**Prospective Dosing of Aminoglycosides and Vancomycin for Adults**
**Simplified Hand Calculations**
**Marshall Pierce PharmD**

Calculate the patient body surface area$_{\text{meters squared}}$ =

$$\text{Weight}_{kg}^{0.425} * ((\text{Height}_{inches}*2.54)^{0.725})*0.007184$$

Creatinine clearance individualized:

Males$_{(ml/min)}$ = $\dfrac{(140\text{-age}) * (\text{ Use Lean Body Weight}_{(kg)} \text{ or actual weight if less than LBW}_{(kg)})}{\text{serum creatinine} * 72}$

Females$_{(ml/mn):}$ above x 0.85

ml/min/1.73$_{\text{meters squared}}$ = above * 1.73 / patients surface area

K elimination (hours$^{-1}$)

Aminoglycosides K $_{(\text{hours-1})}$ = 0.0026 * Clcr + 0.014 (Equation derived in adults)

Vancomycin K $_{(\text{hours-1})}$ = 0.00107 * Clcr $_{\text{per 1.73 meters squared}}$ + 0.0052 (Equation derived in adults)

T$_{1/2\ (\text{hours})}$ = 0.693/K

Tau (Dosing Interval)

Tau$_{(\text{hours})}$ = $\dfrac{\text{Ln(peak desired / trough desired)}}{K}$ + Infusion Period in hours

Infusion Period is abbreviated as T'

T' Vancomycin = 1-2 hours (0.5-1 gram per hour), aminoglycosides = 0.5 hour

Round to a convenient interval i.e. 8, 12, 16, 24, 36, 48 hours

For aminoglycosides do not use dosage intervals < 8 hours unless patient has cystic fibrosis.

Vancomycin do not use < 12 hours unless a pediatric patient is being treated.

Dosing weight (kilograms)

Lean body weight (LBW$_{(kg)}$)

Males$_{(kg)}$ = 50$_{(kg)}$ + 2.3$_{(kg)}$ * (height in inches - 60)

Females$_{(kg)}$ = 45.5$_{(kg)}$ + 2.3$_{(kg)}$ * (height in inches - 60)

Adjusted body weight, **aminoglycosides only**, if actual weight > LBW.

Adjusted Body Weight$_{(kg)}$ = LBW$_{(kg)}$ + 0.4 * (Actual Weight$_{(kg)}$ – LBW$_{(kg)}$)

Dosing weight (kg)

Aminoglycosides

Is the adjusted body weight if overweight

or

Is the actual body weight if actual weight $\le$ LBW

Vancomycin use total body weight

Volume of distribution (Vd)

Aminoglycosides$_{(\text{liters})}$ = 0.25$_{(L/kg)}$ * dosing weight$_{(kg)}$ (Equation derived in adults)

Vancomycin$_{(\text{liters})}$ = 0.65$_{(L/kg)}$ * total body weight$_{(kg)}$ (Equation derived in adults)

Loading dose (milligrams) **assumes no drug on board**

Loading dose$_{(mg)}$ = Cpmax desired$_{(mg/L)}$ * Vd $_{(\text{Liters})}$

Quick estimate

Aminoglycosides(gentamicin/tobramycin): 1.75-2 mg/kg of dosing weight

Vancomycin: 20-25 mg/kg * total body weight

Maintenance $Dose_{(milligrams)}$ = Cp maximum $Desired_{(mcg/ml)}$ * $Vd_{(liters)}$ * $(1-e^{(-K * Tau)})$

Predicted steady state peak and trough for the rounded dose

$$Cpmax\ predicted_{(mcg/ml)} = \frac{Dose_{(mg)}}{Vd * (1-e^{(-K * Tau)})}$$

$$Cpmin\ Predicted_{(mcg/ml)} = Cpmax\ Predicted * e^{(-K * Tau)}$$

Time for a level to fall from a known value to a desired level.

