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APPENDICES

APPENDIX A.

Gentamicin Dosing Guidelines

The written guidelines focus on two of the most often encountered clinical situations: (1) initiation of drug therapy, and (2) consultation after therapy has been initiated by the physician.

Review Chart

A. Collect physical data on patient

1. Age in years: If over 69, treat as a high risk patient.
2. Weight in kg
3. Height in cm
4. Sex: Female patients over 55 are high risk.

B. Extract clinical data from chart to determine the risk factors and some setting values

If the patient meets any of the following criteria, then treat as a high risk patient (Donahue and Yates, 1988)

1. The patient has had aminoglycoside therapy in the last 10 days, including any irrigating solutions.
2. The most recent serum creatinine (S_{cr}) is over 2 mg/dl.
3. The most recent S_{cr} is 0.5 mg/dl or more different from a prior S_{cr}.

4. The patient is diabetic.
5. The patient meets any three of the following criteria for abnormal liver function.
   a. Albumin < 3 g/dl
   b. Total bilirubin > 2.5 mg/dl
   c. Aspartate transaminase (SGOT or AST) > 38 IU/L
   d. A history of hepatic insufficiency
   e. The presence of ascites
6. The physician notes liver disease.
7. The patient meets the criteria for shock. Shock will be defined as either:
   a. A systolic blood pressure of < 80 mmHg with a 24 hour urine output of < 500 ml
   b. A fall in systolic blood pressure of more than 50 mmHg if the final blood pressure is less than 100 mmHg
8. The physician notes shock.
9. The patient is on concurrent vancomycin or amphotericin B.

Assess the patient's hydration status for estimation of volume of distribution (V_d.) (Table A-1).

Assess the patient's renal function to set up some essential values for initiation of therapy (Table A-2) if S_{cr}, primary test for renal function, is not available.

Table A-1 Estimating Volume of Distribution (V_d.)

Hydration Status	V_d. (L/kg)
Normal hydration	0.20
Dehydrated*	0.15
Edematous, overhydrated**	0.30

from Matzke, Burkle, and Lucarotti, 1983.

* Patient had a high temperature or experienced considerable vomiting or diarrhea and/or has been over diuresed.

** Intake and output indicate overhydration, or patient has evidence of pulmonary edema, uncontrolled congestive heart failure, or peripheral edema.

Table A-2 Setting Values for Initiation of Therapy

Renal Function	Setting Values
Normal function	Age-related Clcr (ml/min/1.73 m^2) in normal subjects:*
	If age is > 6 months old, Cl_{cr} = 100,
	1 week < age < 6 months, Cl_{cr} = 80,
	1 day < age < 1 week, Cl_{cr} = 45
Chronic renal failure	S_{cr} = 2 mg/dl**
End-stage renal failure	half-life = 58 hours***

* from Bennett and Scott, 1980. Cl_{cr} is creatinine clearance adjusted to an average body surface area of 1.73 m^2. Because of the passage of maternal creatinine into the infant serum at birth, no estimate of renal function is attempted if the newborn is less than one day old.

** from Kaka and Buchanan, 1983.

*** from Thompson et al., 1982; Robinson et al., 1984

C. Complete laboratory data for further evaluation

1. Renal function monitors

a. Serum creatinine concentration (S_{cr}) in mg/dl

b. Urine creatinine concentration (U_{cr}) in mg/dl

c. 24-hour urine volume (V_{24}) in ml

2. Gentamicin level monitors

After therapy has been initiated, serial serum concentrations should be determined to define each individual patient's pharmacokinetic profile.

a. previous dose (mg) and trough level (mcg/ml or mg/L, measured just prior to the test dose) for subsequent calculation of V_d

b. test dose (mg) and the corresponding postdose levels (mcg/ml or mg/L)

All data must be recorded exactly their measurement times. For V_{24} and especially previous dose and test dose, both the start and finish times must be noted.

D. Treatment data

1. Objective of treatment

The guidelines assist the pharmacist in selecting a dosage regimen based on the peak and trough serum gentamicin concentrations desired for the suspected/documented site of infections (Table A-3).

