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Humankind has used tools for eons. In the hands of a knowledgeable and careful person, a tool can be a life-saving device. But without the knowledge of what it does and how it works, any tool can be dangerous.

Such is the case with this computer program, it is merely a tool to assist you in designing appropriate dosage regimens. You must have a thorough understanding of one-compartment models and practical experience with pharmacokinetic dosing. Putting it another way, if you do not understand the basic principles of pharmacokinetics and pharmacodynamics then you cannot safely use this computer program.

If you accept responsibility for your actions, then you may use this program, if not, then exit and uninstall the program now.

The disclaimer screen also serves as a shareware "nag screen" which will appear each time you switch back to the AbPK program from any other Palm application.

Antibiotic Kinetics© is fully functional, it is not a trial version, and it does not expire. It is marketed under the shareware concept.

Please feel free to copy (beam) the program to your colleagues.

If you find the program useful then please register your copy to support my programming efforts! The registration fee is only $25. You will receive a serial number to register your copy which will remove the nag screens and unlock additional functions.

You must provide the User Name from this screen to RxKinetics when purchasing your registration. The User Name is the same as your HotSync ID.

If the user name you provide is incorrect, your registration will not validate.

Case, spelling, spacing, and punctuation are all relevant.
Preferences screen

This screen displays the default parameters for the program. 

**Please note:** this screen is only active after you register.

<table>
<thead>
<tr>
<th>Preference</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use in/lbs for ht/wt</td>
<td>Sets the default height &amp; weight input to inches / pounds instead of cm / kg.</td>
</tr>
<tr>
<td>Use units for creatinine</td>
<td>Sets the default creatinine input to units instead of mg%.</td>
</tr>
<tr>
<td>Show disclaimer at startup</td>
<td>Uncheck to bypass the disclaimer screen.</td>
</tr>
<tr>
<td>Adult CrCl method</td>
<td>Set the default creatinine clearance method. Other methods are available by clicking the <strong>CrCl</strong> button on the Patient data screen.</td>
</tr>
</tbody>
</table>

Patient data screen

Enter patient demographics by tapping on a field (.....) and then entering the data in the writing area of the Palm.

Shortcuts to other screens are available by tapping **Go to** on the title bar.

- **Register** = Enter serial number to register your copy
- **Preferences** = Edit program preferences
- **Models** = Edit the drug model database

**Please note:** only the current patient data is saved when you exit the program. If you need to track several patients, **APK for Palm** provides full patient database functionality, including data sync to the desktop.

To choose an age unit, Tap the drop down selector to display and select the appropriate age unit for the patient: years, months, days.

**Creatinine clearance** is calculated with the Swartz equation for peds. For adults, you may select the default method on the Preferences screen, otherwise, the Cockcroft and Gault equation based on adjusted body weight is used.

Tap the **CrCl** button for other creatinine clearance calculation methods.

**To select a drug model,** Tap the drop down selector to display and select the drug model.

Tap the **Calc** button to calculate and display lean body weight and body surface area.

Tap the **CrCl** button to display alternate creatinine clearance methods for adults.
Tap the **Next** button to continue to the model entry screen. It is at this point that the program checks for acceptable and appropriate patient data. If the patient data is within the acceptable range, then the model screen is called.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Acceptable range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1 day to 110 years</td>
</tr>
<tr>
<td>Height</td>
<td>35 to 213 cm</td>
</tr>
<tr>
<td>Weight</td>
<td>2 to 251 kg</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>0.3 to 22 mg %</td>
</tr>
</tbody>
</table>

### Patient data screen menu

Because the Palm screen is so small, several functions are found in the menu tree of each screen. If you can't find a button to do what you want to do, always check the menus.

