In this lab the following topics would be covered with **focusing mainly on mathematical equations and its application:**

A- Initial dose determination of aminoglycosides

1- Pharmacokinetic Dosing Method.

2- Hull and Sarubbi Nomogram Method.

3- Hartford Nomogram Method for Extended-Interval Dosing.

4- Literature-Based Recommended Dosing.

B- Use aminoglycosides serum concentration to change the dose

1- Linear Pharmacokinetics Method.

2- Pharmacokinetic Concepts Method.

3- Sawchuk-Zaske Method

C- Solving the problems of chapter <u>Four</u>; The Aminoglycoside Antibiotics (the main task of the Lab.)

Dear student; all the necessary equations and the covered topics are within **chapter four** in your textbook;**"Applied Clinical Pharmacokinetics, Second Edition, 2008 by Larry A. Bauer."**

Dosage intervals should be rounded to clinically acceptable intervals of 8 hours, 12 hours, 18 hours, 24 hours, 36 hours, 48 hours, 72 hours, and multiples of 24 hours thereafter.

[IBWfemales (in kg) = 45 + 2.3(Ht − 60 in)

{IBWmales = 50 + 2.3(Ht - 60 in)

% overweight = [100(76 kg - 68 kg)] / 68kg

The Salazar and Corcoran equation for CrCl calculation for obese patients.

$$CrCl_{est(female)} = \frac{(146 - age)[(0.287 \cdot Wt) + (9.74 \cdot Ht^2)]}{(60 \cdot S_{Cr})}$$

$$CrCl_{est(male)} = \frac{(137 - age)[(0.285 \cdot Wt) + (12.1 \cdot Ht^2)]}{(51 \cdot S_{Cr})}$$

Ht = * 2.54 cm/in / (100 cm/m) from inch to meter

Ht *12 to convert from feet to inches

% overweight=acual wt-ideal wt/ideal wt*100

Pharmacokinetic Dosing Method

1. *Estimate creatinine clearance.*

The Cockcroft-Gault equation:

CrClest = [(140 − age) BW] / (72 · SCr). Multiply by 0.85 for female.

2. *Estimate elimination rate constant (ke) and half-life (t1/2).*

ke = 0.00293(CrCl) + 0.014 , t1/2 = 0.693/ke

3. *Estimate volume of distribution (V).*

0.26 L/kg, obese (30% over IBW) V =0.26[IBW + 0.4(TBW −IBW)]

4. *Choose desired steady-state serum concentrations.*

5. *Use right equation to compute dose.*

6. *Compute loading dose (LD), if needed.*

TABLE 4-2A One-Compartment Model Equations Used with Aminoglycoside Antibiotics

ROUTE OF ADMINISTRATION	SINGLE DOSE	MULTIPLE DOSE	STEADY STATE
Intravenous bolus	$C = (D/V)e^{-k_e t}$	$C = (D/V)e^{-k_e t}[(1 - e^{-nk_e \tau}) / (1 - e^{-k_e \tau})]$	$C = (D/V)[e^{-k_e t} / (1 - e^{-k_e \tau})]$
Intermittent intravenous infusion	$C = [k_0 / (k_e V)](1 - e^{-k_e t'})$	$C = [k_0 / (k_e V)](1 - e^{-k_e t'}) \cdot [(1 - e^{-nk_e \tau}) / (1 - e^{-k_e \tau})]$	$C = [k_0 / (k_e V)][(1 - e^{-k_e t'}) / (1 - e^{-k_e \tau})]$

TABLE 4-2B Pharmacokinetic Constant Computations Utilizing a One-Compartment Model for Aminoglycoside Antibiotics

ROUTE OF ADMINISTRATION	SINGLE DOSE	MULTIPLE DOSE	STEADY STATE
Intravenous bolus	$k_e = -(\ln C_1 - \ln C_2) / (t_1 - t_2)$ $t_{1/2} = 0.693 / k_e$ $V = D/C_0$ $Cl = k_e V$	$k_e = -(\ln C_1 - \ln C_2) / (t_1 - t_2)$ $t_{1/2} = 0.693 / k_e$ $V = D / (C_0 - C_{predose})$ $Cl = k_e V$	$k_e = -(\ln C_1 - \ln C_2) / (t_1 - t_2)$ $t_{1/2} = 0.693 / k_e$ $V = D / (C_0 - C_{predose})$ $Cl = k_e V$
Intermittent intravenous infusion	$k_e = -(\ln C_1 - \ln C_2) / (t_1 - t_2)$ $t_{1/2} = 0.693 / k_e$ $V = [k_0(1 - e^{-k_e t'})] / \{k_e[C_{max} - (C_{predose}e^{-k_e t'})]\}$ $Cl = k_e V$	$k_e = -(\ln C_1 - \ln C_2) / (t_1 - t_2)$ $t_{1/2} = 0.693 / k_e$ $V = [k_0(1 - e^{-k_e t'})] / \{k_e[C_{max} - (C_{predose}e^{-k_e t'})]\}$ $Cl = k_e V$	$k_e = -(\ln C_1 - \ln C_2) / (t_1 - t_2)$ $t_{1/2} = 0.693 / k_e$ $V = [k_0(1 - e^{-k_e t'})] / \{k_e[C_{max} - (C_{predose}e^{-k_e t'})]\}$ $Cl = k_e V$

TABLE 4-2C Equations Used to Compute Individualized Dosage Regimens for Various Routes of Administration Used with Aminoglycoside Antibiotics

ROUTE OF ADMINISTRATION	DOSAGE INTERVAL (τ), MAINTENANCE DOSE (D OR K_0), AND LOADING DOSE (LD) EQUATIONS
Intravenous bolus	$\tau = (\ln Css_{max} - \ln Css_{min}) / k_e$ $D = Css_{max} V(1 - e^{-k_e \tau})$ $LD = Css_{max} V$
Intermittent intravenous infusion	$\tau = [(\ln Css_{max} - \ln Css_{min}) / k_e] + t'$ $k_0 = Css_{max} k_e V[(1 - e^{-k_e \tau}) / (1 - e^{-k_e t'})]$ $LD = k_0 / (1 - e^{-k_e \tau})$

Symbol key: Css_{max} and Css_{min} are the maximum and minimum steady-state concentrations, k_e is the elimination rate constant, V is the volume of distribution, k_0 is the continuous infusion rate, t' is the infusion time.