$$Time_{(hours)} = \frac{\ln (Level\ known/\ level\ desired)}{K}$$

Fraction of steady state achieved: $1- e^{(-\ number\ of\ doses\ given\ *\ K\ *\ Tau)}$, assumes same dose given for each dose

## Retrospective Dosing of Aminoglycosides and Vancomycin Using Steady State Serum Levels For Adults and Pediatrics, Simplified Hand Calculations

**Marshall Pierce PharmD**

Calculate K Elimination ($hour^{-1}$)

$$K_{(hours-1)} = \frac{Ln(Cpmax\ lab\ /\ Cpmin\ lab)}{Time\ (hours)\ between\ levels\ (as\ if\ both\ levels\ were\ drawn\ after\ the\ same\ dose)}$$

$T_{1/2\ (hours)}$ = 0.693/K

Volume of distribution using steady state levels:

$$Vd_{(liters)} = \frac{Maintenance\ dose * e^{(-K * Time\ (hours)\ level\ drawn\ post\ dose)}}{Cpmax\ lab\ level * (1-e^{(-K * Tau)})}$$

$$Vd_{(liter/kg)} = \frac{Vd_{(liters)}}{Dosing\ Weight_{(kg)}}$$

New dosing interval (Tau in hours) if needed

$$Tau_{(hours)} = \frac{Ln(peak\ desired/trough\ desired)}{K} + Infusion\ Period\ (hours)$$

T' for Vancomycin = 1-2 hours (0.5-1 gm per hour), aminoglycosides = 0.5 hour

Round to a convenient interval i.e. 8, 12, 16, 24 hours

Calculate maintenance dose

$$Maintenance\ dose_{(mg)} = Cpmax\ Desired * Vd\ (1-e^{(-K * Tau)})$$

Calculate predicted peak and trough for the rounded dose

$$Cpmax\ predicted_{(mcg/ml)} = \frac{Rounded\ Dose_{(mg)}}{Vd * (1-e^{(-K * Tau)})}$$

$$Cpmin\ predicted_{(mcg/ml)} = Cpmax\ Predicted * e^{(-Kel * Tau)}$$

Calculation of time to a desired level after a known level

$$Change\ in\ time_{(hours)} = \frac{Ln\ (known\ level/level\ desired)}{K}$$

Fraction of steady state achieved: $1- e^{(-number\ of\ doses\ given\ *\ K\ *\ Tau)}$, assumes same dose given for each dose

Key:

K = elimination rate constant in $hours^{-1}$

LD = Loading Dose in milligrams

MD = Maintenance Dose in milligrams

T' = Infusion Period in Hours

Tau = Dosage interval in Hours

**Lithium Prospective Dosing**
**Marshall Pierce PharmD**

Creatinine clearance individualized (Clcr):

$$Males_{(ml/min)} = \frac{(140\text{-age}) * (\text{Use Lean Body Weight}_{(kg)} \text{ or actual weight if less than } LBW_{(kg)})}{\text{serum creatinine} * 72}$$

$Females_{(ml/mn):}$ above x 0.85

Clearance

$Lithium_{(L/hr)} = 0.25 * Clcr * (60/1000_{\text{Converts ml/min to L/hr}})$

If concurrent hydrochlorothiazide multiply by 0.5

If concurrent indomethacin multiply by 0.7

If concurrent ACEI multiply by 0.5

If multiple factors use the one with the largest impact

Sodium depletion decreases clearance

Volume of distribution (Vd)

$Lithium_{(liters)} = 0.7_{(L/kg)} * \text{total body weight}_{(kg)}$

K elimination ($hours^{-1}$)

$Cl_{(L/hr)} / Vd_{(liters)}$

$T_{1/2\ (hours)} = 0.693/K$

Normal half-life 18-24 hours

Tau (Dosing Interval)

Usually dosed twice daily

Use a convenient interval i.e. 6, 8, 12, 24 hours

Dosing weight (kilograms)

Lean body weight ($LBW_{(kg)}$)