- Tap on the Palm **Menu** button to display the menu for the current screen.
- To clear patient data:
  - Tap **File**, then **New patient** on the screen menu.
- To set height/weight entry to Metric or U.S. measurement:
  - Tap **Edit**, then **Preferences** on the screen menu.
- To edit the drug model database:
  - Tap **Edit**, then **Models** on the screen menu.
- To enter your registration number:
  - Tap **Register**, then **Enter SN** on the screen menu.

### Other CrCl Methods

Tap the **CrCl** button on the patient data screen to display this window (for adults only).

For specific information please see the equations sections of this manual.

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C&amp;G ABW</td>
<td>Variation of the Cockcroft and Gault equation using Adjusted Body Weight, a good general equation.</td>
</tr>
<tr>
<td>C&amp;G TBW</td>
<td>Variation of the Cockcroft and Gault equation using Total Weight. May overestimate CrCl in obese patients.</td>
</tr>
<tr>
<td>C&amp;G Normalized</td>
<td>Variation of the Cockcroft and Gault equation which removes weight. May be useful for obese patients.</td>
</tr>
<tr>
<td>Jelliffe Multistep</td>
<td>A good general equation.</td>
</tr>
<tr>
<td>Jelliffe 1973</td>
<td>Weight is not used in this equation either, therefore may be useful in obese patients.</td>
</tr>
<tr>
<td>MDRD</td>
<td>A good general equation.</td>
</tr>
<tr>
<td>Salazar/Corcoran</td>
<td>A method specifically derived for obese patients.</td>
</tr>
</tbody>
</table>
This screen displays the default parameters for the model you selected on the patient data screen.

**Please note:** you may edit the default drug models and also enter your own drug models on the Drug model database screen.

On this screen you may edit these model parameters:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vd per kg</td>
<td>Liters per kg</td>
</tr>
<tr>
<td>Dosing wt</td>
<td>Weight, in kg, used for the Vd equation: Vd = DW x Vd per kg</td>
</tr>
<tr>
<td>Kel or CL renal</td>
<td>Renal constant of Kel or CL equation: Kel or CL = NonRenal + (CrCl x Renal)</td>
</tr>
<tr>
<td>Kel or CL nonrenal</td>
<td>Nonrenal constant of Kel or CL equation.</td>
</tr>
<tr>
<td>Target peak</td>
<td>Target peak level (mcg/ml)</td>
</tr>
<tr>
<td>Peak time</td>
<td>The time in minutes, after the infusion, at which you will be targeting your peak level.</td>
</tr>
<tr>
<td>Target trough</td>
<td>Target trough level (mcg/ml)</td>
</tr>
<tr>
<td>Infusion time</td>
<td>Length, in minutes, of the infusion.</td>
</tr>
</tbody>
</table>

Tap the **Pro** button to dose the current patient prospectively, prior to obtaining serum level data.

Tap the **Retro** button to enter and analyze serum level data for the current patient.

Tap the (<<) button to return to the previous screen.

Tap the (? ) button to view help for this screen.

**Model screen menu**

Tap on the Palm **Menu** button to display the menu for the current screen.

To restore the model defaults:

  Tap **Restore**, then **Model** on the screen menu.

To view calculated patient demographics:

  Tap **View**, then **Calculated data**

To view help about this screen:

  Tap **Help**, then **Tips**
Serum level data screen

This screen is displayed if you selected Retrospective on the previous screen.

**Please note:** Bayesian option is not active until you register the program.

To select an analysis method, Tap the appropriate button:

