Clinical Pharmacokinetic Equations

Adults: (≥ 17 years)

$$\text{CrCl (ml/min)} = \frac{(140\text{-Age}) \cdot CrClWt}{72 \cdot SrCr} \cdot (0.85 + Sex \cdot 0.15)$$

If the patient is < IBW, use Wt = ABW.
If the patient is > IBW and BMI < 25 Kg/m^2, Wt = IBW
If the patient has a BMI ≥ 25 Kg/m^2, Wt = AdjWT

IBW (males)
50 Kg + 2.3 Kg/inch over 5 feet
IBW (females)
45.5 Kg + 2.3 Kg/inch over 5 feet

BMI = Wt (Kg) / (Ht (In) * 0.0254)^2

If ActBW is > 30% over IBW, then
DWT = IBW + 0.4*(ActBW – IBW)
If BMI ≥ 25 Kg/m^2, then
CrCl-WT = IBW + 0.4*(ActBW – IBW)

Neonates: (<2 months)

$$CrCl(\text{ml/min/1.73m}^2) = \frac{0.45 \cdot (CmHt.)}{SrCr}$$

Pediatrics: (2 months – 16 years)

$$CrCl(\text{ml/min/1.73m}^2) = \frac{3.5 \cdot Age + 23.6}{SrCr}$$

$$BSA = Wt^{0.5378} \cdot Ht^{0.3964} \cdot 0.024265$$

CrCl Norm = CrCl * 1.73 /BSA

$$GFR = 175 \cdot SrCr^{-1.154} \cdot Age^{-0.203} \cdot (0.742 + Sex \cdot 0.258) \cdot (1 + 0.21 \cdot Black)$$

Black = 1, else = 0,
Sex: Male = 1, female = 0

$$GFR\ (CKD - EPI) = (144 - (Sex * 3)) * (1 + 0.155 * Black) * 0.993^{Age} * \left(\frac{SrCr}{(0.7 + (0.2 * Sex))} \right)^{-0.329 - SrCrExp}$$

[where Sex = 1 for male, 0 for female, Black = 1 for Black, 0 for other races. and
If SrCr > (0.7 + 0.2*Sex) Then SrCrExp = 0.88 , Else SrCrExp = Sex*0.082]

Population Estimates

Volume of distribution (V)

Aminoglycosides:
V_{ss} (L) = 0.225 L/kg x DWT
V_{ss} (dehydrated) = 0.15 L/kg x DWT
V_{ss} (Fluid overload) = 0.30 L/kg x DWT
Vancomycin:
V_{ss} (L) = 0.7 L/Kg x ActWT

Elimination rate constant (k)

Gentamicin
Ke = 0.015 + (0.00285 x CrCl)
Tobramycin
Ke = 0.010 + (0.0031 x CrCl)
Amikacin
Ke = 0.010 + (0.0024 x CrCl)
Vancomycin
Ke = [44 + (8.3 x CrCl)] / 10000

1. Calculate the elimination rate constant.

$$k_e = \frac{\ln C_1 - \ln C_2}{t_2 - t_1} = \frac{\ln C_{pk} - \ln C_{tr}}{t_{tr} - t_{pk}} = \frac{\ln(C_{pk}/C_{tr})}{\tau - t_{inf} - t_{pi}}$$

2. Calculate C_0 (t_{pk} = elapsed time from start of infusion)

$$C_0 = \frac{C_{pk}}{e^{-k_e (t_{pk} - t_{\text{inf}})}}$$

3. Calculate the half-life.

$$t_{½} = \frac{\ln 2}{k_e}$$

4. Calculate the volume of distribution.

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

5. Calculate the dosing interval.

$$\tau = \frac{\ln(C_{Max,desired}/C_{Min,desired})}{k_e} + t_{\text{inf}}$$

6. Calculate the new infusion rate.

$$\boldsymbol{R_0 = C_{Max,desired} \cdot k_e \cdot V_{ss} \cdot \frac{\left(1 - e^{-k_e \tau}\right)}{\left(1 - e^{-k_e t_{\text{inf}}}\right)}}$$

7. Calculate the new peak.

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

8. Calculate the new trough.

$$C_{ss,tr} = C_{ss,pk} \cdot e^{-k_e (\tau - t_{\text{inf}})}$$

TR Only: $\left({}^{\text{Dose}}/_{\text{Tau}}\right)_{\text{new}} = \left({}^{\text{Dose}}/_{\text{Tau}}\right)_{\text{current}} * {}^{C_{\text{desired}}}/_{C_{\text{measured}}}$ [$C_{desired}$ = Target 15 mg/L]