$Males_{(kg)} = 50_{(kg)} + 2.3_{(kg)} * (\text{height in inches} - 60)$

$Females_{(kg)} = 45.5_{(kg)} + 2.3_{(kg)} * (\text{height in inches} - 60)$

Dosing weight (kg)

Lithium use <u>total body weight</u>

Fraction Absorbed (Bioavailability)

| | |
|---|---|
| Immediate Release | 1 |
| Sustained Release | 0.9 |

Loading doses are <u>not</u> used as this would cause toxicity

$\text{Maintenance Dose}_{(milligrams)} = Cp_{(mEq/L)} * Cl_{(L/hr)} * Tau_{(hours)} * 300/(8.12 * \text{Fraction Absorbed})$

Desired Level is approximately 0.8 mEq/L

Note: there is 8.12 mEq per 300 mg of Lithium carbonate

Predicted average steady state $level_{(mEq/L)}$

$Cp_{(mEq/L)} = \text{Maintenance Dose}_{(milligrams)} * 8.12 * \text{Fraction Absorbed} / (Cl_{(L/hr)} * Tau_{(hours)} * 300)$

Predicted steady state peak and trough for the rounded dose

$$\text{Cpmax predicted}_{(mEq/L)} = \frac{Dose_{(mg)} * 8.12}{Vd_{(Liters)} * 300 * (1-e^{(-K * Tau)})}$$

$\text{Cpmin Predicted}_{(mEq/L)} = \text{Cpmax Predicted} * e^{(-K * Tau)}$

$Cpmin_{12hours\ post\ dose}\ Predicted_{(mEq/L)} = \text{Cpmax Predicted} * e^{(-K * 12)}$

Time for a level to fall from a known value to a desired level.

$$Time_{(hours)} = \frac{\ln(\text{Level known}/\text{level desired})}{K}$$

Fraction of steady state achieved: $1 - e^{(-\text{ number of doses given} * K * Tau)}$, assumes same dose given for each dose

Therapeutic Levels:

Chronic Therapy 0.6-0.8 mEq/L

Acute Mania 0.8-1.2 mEq/L

Samples should be drawn 12 hours after the last evening dose as therapeutic and toxic levels were defined using this sampling method.

Therapeutic Effects:

Full therapeutic effects are usually seen in 14-21 days.

Toxic Levels

$\geq$1.5 mEq/L: CNS (lethargy, fatique, muscle weakness, tremor)

## Digoxin Prospective Dosing
## Marshall Pierce PharmD

Creatinine clearance individualized:

$$Males_{(ml/min)} = \frac{(140\text{-age}) * (\text{ Use Lean Body Weight}_{(kg)} \text{ or actual weight if less than LBW}_{(kg)})}{\text{serum creatinine} * 72}$$

$Females_{(ml/mn):}$ above x 0.85

Clearance

$Digoxin_{(L/hr)NonCHF} = (0.8\ LBW + Clcr) * (60/1000_{\text{Converts ml/min to L/hr}})$

$Digoxin_{(L/hr)CHF} = (0.33\ LBW + 0.9*Clcr) * (60/1000_{\text{Converts ml/min to L/hr}})$

If concurrent amiodarone multiply by 0.5

If concurrent quinidine multiply by 0.5

If concurrent verapamil multiply by 0.75

If clinically hypothyroid multiply by 0.7

If clinically hyperthyroid multiply by 1.3

Volume of distribution (Vd)

$Digoxin_{(liters)} = (3.8_{(L/kg)} * \text{lean body weight}_{(kg)}) + (3.12 * Clcr_{(ml/min)})$

If concurrent quinidine multiply by 0.7

If clinically hypothyroid multiply by 0.7

If clinically hyperthyroid multiply by 1.3

K elimination ($hours^{-1}$)

$Cl_{(L/hr)} / Vd_{(liters)}$

$T_{1/2\ (hours)} = 0.693/K$

Tau (Dosing Interval)