<table>
<thead>
<tr>
<th>Button</th>
<th>Description</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trad</td>
<td>Steady-state 2 point series</td>
<td>Traditional steady-state trough before and peak after an infusion.</td>
</tr>
<tr>
<td>3pt</td>
<td>Non-steady state 3 point series</td>
<td>Non-steady-state trough before the dose, and 2 levels after a dose.</td>
</tr>
<tr>
<td>1st</td>
<td>First dose 2- or 3-point series</td>
<td>2 or 3 Levels drawn after a loading dose. If 3 levels then data is fitted with least squares linear regression.</td>
</tr>
<tr>
<td>Post</td>
<td>2- or 3-point post dose series</td>
<td>2 or 3 levels drawn after a steady-state dose. If 3 levels then data is fitted with least squares linear regression.</td>
</tr>
<tr>
<td>B</td>
<td>Steady state Single point Bayesian</td>
<td>A &quot;random&quot; level drawn within the dosing interval (a trough level is preferred). <strong>Please note:</strong> Bayesian is active only after registration.</td>
</tr>
<tr>
<td>El</td>
<td>Extended interval Bayesian</td>
<td>A &quot;random&quot; level drawn 6 to 16 hours after a once-daily AG dose.</td>
</tr>
</tbody>
</table>

**Please Note:** all times are relative to the start or end of the sample infusion. Let's use a simple example to help illustrate this important point. Let's say that gentamicin is being administered to our patient at a dose of 80mg every 8 hours. Administration times are 0200, 1000, and 1800. The standard at your facility is to administer gentamicin over one hour. A traditional peak and trough series is ordered. The trough level is drawn at 0900, the peak at 1130. Therefore, the time entry for the trough is 60, because it was drawn 60 minutes before the start of the sample infusion. The time entry for the peak is 30, because it was drawn 30 minutes after the end of the one hour infusion.

**Please read the serum level entry screen carefully** when entering time data, some time entries are in minutes while others are in hours!

Tap the [<<] button to return to the previous screen.

Tap the Clear all button to clear all serum level data.

Tap the Calculate button to calculate individualized pk parameters based on your patient's serum level data. It is at this point that the program checks for gross errors in your data. For example, required levels and times cannot be blank, the trough cannot be greater than the peak, and the levels must be drawn within the appropriate time frame. If the serum level data is acceptable, then the dose selection screen is called.

Bayesian analysis is optional with the steady-state methods. When you click Calculate, a dialog will appear which allow you to choose whether to apply Bayesian or not.

**Please note:** Bayesian is active only after registration.
Serum level analysis pictorial

**Trad = Steady state peak and trough series**
- Levels: a trough before the dose and a peak after the dose

**3pt = Non-steady state 3 point series**
- All 3 levels required:
  - A trough level before the dose
  - A peak after the dose
  - A trough after the dose

**1st = First dose 2- or 3- point series**
- 2 or 3 levels drawn after the first (loading) dose

**Post = Steady state 2 or 3 post dose series**
- 2 or 3 levels drawn after a dose

**B = Steady state Single point Bayesian**
- A single level drawn at any time within the dosing interval

**El = one daily AG dosing**
- A single level drawn 5 to 16 hours after an El dose
Dose selection screen

Dose entry
An "ideal" dose is displayed, you then enter a practical dose and interval.

Prospective dosing
If dosing prospectively, you may select a dosing methodology. Tap the appropriate button:

<table>
<thead>
<tr>
<th>Button</th>
<th>Description</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trad</td>
<td>Traditional dosing</td>
<td>Adults: traditional 1-compartment dosing based on the target peak and trough levels you selected on the model screen. Peds: Dose is wt-based (i.e., Gent/Tobra= 2.5mg/kg, Amik= 7.5mg/kg, Vanco= 15mg/kg). Interval is age-based (i.e., neonate= 12hr, peds= 8hr).</td>
</tr>
<tr>
<td>EI</td>
<td>Extended interval AG dosing</td>
<td>AG dose is wt based (i.e., Gent/Tobra= 5mg/kg, Amikacin= 15mg/kg). Interval is based on CrCl (60= 24hr, 40-60= 36hr, 30-40= 48hr). Note: EI dosing is not available in peds patients or adults with a CrCl &lt; 30 ml/min.</td>
</tr>
</tbody>
</table>

Retrospective dosing
You do not have the ability to switch between EI and Trad on this screen if you are dosing retrospectively. The dosing method is selected from the serum level data screen. For example, if you selected EI on the serum level data screen, then only the EI button will be displayed; if you selected any other method then only the Trad button will be displayed.