2. If the patient has been receiving gentamicin, the steady-state peak and trough serum concentrations

Table A-3 Desired Peak and Trough Serum Concentrations for Gentamicin

Infectious Process	Concentration (mcg/ml)	
	Desired Peak	Desired Trough
Pneumonia, biliary tract infection (cholangitis), extraabdominal abscess, peritonitis, endocarditis	7-8	
Wound infections, sepsis, diverticulitis	6-7	
Cellulitis, pyelonephritis	5-6	
Cystitis	4-5	
Neutropenia (< 500 polymorphonucleocytes plus bands)		1.5-2.0
Non-neutropenia		0.5-1.5

from Matzke, Burkle, and Lucarotti, 1983.

should be estimated and evaluated, using actual dosage regimen as input.

a. Loading dose (LD) in mg, if it had been ordered, and the start time
b. Maintenance dose (MD) in mg, and the start time
c. Dosing interval (T) in hr
d. Infusion time or period (t') in hr

Condition 1: Initiation of Drug Therapy

A loading dose (LD) should be recommended for all patients. Then after administration of the LD, a series of three serum gentamicin concentrations are obtained to characterize each individual patient's pharmacokinetic parameters including gentamicin half-life, elimination rate constant, total body clearance, and volume of distribution. These values are then used to individualize the dosing regimen where it is required to maintain serum concentrations of the drug within a desired range.

Rarely will the results of the serum gentamicin concentration be available for analysis prior to the patient's need for a subsequent dose of the drug. Therefore, the pharmacist should calculate the patient's maintenance dosage regimen with the equations of Sawchuk and Zaske, using an estimation of V_d based on the patient's hydration status and body weight; an estimate of the patient's k_{el} based on the drug-specific relationship between k_{el} and Cl_{cr}; and the desired steady - state peak and trough serum levels. Alternatively, the pharmacist states or chooses any dosage

regimen and evaluate whether the corresponding predicted steady-state peak and trough serum concentrations are in the desired range.

A. Determining the loading dose and the interim maintenance dosage regimen based on literature averages of pharmacokinetic parameters

1. Calculate the patient's dosing weight (DW), or adjusted body mass (ABM) as follows.

a. For adults (age > 18 years), calculate lean body weight (LBW), and dosing weight (DW) via these equations (Donahue and Yates, 1988):

males: LBW = 50 + 2.3 (ht in inches - 60)

females: LBW = 45.5 + 2.3 (ht in inches - 60)

(Devine, 1974)

1) If ABW < LBW, then DW = ABW.

2) If ABW/LBW <= 1.15, then DW = LBW.

3) If ABW/LBW > 1.15, then

DW = LBW + 0.4 (ABW - LBW)

(Schwartz, et al., 1978)

where ABW is actual body weight of the patient in kg, LBW is lean body weight of the patient in kg, ht is the patient's height in inches, and height is the patient's height in cm.

b. For children aged 1-18 years, ideal body mass (IBM) are estimated and adjusted (ABM) subsequently according to the following formulae. (Traub and Johnson, 1980)

1) Children less than 5 feet tall:

$$IBM\ (kg) = 2.05\ e^{0.02(height)}$$

where IBM is in kg and height is in cm.

2) Children 5 feet or taller:

males: IBM = 39 + 2.27(ht in inches-60)

females: IBM = 42.2 + 2.27(ht in inches-60)

where IBM is in kg, and ht is height in inches.

3) Adjusted Body Mass (ABM):

a) If total body mass (TBM) is greater than IBM, then ABM = IBM.

b) If total body mass (TBM) is less than or equal to IBM, then ABM = TBM.

2. Estimate patient's volume of distribution (V_d) based on hydration status (Table A-1) and DW or ABM.

$$V_d\ (L) = V_d \times DW\ (or\ ABM)$$

3. Gentamicin clearance is derived directly from the patient's creatinine clearance (Cl_{cr}). A measured Cl_{cr} would be preferred because it provides a clinically acceptable estimate of glomerular filtration rate; however, if it is not available, the patient's Cl_{cr} can be estimated.

a. Measured Cl_{cr} can be calculated from standard equation (Andreoli et al.,1986):

$$Cl_{cr}\ (ml/min) = \frac{U_{cr} \times V_{24} \times 100}{1440\ S_{cr}}$$

where U_{cr} = urine creatinine concentration in 24 hour urine sample (mg/dl),

V_{24} = 24-hour urine volume (ml), and

S_{cr} = serum creatinine concentration drawn at mid point of the urine collection period (mg/dl).

b. Estmation of Cl_{cr} without urine collection could be done by using S_{cr} and other parameters. The following formulae are recommended.