Usually dosed daily

Dosing weight (kilograms)

Lean body weight ($LBW_{(kg)}$)

$Males_{(kg)} = 50_{(kg)} + 2.3_{(kg)} * (\text{height in inches} - 60)$

$Females_{(kg)} = 45.5_{(kg)} + 2.3_{(kg)} * (\text{height in inches} - 60)$

Dosing weight (kg)

Digoxin use lean body weight

Fraction Absorbed (Bioavailability)

| | |
|---|---|
| Tablets | 0.7 |
| Elixir | 0.8 |
| Injection | 1 |
| Soft Gelatin Capsule | 1 |

Loading doses

$Dose_{(mg)} = Vd_{(liters)} * Cp(ng/ml) / (\text{Fraction Absorbed} * 1000)$

Maintenance $Dose_{(milligrams)} = Cp_{(ng/ml)} * Cl_{(L/hr)} * Tau_{(hours)} / (\text{Fraction Absorbed} * 1000)$

Predicted average steady state $level_{(ng/ml)}$

$Cp_{(ng/ml)} = \text{Maintenance } Dose_{(milligrams)} * \text{Fraction Absorbed} * 1000 / (Cl_{(L/hr)} * Tau_{(hours)})$

Predicted steady state peak and trough for the rounded dose

$$Cpmax\ predicted_{(ng/ml)} = \frac{Dose_{(mg)} * \text{Fraction Absorbed} * 1000}{Vd_{(Liters)} * (1-e^{(-K * Tau)})}$$

$Cpmin\ Predicted_{(ng/ml)} = Cpmax\ Predicted * e^{(-K * Tau)}$

Time for a level to fall from a known value to a desired level.

$$Time_{(hours)} = \frac{\ln(\text{Level known/ level desired})}{K}$$

Fraction of steady state achieved: $1- e^{(-\text{ number of doses given } * K * Tau)}$, assumes same dose given for each dose

Therapeutic Levels:

- Atrial Fibrillation Trough 1.5-2 ng/ml, Predicted or Calculated Peak < 2.5 ng/ml
- CHF Trough 0.8-1.2 ng/ml, Predicted or Calculated Peak < 1.5 ng/ml
- Samples should be drawn no sooner than 6 hours after an IV dose and 8 hours after an oral dose due to slow distribution into tissue.

**Theophylline Prospective Dosing**
**Marshall Pierce PharmD**

Clearance

Theophylline $Clearance_{(L/hr)}$ = L/kg/hour * $kg_{(lean\ body\ weight)}$

| | |
|---|---|
| If age >=1 and age <= 9, | 0.08 * LBW |
| If age >9 & <=12, | 0.07 * LBW |
| If age > 12 & <= 50 & smoker, | 0.07 * LBW |
| If age >12 & <=16 & nonsmoker, | 0.05 * LBW |
| If age > 50 & smoker, | 0.064*LBW |
| If age > 16 & nonsmoker, | 0.04 * LBW |

If concurrent CHF multiply by 0.4, maximum daily dose 400 mg without a level
If concurrent Cystic Fibrosis multiply by 1.5
If acute pulmonary edema multiply by 0.5
If acute viral illness multiply by 0.5
If hepatic cirrhosis multiple by 0.5, maximum daily dose 400 mg without a level
If severe obstructive pulmonary disease multiply by 0.8
If concurrent cimetidine multiple by 0.6
If concurrent ciprofloxacin multiple by 0.7
If concurrent erythromycin multiple by 0.75
If concurrent phenobarbital multiple by 1.3
If concurrent phenytoin multiple by 1.6
If concurrent propranolol multiple by 0.6
If concurrent rifampin multiple by 1.3

Volume of distribution (Vd)

$Theophylline_{(liters)} = 0.5_{\ (L/kg)}$ * lean body $weight_{(kg)}$

K elimination ($hours^{-1}$)