<table>
<thead>
<tr>
<th>Button</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ View model ]</td>
<td>View calculated model parameters.</td>
</tr>
<tr>
<td>[ View levels ]</td>
<td>View projected serum levels from your chosen dose.</td>
</tr>
<tr>
<td>[ View graph ]</td>
<td>View a serum level plot of your chosen dose.</td>
</tr>
<tr>
<td>[ &lt;&lt; ]</td>
<td>Return to the previous screen</td>
</tr>
<tr>
<td>[ New Drug ]</td>
<td>Return to main screen.</td>
</tr>
<tr>
<td>[ Print ]</td>
<td>Print a hard copy of your dosing consult. Please note: Print function requires PalmPrint from Stevens Creek software.</td>
</tr>
</tbody>
</table>
This screen calculates antibiotic PK/PD parameters based on the MIC. Enter the MIC then Tap the “Calc PK/PD” button. Tap the “Close” button to return to the previous screen.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cp max</td>
<td>Maximum plasma concentration (true peak).</td>
</tr>
<tr>
<td>Cp min</td>
<td>Minimum plasma concentration (true trough).</td>
</tr>
<tr>
<td>AUC</td>
<td>24 hour area under the curve.</td>
</tr>
<tr>
<td>Time &gt; MIC</td>
<td>Time above MIC expressed as percentage of dosing interval. An important parameter for time dependent antibiotics such as beta-lactams.</td>
</tr>
<tr>
<td>Pk/MIC</td>
<td>Peak to MIC ratio. An important parameter for concentration dependent antibiotics such as Aminoglycosides.</td>
</tr>
<tr>
<td>24h AUC / MIC</td>
<td>The 24 hour AUC / MIC ratio. An important parameter for mixed property antibiotics such as Vancomycin.</td>
</tr>
</tbody>
</table>

Palm OS does not support printing, therefore you must purchase a program in order to print from your Palm.

Antibiotic Kinetics interfaces with PalmPrint from Stevens Creek software, it costs $40, but I feel it is well worth the cost. PalmPrint can be used with a wide variety of printers, please visit their web site for a list of supported printers. I recommend an "infrared" printer. These printers use the IR port on your Palm, allowing you to "beam" to your printer without cables or wires.

To print your consult:
1. Line up the Infrared ports on your Printer and on your Palm.
2. Turn on the Printer.
3. Enter the Patient name and your name.
4. Tap the "Print" button
Drug model database

This screen allows you to edit all of the drug model parameters. You can add your own drug models, and also add multiple models of the same drug.

Navigation buttons along the top of the screen provide the following functions:

<table>
<thead>
<tr>
<th>Button</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;&lt;</td>
<td>Previous record</td>
</tr>
<tr>
<td>&lt;</td>
<td>Previous record</td>
</tr>
<tr>
<td>+</td>
<td>Add a new model</td>
</tr>
<tr>
<td>-</td>
<td>Delete current model</td>
</tr>
<tr>
<td>v</td>
<td>Save current model. Please note: you must click this icon to save any changes you have made.</td>
</tr>
<tr>
<td>x</td>
<td>Cancel changes to current model</td>
</tr>
<tr>
<td>&gt;</td>
<td>Next record</td>
</tr>
<tr>
<td>&gt;&gt;</td>
<td>Last record</td>
</tr>
</tbody>
</table>