Target Drug Concentrations

	Trough	Peak (Life Threatening infection)	Peak (Serious Infection)	Peak (Synergy/UTI)	Infusion Time
Gentamicin	< 2 mg/L	8 to 10 mg/L	6 to 8 mg/L	4 to 6 mg/L	0.5 Hr.
Tobramycin	< 2 mg/L	8 to 10 mg/L	6 to 8 mg/L	4 to 6 mg/L	0.5 Hr.
Amikacin	< 10 mg/L	25 to 30 mg/L	20 to 25 mg/L	15 to 20 mg/L	0.5 Hr.
Vancomycin	10-20 mg/L		30 to 40 mg/L		1.5 Hr. (≤ 1.25 g) 2 Hr. (1.5 – 2 g)

Extended-Interval Dosing

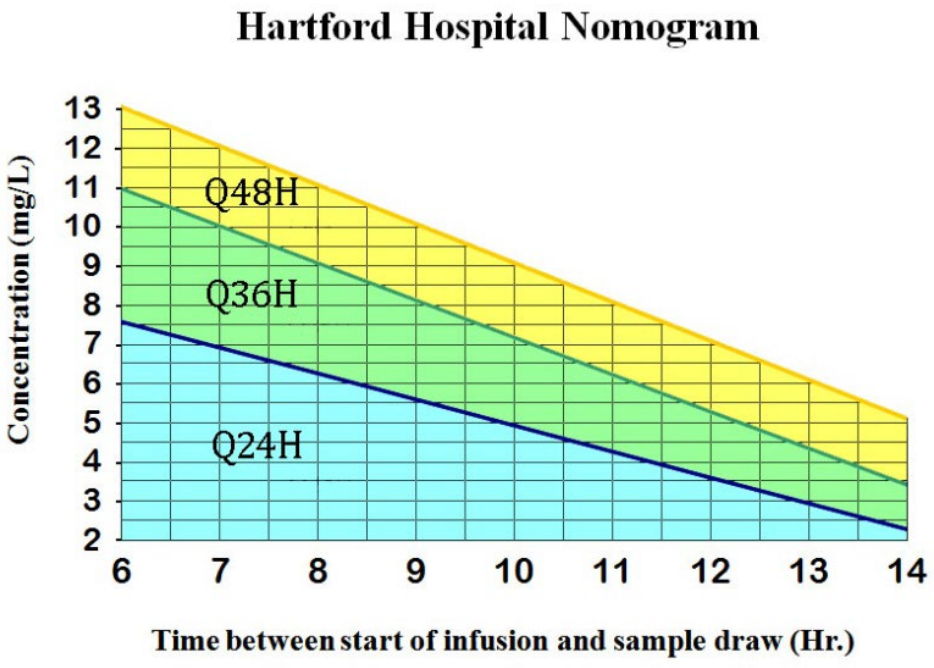
Initial Dosing Regimen - Adults:

Creatinine Clearance	Dose and Dosing Interval
≥ 60 ml/min	7 mg/kg every 24 hours
40 to 59 ml/min	7 mg/kg every 36 hours
20-39 ml/min	7 mg/kg every 48 hours
< 20 ml/min	Use conventional dosing approach.

Dosing is based on ABW, unless the patient is >30% IBW, use DWT

Initial Dosing Regimen - Children:

Age	Dose and Dosing Interval
3 months – 2 years	9.5 mg/kg every 24 hours
2 – 8 years	8.5 mg/kg every 24 hours
> 8 Years	7.0 mg/kg every 24 hours



Hartford nomogram for gentamicin and tobramycin at 7 mg/kg

Monitoring: Obtain a single serum level 6 to 14 hours after the start of infusion following the administration of the first dose. Evaluate according to the nomogram below. If the patient is on a transition line, choose the longer interval. If the level is off the nomogram, hold the next dose and obtain serial levels to calculate drug clearance according to conventional dosing equations.

Patient Exclusion: Extended-interval dosing is not recommended in pediatrics, pregnancy, burn patients (>20%), ascites, dialysis, enterococcal endocarditis, and patients with an estimated creatinine clearance of < 20 ml/min.