$Cl_{(L/hr)} / Vd_{(liters)}$

Ka 1.8 for Theodur, Sustaire, Slobid; products marketed for once daily dosing are not recommended due to potential for dose dumping and incomplete absorption

$T_{1/2\ (hours)} = 0.693/K$

Tau (Dosing Interval)

2-4 times daily depending on product

Dosing weight (kilograms)

Lean body weight ($LBW_{(kg)}$)

$Males_{(kg)} = 50_{(kg)} + 2.3_{(kg)}$ * (height in inches - 60)

$Females_{(kg)} = 45.5_{(kg)} + 2.3_{(kg)}$ * (height in inches - 60)

Dosing weight (kg)

Theophylline use lean body weight

Fraction Absorbed (Bioavailability)

| | |
|---|---|
| Tablets | 1 |
| Elixir | 1 |
| Injection | 1 |
| Sustained Release | 1 |

Salt (Fraction of Dose Active Ingredient)

| | |
|---|---|
| Aminophylline | 0.84 |
| Amindur | 0.84 |
| Choledyl | 0.64 |
| Theophylline | 1 |

Loading doses (aim for 10 mcg/ml, assuming no drug on board)

$Dose_{(mg)} = Vd_{(liters)} * Cp_{(mcg/ml)}$ / (Fraction Absorbed * Salt)

Maintenance $Dose_{(milligrams)} = Cp_{(mcg/ml)} * Cl_{(L/hr)} * Tau_{(hours)}$ /(Fraction Absorbed * Salt)

Predicted average steady state $level_{(mcg/ml)}$

$Cp_{(mcg/ml)}$ = Maintenance $Dose_{(milligrams)}$ * Fraction Absorbed *Salt /($Cl_{(L/hr)} * Tau_{(hours)}$)

Predicted steady state peak and trough for the rounded dose

$$Cpmax\ predicted_{(mcg/ml)} = \frac{Dose_{(mg)} * Fraction\ Absorbed * Salt}{Vd_{(Liters)} * (1-e^{(-K * Tau)})}$$

$Cpmin\ Predicted_{(ng/ml)} = Cpmax\ Predicted * e^{(-K * Tau)}$

Time for a level to fall from a known value to a desired level.

$$Time_{\ (hours)} = \frac{\ln(Level\ known/\ level\ desired)}{K}$$

Fraction of steady state achieved: $1 - e^{(- \text{number of doses given} * K * Tau)}$, assumes same dose given for each dose

Therapeutic Levels:

Maximum peak: 20 mcg/ml

Trough: 5-15 mcg/ml, usually 10 mcg/ml

Sustain Release Product Equations:

Predicted steady state level$_{(mcg/ml)}$ at time t post dose

$$Cp_{(mcg/ml)} = \frac{Salt*Fraction*Dose*ka}{Vd*(ka-k)} * [(e^{-k*t}/(1-e^{-k*tau})) - (e^{-ka*t}/(1-e^{-Ka*tau}))]$$

Time to Cmax at Steady State (hours)

$$Tpmax_{(hours)} = \frac{\ln[ka*(1-e^{-k*tau}) / (k*(1-e^{-ka*tau}))]}{(ka-k)}$$

Equations for Single Dose

$$Cp_{(mcg/ml)} = = \frac{Salt*Fraction*Dose*Ka}{Vd*(ka-k)} * (e^{-k*t} - e^{-ka*t})$$

$$Tpmax_{(hours)} = \frac{\ln(ka / k)}{(ka-k)}$$

Pediatric Equations

Creatinine Clearance

$$Clcr_{(ml/min/1.73\ Meters\ Squared)} = \frac{K * Height_{(cm)}}{Serum\ Creatinine_{(mg/dl)}}$$

$$= \frac{K * Height(inches) * 2.54}{Serum\ Creatinine_{(mg/dl)}}$$

K= 0.45 full term to < 2 years

K= 0.55 children < 13

K= 0.55 females 13-21 years

K=0.7 males 13-21 years