One compartment model parameters

- **Name**: Drug model name. To add multiple models of the same drug add a second word descriptor as pictured in the screen shot.
- **Model calculates**: Choose to have the model parameters calculate Clearance or Elimination rate constant.
- **Nonrenal**: Nonrenal portion of Kel or CL equation: Kel or CL = Nonrenal + (CrCl x Renal)
- **Renal**: Renal portion of Kel or CL equation.
- **Vd L/kg**: Volume of distribution in liters per kg
- **Vd CF**: Vd obesity correction factor, i.e., percent of adipose tissue should be included in the dosing weight.
- **Tgt peak**: Target peak level (mcg/ml)
- **Tgt tr**: Target trough level (mcg/ml)
- **Pk predict**: The time in minutes, after the infusion, at which you will be targeting your peak level.
- **EI dose**: Once daily dose (mg/kg) for "extended-interval" AG dosing. Enter zero for drugs other than AG’s.
- **Ped dose**: Prospective pediatric dose (mg/kg).
- **Ped int**: Prospective pediatric interval.
- **Neo dose**: Prospective neonatal dose (mg/kg).
- **Neo int**: Prospective neonatal interval.
- **Inf time**: Length, in minutes, of the infusion.
- **Level analysis**: Check if serum level analysis is permitted. Leaving this unchecked allows you to enter drug models which are not traditional "PK" drugs, i.e., *Cephalosporins*. 
Patient data calculations

1. Lean body weight
   - **Adult males**
     \[ \text{LBW} = 50 + 2.3 \text{ for each inch over 5 feet} \]
   - **Adult females**
     \[ \text{LBW} = 45.5 + 2.3 \text{ for each inch over 5 feet} \]
   - **Pediatric**
     \[ \text{LBW} = \left( \text{HT}^2 \times 1.65 \right) / 1000 \]
     where
     \[ \text{HT} = \text{height in cm} \]

2. Body surface area
   \[ \text{BSA} = \frac{(\text{HT} \times \text{WT})}{3600} \]
   where
   \[ \text{HT} = \text{height in cm} \]
   \[ \text{WT} = \text{weight in kg} \]

3. Creatinine clearance
   **Adult equations**
   - **Cockroft/Gault ABW**
     \[ \text{CrCl} = \frac{\text{Wt} \times (140 - \text{Age})}{(\text{SCr} \times 72)} \]
     If female then \( \text{CrCl} = 0.85 \times \text{CrCl} \)
     where \( \text{Wt} = \text{LBW plus 20\% of excess weight over LBW} \)
   - **Cockroft/Gault TBW**
     Same as above using Total Body Weight
   - **Cockroft/Gault Normalized**
     \[ \text{CrCl} = \frac{(140 - \text{Age})}{\text{SCr}} \]
   - **Jelliffe 1973**
     \[ \text{CrCl} = \frac{(98 - (0.8 \times (\text{Age}-20)))}{\text{SCr}} \]
     If female then \( \text{CrCl} = 0.9 \times \text{CrCl} \)
   - **Jelliffe Multistep**
     If female then \( \text{CreatProduction} = \text{LBW} \times (25.3 - (0.18 \times \text{Age})) \)
     If male then \( \text{CreatProduction} = \text{LBW} \times (29.305 - (0.203 \times \text{Age})) \)
     \[ \text{CrCl} = \frac{(\text{CreatProduction} \times 0.12)}{(\text{SCr} \times \text{BSA})} \]
   - **MDRD (abbreviated)**
     \[ \text{CrCl Males} = \exp[5.228 - (1.154 \times \log(\text{SCr})) - (0.203 \times \log(\text{Age}))] \]
     \[ \text{CrCl Female} = 74.2\% \text{ of male value} \]
     For African Americans multiply by 1.21
   - **Salazar and Corcoran**
     \[ \text{CrCl Males} = \left\{ (137 - \text{Age}) \times \left[ (0.285 \times \text{Wt}) + (12.1 \times \text{Ht^2}) \right] \right\} / (51 \times \text{SCr}) \]
     \[ \text{CrCl Females} = \left\{ (146 - \text{Age}) \times \left[ (0.287 \times \text{Wt}) + (9.74 \times \text{Ht^2}) \right] \right\} / (60 \times \text{SCr}) \]
   - **Pediatric CrCl**
     \[ \text{CrCl} = \frac{(\text{Ht} \times 0.48)}{\text{SCr}} \]
   - **Infant CrCl**
     \[ \text{CrCl} = \frac{(\text{Ht} \times 0.45)}{\text{SCr}} \]
Prospective dose calculation (population model)

**Traditional method**

1. Determine elimination rate (Kel) or Clearance (CL)
   
   \[ Kel \text{ (or CL)} = \text{NonRenal} + (\text{CrCl} \times \text{Renal}) \]

   where
   
   NonRenal and Renal are the population model constants as described in the drug model database.
   