1) If the patient's age is > 18 years:

a) If the S_{cr} is < 2 mg/dl, then use the method of Cockcroft and Gault (Cockcroft and Gault, 1976; D'Angio, Platt, and Gannon, 1988):

$$\text{males: corrected } Cl_{cr} \text{ (ml/min/72 kg)} = \frac{140 - \text{age}}{S_{cr}}$$

$$\text{females: corrected } Cl_{cr} \text{ (ml/min/72 kg)} = 0.85 \frac{(140-\text{age})}{S_{cr}}$$

where age is in years, and S_{cr} is serum creatinine concentration (mg/dl), Cl_{cr} is creatinine clearance of the patient corrected to an average weight of 72 kg.

b) If the S_{cr} is >= 2 mg/dl, or in patient with chronic renal failure, or in patient with unstable S_{cr} and S_{cr} is

greater than or equal to 0.9 mg/dl then estimate Cl_{cr} from these formulae (Kaka and Buchanan, 1983).

males: E = LBW(29.3 - 0.203 age)

(Siersbaek-Neilsen, et al., 1971)

females: E = LBW(25.1 - 0.175 age)

(Kampmann and Siersbaek-Neilsen, 1974)

E_{corr} = (1.035 - 0.0337 S_{cr})E

Cl_{cr} (ml/min) = E_{corr}/1.44 S_{cr}

(Jelliffe and Jelliffe, 1972)

where E = creatinine excretion (mg/day), E_{corr} = corrected creatinine excretion (mg/day), age is in years, and S_{cr} is the average of serum creatinine levels (mg/dl).

2) If the patient's age is not 1-18 years, then use this equation (Traub and Johnson, 1980):

Cl_{cr} (ml/min/1.73 m^2) = 0.48 height/S_{cr}

where height is in centimeters, S_{cr} is serum creatinine concentration (mg/dl), and Cl_{cr} is creatinine clearance of the patient adjusted to an average body surface area of 1.73 m^2.

4. The patient's first-order elimination rate constant (k_e) can be estimated on the basis of population relationships that relate Cl_{cr} to k_e.

$$k_{el}\ (hr^{-1}) = 0.015 + 0.00238\ Cl_{cr}$$

(Kaka and Buchanan, 1983).

5. The dosing interval (T) then can be determined, based on the desired steady-state peak (Cp'_{max}) and trough (Cp'_{min}) serum concentrations (Table 3) and the patient's k_{el} (Sawchuk and Zaske, 1976).

$$T'\ (hr) = \frac{\ln (Cp'_{max}/Cp'_{min})}{k_{el}} + t'$$

where T' = calculated ideal dosing interval according to desirable Cp'_{max} and Cp'_{min} chosen, and t' (hr) = intravenous infusion time for each dose. When a reasonable interval is approximated, it should be rounded to one of the following practical or acceptable intervals (T): 6, 8, 12, 24, 36, or 48 hours.

6. The loading dose (LD) and maintenance dose (MD), in mg, can be estimated as follows (Sawchuk and Zaske, 1976):

$$LD = t'k_{el}V_d Cp'_{max} \frac{1}{(1 - e^{-k_{el}t'})}$$

$$MD = LD\ (1 - e^{-k_{el}T})$$

or $$MD = t'k_{el}V_d Cp'_{max} \frac{(1 - e^{-k_{el}T})}{(1 - e^{-k_{el}t'})}$$

$$LD = \frac{MD}{(1 - e^{-k_{el}T})}$$

For the present injection dosage forms of gentamicin are vial or ampoule of 80 mg/2 ml or 20 mg/2 ml, the calculated doses should be rounded to the nearest 4 or 8 mg.

