(This summary is designed only for the lecture; it never designed for any exam.)

CLINICAL PHARMACOKINETIC FOR AMINOGLYCOSIDE:

A-Initial dose determination.

B-Use of Aminoglycoside concentration to change the dose.

Initial dose determination:

1- pharmacokinetic dosing method.

2-Hull and Sarubbi nomogram method.

3-Harford nomogram method for extended interval dosing.

4-Literature-based recommended dosing method

1-Pharmacokinetic dosing methods

To get the initial dose using pharmacokinetic dosing method, the following should be known:

1- The actual weight of the patient and its relation to ideal body weight.

$\%\ \boldsymbol{overweight} = \frac{(\boldsymbol{ABW}-\boldsymbol{IBW})}{\boldsymbol{IBW}} \times 100\%$, $\boldsymbol{ABW}$= Actual body weight, $\boldsymbol{IBW}$= Ideal body weight

IBW (male) = 50 + 2.3 (H - 60) **IBW** (female) = 45.5 + 2.3 (H - 60)

Where: H = *height in inches*

IBW (male) = 0.9 H – 88 **IBW** (female) = 0.9 H – 92

Where: H = *height in centimeters*

2-Creatinine clearance

A-If the patient has stable renal function and not obese, use Cockroft and Gault EQ:

$$CrCl\ male = \frac{(140-Age)*wt}{72*Sc}$$

$$CrCl\ female = 0.85\ \frac{(140-Age)*wt}{72*Sc}$$

(Cockroft and Gault) where Age in years, Wt in Kg, and Sc in mg/dL.

B- If the patient has stable renal function and obese (above 30% of its ideal body weight), use Salazar and Corcoran equation:

$$CrCl\ male = \frac{(137-age)[(0.285*Wt)+(12.1*Ht\text{^}2)]}{(51*sc)}$$

$$CrCl\ female = \frac{(146-age)\{(0.287*Wt)+(9.74*Ht\text{^}2)\}}{(60*sc)}$$

where Age in years, Wt in Kg, Ht in meter, and Sc in mg/dL.

Note: Inch= 2.54 cm

3- The volume of distribution of Aminoglycoside in the patient

Adult, normal renal fun	**0.26 L/kg**
Adult, renal failure	**0.26 L/kg**
burn	**0.26 L/kg**
Penicillin therapy	**0.26 L/kg**
Obesity (more than 30% of IBW)	**V= 0.26 [IBW+ 0.4(TBT-IBW)]**
Cystic fibrosis	**0.35**
Acites/overhydration	**V = (0.26 · DBW) + (TBW – DBW)**

4-The elimination rate constant of AG in the patient

ke = 0.00293(CrCl) + 0.014 (h^{-1})

5- The suitable steady state concentration (peak & trough)

Sever infection (Pseudomonas aeruginosa, OR gram-negative pneumonia or septicemia)	8-10 µg/mL for tobramycin, gentamicin, and netilmicin. 25-30 µg/mL for Amikacin.
Moderate infections such as Intraabdominal infection	5-7 µg/mL for tobramycin, gentamicin, and netilmicin 15-25 for Amikacin.
Mild infection or with penecillin in endocarditis	3-5µg/mL for tobramycin, gentamicin, and netilmicin. 12-15 for Amikacin.

6-Dose model (intravenous bolus or intermittent infusion)

For intravenous bolus:

$$\tau = \frac{\text{InCss max} - \text{InCss min}}{\text{Kel}}$$

MD = Css max * Vd $(1-e^{-Kel*\tau})$

LD = Css max * Vd

For intermittent infusion:

- $\tau = \frac{InCss\ max - InCss\ min}{Kel} + t'$
- MD = Css max * kel * Vd $\left(\frac{1-e-Kel*\tau}{1-e-Kel*t'}\right)$
- LD = $\frac{MD}{1-e-Kel*\tau}$

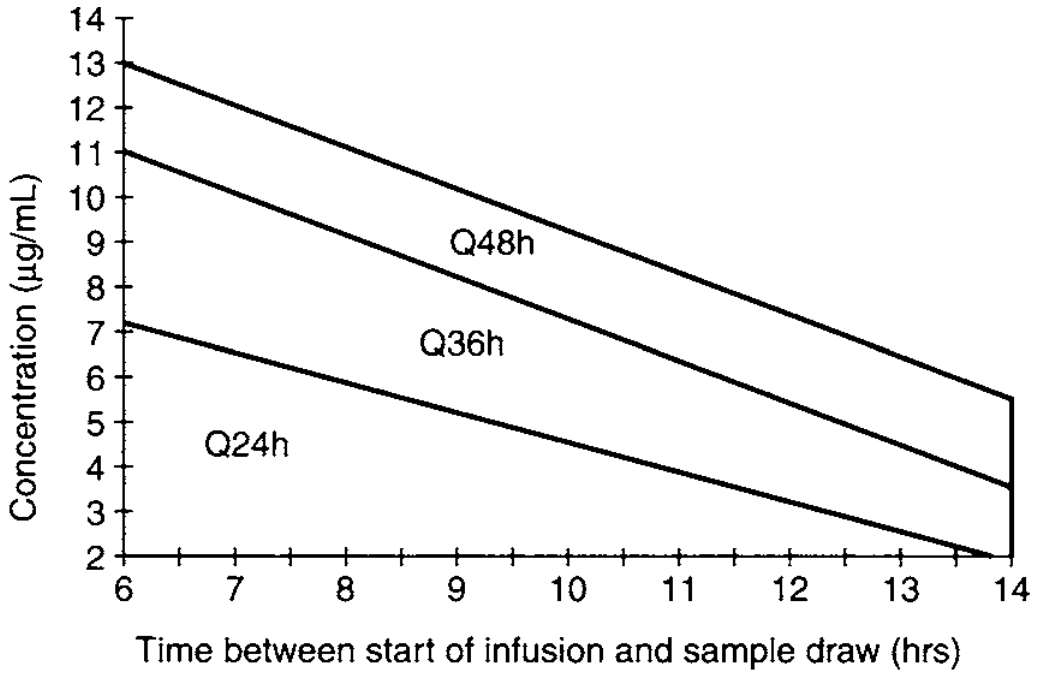
Hartford Nomogram Method for Extended-Interval Dosing

1. Administer 7-mg/kg gentamicin with initial dosage interval

2- According to CLcr, choose the INITIAL DOSAGE INTERVAL

ESTIMATED CrCl	INITIAL DOSAGE INTERVAL
≥60 mL/min	q24 h
40–59 mL/min	q36 h
20–39 mL/min	q48 h
<20 mL/min	monitor serial concentration and give next dose when <1 µg/mL

3- The aminoglycoside concentration should be measured 6–14 hours after dose (ideally first dose), and accordingly, the dose interval may be changed:



USE OF AMINOGLYCOSIDE SERUM CONCENTRATIONS TO CHANGE THE DOSE:

Linear Pharmacokinetics Method:

For this method to be valid, it should:

1-The measured concentration is a steady state

2-Make sure that the trough is within recommended range

D new = (Css,new/Css,old) D old

Css is the peak concentration.

Check the trough, it should be <2 µg/mL for tobramycin, gentamicin or <5–7 µg/mL for Amikacin.

Css,new = (D new/D old) Css,old Css is the trough concentration.