   \( \text{CrCl} = \) Creatinine clearance

2. Determine Volume of distribution (Vd)
   
   \[ Vd = \left[ \text{LBW} + \left( (\text{Wt} - \text{LBW}) \times \text{CF} \right) \right] \times \text{Vd L/kg} \]

   where
   
   LBW = lean body weight
   
   Wt = measured weight
   
   CF = Population model correction factor as described in the drug model database.
   
   Vd L/kg = Population model Vd constant as described in the drug model database.

3. Determine ideal dosing interval (tau)
   
   \[ \tau = t_{inf} + \left( -\frac{1}{\text{Kel}} \right) \times \ln \left( \frac{\text{Cpmin}_{\text{target}}}{\text{Cpmax}_{\text{target}}} \right) \]

   where
   
   tinf = length of infusion
   
   Cpmin_{target} = Target trough
   
   Cpmax_{target} = Target peak

4. Determine ideal maintenance dose (IMD)
   
   \[ \text{IMD} = \text{Kel} \times \text{Vd} \times \text{Cpmax}_{\text{target}} \times \left( 1 - e^{\text{Kel} \times \tau} / 1 - e^{\text{Kel} \times t_{inf}} \right) \]

**Extended interval method**

1. Determine ideal dose
   
   \[ \text{IMD} = \text{DW} \times \text{mg/kg} \]

   where
   
   DW = LBW + [(Wt - LBW) * CF]
   
   mg/kg = Daily dose in mg/kg as described in the drug model database

2. Determine ideal dosing interval

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;= 60 ml/min</td>
<td>24 hours</td>
</tr>
<tr>
<td>40 to 59 ml/min</td>
<td>36 hours</td>
</tr>
<tr>
<td>30 to 39 ml/min</td>
<td>48 hours</td>
</tr>
</tbody>
</table>
Retrospective dose calculation (serum level analysis)

Traditional methods (Trad, Post, 3pt, 1st)

1. Determine elimination rate (Kel)

   Trad, Post, 3pt methods

   \[ Kel = \frac{(\ln Cp_{max}/Cp_{min}')}{\text{time between samples}} \]

   where
   
   \( Cp_{max} = \) Peak level
   
   \( Cp_{min}' = \) If 3pt analysis then Trough after dose, if Trad analysis then Trough is extrapolated

   1st method (first dose analysis)

   Least squares linear regression is utilized to calculate Kel (beta):

   \[
   \beta = \frac{\sum xy}{\sum xx}
   \]

   \[
   S_{xy} = \sum x y - \frac{(\sum x)(\sum y)}{n}
   \]

   \[
   S_{xx} = \sum x^2 - \frac{(\sum x)^2}{n}
   \]

   where
   
   \( x = \) time after infusion
   
   \( y = \ln(\text{serum level}) \)