B. Evaluate a selected dosage regimen

Use the equations of Sawchuk and Zaske (1976) to predict steady-state peak and trough serum concentrations:

$$Cp_{max*} \text{ (mcg/ml)} = \frac{MD \quad (1 - e^{-k_{el}t'})}{t'k_{el}V_d \quad (1 - e^{-k_{el}T})}$$

$$Cp_{min*} \text{ (mcg/ml)} = Cp_{max*}e^{-k_{el}(T - t')}$$

where Cp_{max*} = predicted peak serum level of gentamicin at steady-state,

Cp_{min*} = predicted trough serum level of gentamicin at steady-state,

MD (mg) = calculated (and then rounded), or chosen maintenance dose of gentamicin,

k_{el} (hr^{-1}) = first-order elimination rate constant of gentamicin in the patient,

t' (hr) = intravenous infusion time for each dose,

V_d (L) = apparent volume of distribution of gentamicin in the patient, and

T (hr) = recommended practical dosing interval according to calculated ideal dosing interval, or chosen dosing interval of gentamicin.

Unless otherwise specified by the physician, the target range of steady-state peak is 4-10 mcg/ml and trough is 0.5-2.0 mcg/ml.

E. Drug administration (McEvoy, 1989)

1. For adults, IV infusions are prepared by diluting the calculated dose of gentamicin with 50-200 ml of 0.9% sodium chloride or 5% dextrose injection. The diluted solution should be infused over 30 minutes to 2 hours.
2. For pediatric patients, the volume of infusion fluid depends on the patient's needs, but should be sufficient to allow a gentamicin infusion period of 30 minutes to 2 hours.

F. Blood sampling times

Depending upon the patient's defined risk status, a series of three serum gentamicin concentrations is drawn after administration of the loading dose (See "Initial Laboratory Orders"). The time interval between samples is based on the patient's apparent kidney function and age.

Condition 2: Consultation after Therapy Has Been Initiated by the Physician

A. Evaluate the patient's current dosage regimen

1. Estimating the steady-state peak (Cp_{max*}) and trough (Cp_{min*}) serum concentrations.

When the patient already has received gentamicin, the maintenace dose (MD) and dosing interval (T) are known. Therefore, the pharmacist can calculate the patient's Cp_{max*} and Cp_{min*} with the equations of Sawchuk and Zaske (1976) once the patient's V_d and k_{el} are estimated, as previously described (See "Condition 1 Section A.1-4").

$$Cp_{max*}\ (mcg/ml) = \frac{MD\ (1 - e^{-k_{el}t'})}{t'k_{el}V_d\ (1 - e^{-k_{el}T})}$$

$$Cp_{min*}\ (mcg/ml) = Cp_{max*}e^{-k_{el}(T - t')}$$

where MD (mg) is current maintenance dose of gentamicin , k_{el} (hr^{-1}) is first-order elimination rate constant of gentamicin in the patient, t' (hr) is intravenous infusion time for each dose, V_d (L) is apparent volume of distribution of gentamicin in the patient, and T (hr) is current dosing interval of gentamicin.

2. Interpretation of and response to Cp_{max*} and Cp_{min*}.

Unless the physician specifies otherwise, the target

or accepted range of steady-state peak serum level has been defined as 4 to 10 mcg/ml and trough as 0.5 to less than 2 mcg/ml.

a. If both Cp_{max*} and Cp_{min*} are in accepted range, serial serum gentamicin levels to determine the individual's kinetic parameters should be drawn depending upon the patient's defined risk status (See "Initial Laboratory Orders") when the drug profile reaches steady-state.

   To estimate the time requried to reach steady-state, multiply the estimated half-life ($t_{1/2}$) by five, while $t_{1/2} = (\ln 2)/k_{el}$.

b. If Cp_{max*} and/or Cp_{min*} are unacceptable, a new dosage regimen should be calculated to achieve the desired steady-state peak and trough serum concentrations (See "Condition 1"). This information should be conveyed to the physician, as soon as possible, along with the recommended serum gentamicin concentration sampling plan. The (new) estimated dose should be given at a time after the last dose equal to the (new) calculated dosing interval. A predose blood sample, for subsequent calculation of the patient's volume of distribution (V_{d*}), as well as postdose serum concentrations after the administration of the calculated dose also should be recommended. See "Section D. Timing of

serum gentamicin concentrations" in "Initial Laboratory Orders" and "Section A.1.c. Rising serum creatinine" in "Subsequent Laboratory Orders."

