1.5. Aminoglycoside Antibiotics

Pharmacokinetic Parameters

Table 1.5-1. Volume of Distribution by Age Group

Age	Volume (V) (mean ± SD)[a,b]
Neonates[1–6]	0.45 ± 0.1 L/kg[c,d]
Infants[7]	0.40 ± 0.1 L/kg[d]
Children[8,9]	0.35 ± 0.15 L/kg[e]
Adolescents[8,9]	0.30 ± 0.1 L/kg[e]
Adults and geriatrics[10–13]	0.30 ± 0.13 L/kg

[a]The values approximate those in the original studies.

[b]Studies are inconsistent in the reporting of V relative to body weight. Volume may be related to actual (ABW), ideal (IBW), or an adjusted dosing weight (BW_{adj}); many studies have patients both above and below ideal weight. $BW_{adj} = IBW + 0.4(ABW - IBW)$.

[c]Premature neonates tend to have a larger V (nearer 0.50–0.55 L/kg and perhaps even larger), while full-term neonates tend to have smaller values (nearer 0.40–0.45 L/kg).

[d]Use actual body weight (ABW) to estimate the V for neonates and infants.

[e]For children and adolescents, ideal body weight (IBW) is suggested for estimating V, although one study found that an adjusted body weight (BW_{adj}) might need to be used in obese children.

Estimating Aminoglycoside Clearance and the Elimination Rate Constant (k)

Aminoglycoside clearance (CL_{ag}) has been found to be approximately equal to creatinine clearance (CrCl). Thus, k may be determined after measuring or estimating CrCl using the following equation:

$$k = \frac{CL_{ag}}{V}$$

where CL_{ag} (= CrCl) is in liters per hour (L/hr), k in hours^{-1}, and V in liters (L).

Self-Assessment Problems

1. The following *steady state* gentamicin concentrations are drawn on an 85-kg patient receiving 140 mg every 12 hours. Doses are given as 0.5-hour infusions at 10 a.m. and 10 p.m.

C (mg/L)	1.1	6.1
Time	9:30 a.m.	11 a.m.

   Determine the patient's half-life (in hours) and volume of distribution (in L/kg).

2. A 50-year-old woman, height 5'9", weight 75 kg, is started on tobramycin 160 mg every 12 hours for *E. coli* septicemia. She is also receiving cefazolin 1 g every 8 hours. The patient's estimated creatinine clearance is 60 mL/min. Estimate the patient's steady state peak and trough tobramycin concentrations on this dosage regimen. The patient's IBW is 66.2 kg; use ABW for calculating V.

   Note: At your hospital, it is traditional to collect peak concentrations 30 minutes after the end of 30-minute infusions, and troughs 30 minutes before the next dose.

3. A 62-year-old woman, height 5'4", weight 90 kg, is started on tobramycin 120 mg every 12 hours for *Pseudomonas* septicemia. On admission she reported "feeling really bad" and that she was having chills. She is also to receive ticarcillin 3 g every 6 hours. You are asked to consult on the patient. After speaking with the woman you note that, though overweight, she does appear to be in fairly good physical condition. Because of this, use BW_{adj} (accounting for 40% of difference between actual and ideal) for her weight when determining dosing weight and V. The following is gleaned from her chart:

   3/2 Begin tobramycin 120 mg every 12 hours IV (give as 30-minute infusions)—first dose at 10 a.m.

   3/2 Begin ticarcillin 3g every 6 hours IV—first dose at 12 noon

Patient Data	Value	Date/Time
Creatinine	2.1	3/1 0600
eGFR	30 mL/min	3/1 0600
BUN	22	3/1 0600
WBC	18 k/mm^3	3/1 0600
Intake/output	2300/1600 mL	3/1 24-hour observation period
Temperature	101°	3/1 1800
Temperature	102°	3/2 0600
Blood pressure	110/60	3/2 0600

   Note: At your hospital, it is traditional to collect peak concentrations 30 minutes after the end of 30-minute infusions and troughs 30 minutes before the next dose. These are usually done as trough—dose—peak for convenience. Desired peaks are ~8 to 10 mg/L range in the institution and desired troughs are ~0.5 to 1.5 mg/L (but definitely <2 mg/L).

   A. Predict the steady state peak concentration on 120 mg every 12 hours.

   B. Predict the steady state trough concentration on 120 mg every 12 hours.

4. The patient you saw in Problem 3 was changed to tobramycin 160 mg every 12 hours on 3/3. The case description is the same with added information on labs and orders. The following new data are gleaned from the chart:

   3/3 Change tobramycin to 160 mg IV every 12 hours—first dose at 10 a.m.

   3/3 Get peak and trough tobramycin concentrations around the fourth 160-mg dose.

Patient Data	Value	Date/Time
Creatinine	1.7	3/2 1800
eGFR	37 mL/min	3/2 1800
Temp	100°	3/3 0600
WBC	15 k/mm^3	3/3 0600
Tobramycin	3.1 mg/L	3/4 2130
Tobramycin	10.1 mg/L	3/4 2330