2. Determine Volume of distribution (Vd)

   \[
   V_D = \frac{[\text{Dose} / \text{tinf}] / Kel \times (1 - e^{Kel \times t'})}{Cp_{max} - (Cp_{min} \times e^{-Kel \times t'})}
   \]

   where
   
   \( \text{Dose} = \) dose of sample infusion
   
   \( \text{tinf} = \) length of infusion
   
   \( Cp_{max} = \) Peak level
   
   \( Cp_{min} = \) Trough level before the dose
   
   \( t' = \) hours between time Cpmin drawn and end of infusion

3. Determine ideal dosing interval (tau)

   \[
   \tau = \text{tinf} + (-1 / Kel) \times \ln \left( \frac{Cp_{min \_target}}{Cp_{max \_target}} \right)
   \]

   where
   
   \( Cp_{min \_target} = \) Target trough
   
   \( Cp_{max \_target} = \) Target peak

4. Determine ideal maintenance dose (IMD)

   \[
   IMD = Kel \times Vd \times Cp_{max \_target} \times \left( 1 - e^{Kel \times \tau} / 1 - e^{Kel \times \text{tinf}} \right)
   \]
Retrospective dose calculation (cont’d)

Bayesian analysis

The selection of a drug dosage regimen in the absence of measured drug levels is based on estimates of the patient’s pharmacokinetic parameters adjusted for patient characteristics (e.g., weight, age, sex, serum creatinine). This is also referred to as population or a priori kinetics. An example of a priori kinetics is the Hull and Sarrubi nomogram for aminoglycoside dosing.

The traditional use of measured drug levels is to estimate the patient’s pk parameters from the measured drug levels without relying in any way on the population kinetics. This is referred to as a posteriori kinetics. An example of a posteriori dosing is the Sawchuk and Zaske method for aminoglycoside dosing.

The Bayesian approach incorporates both sets of data for estimating the patient’s pharmacokinetic parameters. It uses the a priori pharmacokinetic parameters of the population as the starting estimate for an individual; it then adjusts these estimates based on the patient’s measured drug levels taking into consideration the variability of the population parameters and the serum level data. A priori information is not discarded, but it is appropriately incorporated into the estimation procedure. The appeal of this approach is that it mimics human thinking. That is, the result of any clinical test should be interpreted in light of both the a priori expectations and knowledge of the variability of the test itself.

The Bayesian approach estimates the pharmacokinetic parameters, kel and Vd, that will be most consistent with serum levels predicted by both the population model and the actual measured serum levels. To achieve that end, the least squares method based on the Bayesian algorithm estimates the parameters which minimize the following function:

$$SS = \sum_{i=1}^{n} \frac{(C_i - f(t_i, P))^2}{\sigma_i^2} + \sum_{j=1}^{m} \frac{(\bar{p}_j - p_j)^2}{\omega_j^2}$$

where

- $n$ number of data points
- $m$ number of parameters
- $C$ measured serum level
- $f(t, P)$ predicted serum level from population model
- $\sigma$ standard deviation of serum level data
- $\bar{p}$ population parameter
- $p$ estimated parameter
- $\omega$ standard deviation of population parameter

Bayesian Precautions

In general, the Bayesian approach to the determination of individual drug-dosage requirements performs better than other approaches. However, it should be emphasized that the population model must be appropriate for the patient. It is wrong to use a drug model derived from a dissimilar patient population. For example, you should never use a model based on data from otherwise healthy adults in a frail elderly patient.

Likewise, outlying patients in a population (i.e., those patients whose pharmacokinetic parameters lie outside of the 95th percentile of the population) may be put at risk.

Bad data will corrupt the analysis. As is always the case, the computerized algorithms outlined below can only assist in the decision-making process and should never become a substitute for rational clinical judgment.
Retrospective dose calculation (cont’d)

EI method

With extended interval (EI) AG dosing, the interval is changed depending on whether the "random" level falls above or below the interval break points on the dosage adjustment graph. The AG dose is not changed, only the interval.

Obtain a mid-interval drug level 6 to 16 hours after the initial dose, then evaluate the level using the interval adjustment nomogram. If the 6 to 16 hour level is undetectable and the infection is not responding, consider changing to a traditional dosing method. The three interval break points on the Hartford interval adjustment nomogram are the approximate decay curves from a 7mg/kg gentamicin dose. These decay curves were calculated using a one compartment model with a volume of distribution of 0.25 L/kg and an elimination rate calculated from creatinine clearances of 25, 40, and 60 ml/min for 48, 36, and 24 hour intervals respectively. The authors of the Hartford nomogram then flattened these decay curves to simplify the nomogram. This nomogram is utilized by Antibiotic Kinetics if your model EI dose is 7mg/kg.