B. Adjust current dosage regimen (or establish a new dosage regimen) if necessary

One of the following dosage regimen decisions should be made if Cp_{max*} and/or Cp_{min*} are unacceptable (Haslett and Reynolds, 1988):

1. high peak with acceptable trough: decrease maintenance dose,
2. low peak with acceptable trough: increase maintenance dose,
3. high trough with acceptable peak: prolong dosing interval,
4. low trough with acceptable peak: shorten dosing interval,
5. high trough and high peak: decrease dose alone or decrease dose and prolong dosing interval,
6. low trough and low peak: increase dose alone or increase dose and shorten dosing interval
7. high peak and low trough: decrease dose and shorten dosing interval,
8. low peak and high trough: increase dose and prolong dosing interval.

Initial Laboratory Orders

A. All patients shall have a serum creatinine ordered upon initiation of gentamicin therapy if they have not had one drawn in the past 24 hours. The creatinine should be reported to the pharmacist within 6 hours so that the maintenance dose can be calculated and further laboratory tests ordered.

B. Low risk patients

1. Order drug levels so that lab will be able to report on the next scheduled batch day.
2. Order serum creatinine every 3 days.

C. High risk patients

1. Order drug levels on the first dose if the patient is known to be high risk at that time. If the patient is determined to be high risk after the S_{cr} is reported, then order levels on the next dose.
2. Order serum creatinine daily if:
   a. The patient is over 55 and diabetic.
   b. The initial or recent S_{cr} is 2.0 mg/dl or greater.
   c. The S_{cr} shows a rising trend (e.g., a rise of 0.5 mg/dl over 3-5 days).
   d. The patient is on concurrent IV vancomycin or amphotericin B.
   e. The patient is in shock.
3. Order serum creatinine every other day if:
   a. The patient is over 69 years old.

b. The patient is diabetic.

c. The patient has abnormal liver function.

d. The patient is a female over 55 years old.

D. Timing of serum gentamicin concentration measurements

1. If the first level is drawn on the first dose, then draw drug levels according to the following schedule

a. Drawing times for patients with apparently normal renal function (S_{cr} < 2 mg/dl)

Table A-4 Recommended Blood Sampling Times

Age (years)	Blood Sampling Times
Under 30	0.5, 1, and 2 hours post dose
30 to 55	0.5, 2, and 3 hours post dose
Over 55	0.5, 3, and 5 hours post dose

from Donahue and Yates, 1988.

b. For patients with abnormal renal function (S_{cr} greater than or equal to 2 mg/dl):

1) S_{cr} 2 to 3

Draw 1, 6, and 10 hour postdose levels.

2) S_{cr} > 3

Draw 2, 12, and 22 hour postdose levels.

2. If the first level is drawn on any other than the first dose:

a. If the patient is at steady-atate, then draw three postinfusion levels as explained above (Section D.1).

b. If the patient is not at steady-atate, then draw a predose or preinfusion level plus two or three postinfusion levels:

1) For patients with normal renal function:

Table A-5 Recommended Blood Sampling Times

Age (years)	Blood Sampling Times
Under 30	preinfusion, 0.5, and 2 hours post dose
30 to 55	preinfusion, 0.5, and 3 hours post dose
Over 55	preinfusion, 0.5, and 5 hours post dose

from Donahue and Yates, 1988.

2) For patients with abnormal renal function, draw a predose or preinfusion level plus three postinfusion levels as explained above (Section D.1.b). Notify physician and get approval to continue protocol before writing orders. Check with M.D. to see if he or she wants to hold the drug until levels are reported by lab.

If the sampling times fall outside the patient's current dosing interval (e.g., 1, 6, 10 hours postdose but the patient's is on a q 8 h schedule), recommend that the next dose should be held to accommodate all blood sampling times. Then restart the drug at the dose and interval that were calculated to yield the desired peaks and troughs.

3. Nursing Alert:

In addition to chart orders for serum levels to be drawn on a specific dose, the pharmacist dispensing the dose shall communicate special handling and instructions to the nurse administering the dose.

