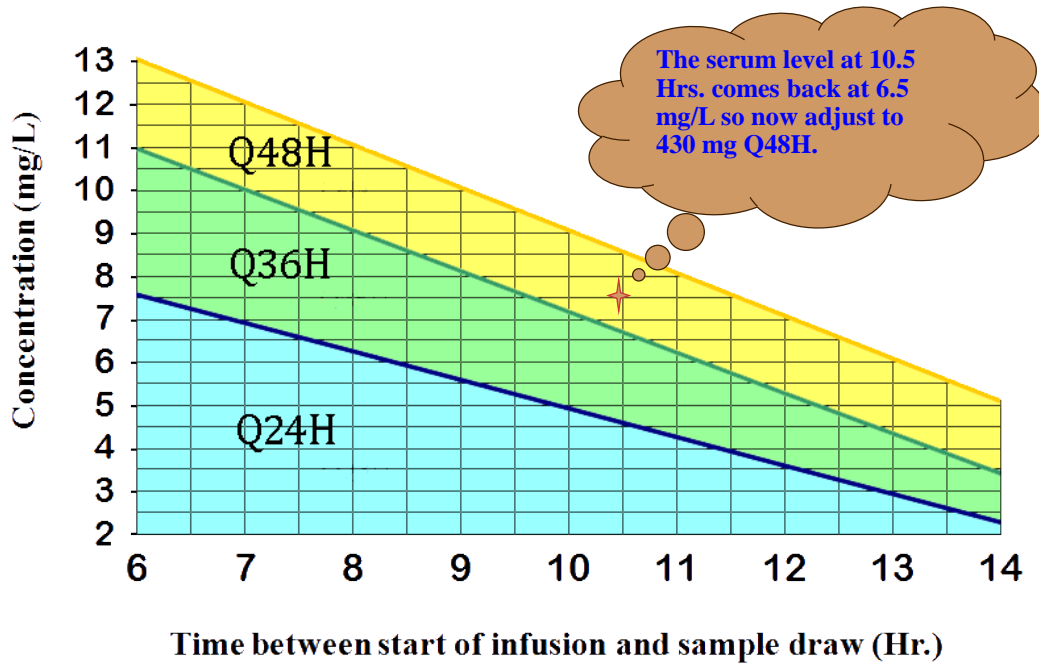
You have a 64 YO WF who will have abdominal surgery and the physician wants to initiate EID Gentamicin. The patient weighs 79 Kg and is 5'2" and has a SrCr of 1.3. What should be her EID?

#### Steps to use your Dosing Calculator

1. Start the program and input patient information
  - a. Age - 64
  - b. Wt - 79
  - c. Ht - 62
  - d. SrCr – 1.3
  - e. Sex - F
2. It displays the patients estimated CrCl as 42.6 ml/min.
3. WinPK - from the menu bar select File, then Prospective PK then select Genamicin-EID
4. PK-App - select the bottom button “Select Drug” then choose Gentamicin-EID, Prospective and Results.
  - a. Based on the DWT it calculates the dose of 430 mg
  - b. Based on the CrCl it calculates the interval of 36 hr
5. If a level was done 10.5 hours after the start of infusion, and came back at 7.5 mg/L.
  - a. You need to use the nomogram, or if you do not have it with you, you can go to the menu bar select File, then Retrospective PK.
6. WinPK
  - a. Go to the menu bar, select File, then Retrospective PK
  - b. Change the dose to 430 mg, change the interval to 36 hours, change the level to 7.5 mg/L, change the time to 10.5 hours and then press the Enter button.
7. PK-App
  - a. Select the bottom button, then change to Retrospective.
  - b. Change the dose to 430 mg, change the interval to 36 hours, change the level to 7.5 mg/L

8. The recommended level displays 430 mg Q48H and that is also what the nomogram indicates.

### Hartford Hospital Nomogram



#### Conclusions

The application of basic pharmacokinetic principles to prospectively and retrospectively dose vancomycin and aminoglycosides can be greatly facilitated by the use of a smart device dosing calculator or a desktop calculator.