It is important to note that the Hartford interval adjustment nomogram is only valid for a 7mg/kg dose. A nomogram for the less aggressive dose of 5mg/kg/day was developed by a consensus panel. For 15mg/kg doses of amikacin multiply the drug-level scale by a factor of three. This nomogram is utilized by Antibiotic Kinetics if your model EI dose is 5mg/kg.

This same consensus panel argues that the 48 hour interval should be abandoned, that patients with a CrCl < 40ml/min should be dosed by traditional pharmacokinetic methods. The consensus panel also suggests that younger patients with excellent renal function may require Q 12 hour dosing. A new dosing algorithm for this subpopulation has been proposed by Urban and Craig. However, this nomogram is not utilized by Antibiotic Kinetics, it is show here for your reference.

Some have questioned the validity of all ODA nomograms because they are based on one-compartment parameters derived from traditional dosing methods. Some pk studies have shown that the pharmacokinetics of aminoglycosides at high doses differ significantly from those at traditional doses. Therefore, it is argued that nomograms based on an assumption of similar kinetics are invalid.
Frequently asked questions

**Question:** Why does the Palm version run so slow?

**Answer:** Unfortunately the Palm program does run slow on older, inexpensive devices like the Palm M105 or the Visor Deluxe. This is a because of the slow processor speeds in these models.

**Question:** I've made changes in the model editor screen, but they don't show up when I dose.

**Answer:** Models are not automatically saved. You must tap the "Save" icon before exiting the editing screen.

**Question:** When I change height, weight or SCr the creatinine clearance does not change.

**Answer:** Unlike Windows, Palm OS does not have an "on change" event. When you change the height or weight, you must tap to the next field, select a drug, or tap either the "Calc" or "Next" buttons to re-calculate creatinine clearance. Changing ht/wt/cr does not automatically trigger recalculation, like a Windows program would. This is a limitation of the operating system, not a bug, or a reflection of my incomplete skills as a programmer.

**Question:** In the description of your program it shows "EI" AG dosing but when dosing Gentamicin I only see the "TRAD" button.

**Answer:** The program only allows Extended Interval dosing in adults with creatinine clearance > 30. However this is the most basic requirement. EI dosing should be avoided in many other patient groups. Please familiarize yourself with consensus guidelines for pulse dosing of aminoglycosides.

**Question:** Why does the creatinine clearance from the Antibiotic Kinetics® program differ from what I calculate by hand?

**Answer:** The difference is most likely due to the weight that you are using in your hand calculation. Because creatinine is produced by muscle tissue, not fat, most experts recommend that you use lean body weight in normal patients and adjusted body weight in morbidly obese patients.

**Question:** Why are there two vancomycin models?

**Answer:** Vancomycin is a difficult drug to dose, no model is perfect for every patient population. Even the experts can't agree on a model or dosing method.

? The Kel model calculates a rate constant via the Matzke method.

? The CL model calculates clearance via the Winter method.

**Question:** How do I dose IM gentamicin?

**Answer:** Enter an infusion length of 90 minutes, which is the average time for IM absorption of aminoglycosides. Be sure to draw your peaks at least 90 plus 15 minutes after the injection.

Feedback

If you have any comments or suggestions for improving the program, email ricktharp@rxkinetics.com. Thank you and happy dosing, Rick.

Web links

Once daily aminoglycoside dosing  [http://www.rxkinetics.com/oda.html](http://www.rxkinetics.com/oda.html)
Palm Print utility from Stevens Creek software  [http://www.stevenscreek.com/palm/palmprint.shtml](http://www.stevenscreek.com/palm/palmprint.shtml)