Analysis of The Gentamicin Serum Concentration Time Data

Once the serum gentamicin concentrations are reported by the laboratory, each individual patient's pharmacokinetic parameters can be directly estimated (Sawchuk and Zaske, 1976; Sawchuk et al., 1977). The following procedures shall be implemented:

1. If there are 3 postinfusion levels (or more), the pharmacist could use regression analysis of the serum concentration time data to determine the k_{el} and Cp_{max} (i.e., graphically or mathematically via calculator or microcomputer). k_{el} is the slope of while Cp_{max} is the concentration on the regression line(Y-intercept).

   If there are only two postinfusion levels, this should be simply obtained by:

$$k_{el\#} = \frac{\ln (Cp_1/Cp_2)}{t_2 - t_1}$$

$$Cp_{max} = \frac{Cp_1}{e^{-k_{el\#}(t_1 - t')}}$$

where $k_{el\#}$ (hr^{-1}) is individualized first-order elimination rate constant derived from postinfusion serum level measurements, Cp_1 and Cp_2 (mcg/ml) are serum gentamicin levels measured during the postinfusion phase at first (t_1) and second (t_2) time points taken from the beginning of the infusion, Cp_{max} (mcg/ml) is peak serum level of gentamicin at the end of any infusion period calculated based on the measured serum concentrations, and t' (hr) is intravenous infusion time of this dose.

2. The one-compartment model method of Sawchuk and Zaske then can be employed to estimate the patient's $V_{d\#}$.

$$V_d\# = \frac{D \quad (1 - e^{-k_{el\#}t'})}{t'k_{el\#} (Cp_{max} - Cp_0 e^{-k_{el\#}t'})}$$

where $V_{d\#}$ (L) is apparent volume of distribution of gentamicin in the patient estimated based on measured serum levels, D (mg) is test dose or infused dose that generates the measured postinfusion serum levels, and Cp_0 (mcg/ml) is preinfusion or trough gentamicin level measured just before infusion of the test dose.

If data from other than the first infusion interval are used, the concentration remaining from a previously

administered dose or preinfusion level (Cp_o) must also be known. If the patient is at steady-state, however, an estimate of this preinfusion level can be made by the serum concentration measured (or predicted by: $Cp_o = Cp_{min\#} = Cp_{max\#} e^{-k_{el\#}(T - t')}$ as in Section 2. where $Cp_{min\#}$ and $Cp_{max\#}$ are steady-state peak and trough serum levels calculated based on the measured serum levels) at the end of the dosing interval.

3. The total body clearance of gentamicin in the patient (TBC) then can be calculated as follows:

$$TBC = k_{el\#} \times V_{d\#}$$

4. Steady-state peak ($Cp_{max\#}$) and trough ($Cp_{min\#}$) serum levels, and half-life ($t_{1/2\#}$) then can be determined:

$$Cp_{max\#} \text{ (mcg/ml)} = \frac{MD \quad (1 - e^{-k_{el\#}t'})}{t'k_{el\#}V_{d\#} \quad (1 - e^{-k_{el\#}T})}$$

$$Cp_{min\#} \text{ (mcg/ml)} = Cp_{max\#}e^{-k_{el\#}(T - t')}$$

$$t_{1/2\#} \text{ (hr)} = \frac{\ln 2}{k_{el\#}} = \frac{0.693}{k_{el\#}}$$

where T (hr) is ordered dosing interval.

Monitoring of Therapy

A. Initial Evaluation

1. If the expected steady-state peak and trough serum gentamicin concentrations are obtained (i.e., the estimates based on

measured serum concentrations, $Cp_{max\#}$ and $Cp_{min\#}$, are $\pm$ 10 and 20 percent of those estimates based on literature averages of pharmacokinetic parameters, $Cp_{max\#}$ and $Cp_{min\#}$, respectively), and the patient is improving clinically, with stable renal function, the present dosage regimen may be continued.

2. If the expected steady-state peak and trough serum gentamicin concentrations are not obtained, a new dosage regimen based on the patient's pharmacokinetic parameters which were directly estimated from measured serum concentrations should be calculated (as described above, but use $k_{el\#}$ and $V_{d\#}$ instead of k_{el} and V_d, respectively) and recommended for the patient.

B. Follow-Up

For all patients, follow-up serum gentamicin concentration determinations are recommended to ensure that therapeutic, yet nontoxic, concentrations are achieved and to assess the accuracy of the pharmacokinetic model. Two serum gentamicin concentration determinations should be carried out after the initial evaluation, when the patient has reached steady-state (i.e., approximately five half-lives) on the current dosage regimen for those patients with stable renal function, or after a dose for patients with fluctuating renal function. The timing is outlined in table A-6.

This process (recommendation, assessment) will need to be repeated until a predictable kinetic pattern is established. Serum gentamicin concentrations should then be reassesed in three to

five days, provided there are no drastic changes in the patient's clinical status.

Subsequent Laboratory Orders

A. Renal function monitors

1. Criteria for ordering serum creatinine (S_{cr}):

a. Low risk patients shall have S_{cr} monitored every 3 days.

b. High risk patients shall be monitored as defined below.

1) If the patient's initial S_{cr} is between 1.6 and 2.0 mg/dl

a) If stable (i.e., < 25 % change from baseline while receiving gentamicin), order S_{cr} every other day.

b) If unstable (i.e., > 25 % change from baseline while receiving gentamicin), order S_{cr} daily until stable. Then if the stable S_{cr} is between 1.6 and 2.0 mg/dl, change the S_{cr} orders to every other day.

2) If the patient's initial S_{cr} is greater than or equal to 2 mg/dl

a) Call the physician to see if the protocol is to be continued.

b) If the protocol is continued:

(1) Order gentamicin levels as defined in Section B.

(2) Order S_{cr} daily.

c. Rising serum creatinine

1) If the patient's S_{cr} rise 0.3 or 0.4 mg/dl from the start of therapy, alert the physician to order an extra S_{cr} within 24 hours.

2) If the patient's S_{cr} rise 0.5 to 0.9 mg/dl during the course of therapy, this is a sign of possible drug induced nephrotoxicity.

a) Contact the physician to see if the protocol is to be continued.

b) If the protocol is continued:

(1) Order gentamicin levels as soon as possible. See Section B.

(2) Order S_{cr} daily.

3) If the patient's S_{cr} rise 1 mg/dl or more during the course of therapy:

a) Contact the physician to see if the protocol is to be continued.

b) If the protocol is continued:

(1) If the dosing interval is 12 hours or less, then

(a) Hold the drug for one dosing interval (e.g., for 6, 8 or 12 hours).

(b) Give the next scheduled dose.

(c) Draw gentamicin levels just prior to dose, 1 hour after infused, and one level at a time equal to halftime of the previous dosing interval.

(d) Do not give another dose until the results are back from the laboratory.

(e) Adjust the dose if necessary.

(f) Order S_{cr} daily.

(2) If the dosing interval is 24 hours or more, then

(a) Hold the next scheduled dose of gentamicin.

(b) Draw a gentamicin level at the time the dose would have been given.

(c) If the lab reports the level as below the normal trough values, then give the same dose as soon as possible and order levels prior to, 1 hour after and 24 hours after the dose to redefine the kinetic parameters.

(d) If the reported level is higher than the normal trough, then continue to hold gentamicin, order one more level within 12 hours, and follow "(c)" above.

(e) Adjust the dose if necessary.

(f) Be sure S_{cr} is ordered daily.

2. Other renal monitors

a. Tests which might have a major role in the monitoring of proximal tubular effect include urinary excretion of beta-2-microglobulin, renal enzymes, protein, and casts; rank order from most sensitive to least.

b. Urine Output

If the urine output drops below 700 ml in 24 hours and the intake is greater than 1500 ml, then order a serum creatinine (if not already ordered for that day) and alert the physician.

c. Urinalysis

If a urinalysis shows granulated casts in urine, this may be an early sign of nephrotoxicity and may warrant additional serum creatinine or gentamicin levels (at next regular batch time).

B. Gentamicin level monitors

Normally, all follow-up gentamicin levels should be a peak followed by a trough on a single dose. However, in cases where the predicted trough is less than one it may be more helpful to order a peak and another level about half-way through the dosing period. The trough can be extrapolated.

When circumstances dictate, a trough may be drawn, the dose given, and the peak drawn. This may be necessary due to the timing of a dose in relationship to the time the laboratory is scheduled to run the day's gentamicin batch.

Table A-6 Follow-Up Blood Sampling Times

Ordered Dosing Interval	Recommended Blood Sampling Times
q 4 h	0.5 and 2 hours post dose
q 6 h	0.5 and 3 hours post dose
q 8 h	0.5 and 4 hours post dose
q 12 h	1 and 6 hours post dose
q 24 h	2 and 12 hours post dose
q 36 h	2 and 18 hours post dose
q 48 h	2 and 24 hours post dose
q > 48 h	2 and T/2 hours post dose

T = Ordered Dosing Interval, h = hour

from Matzke et al., 1983; Donahue and Yates, 1988

Appendix B.

Examples of Screens and Printouts

This appendix demonstrates an operation of the developed program in a series of figures of several screens and printouts.

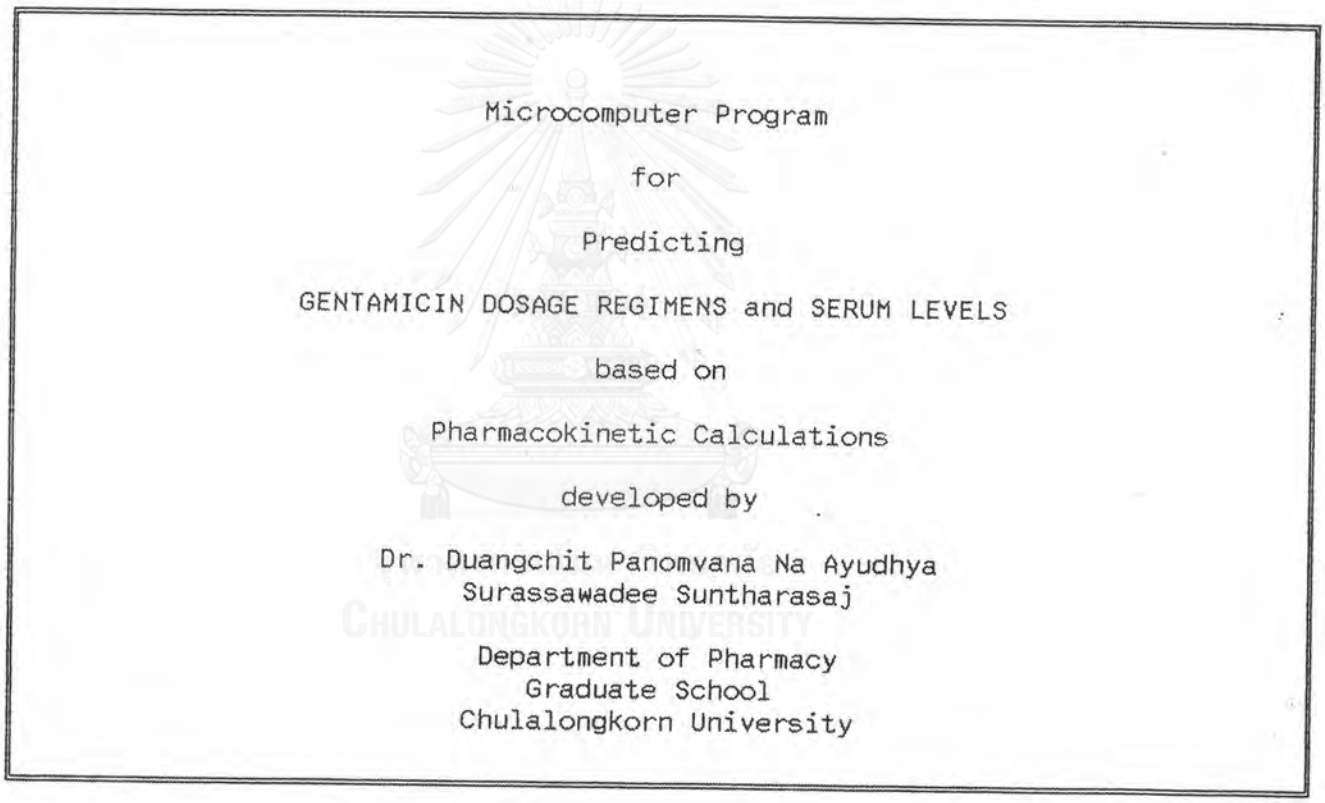


Figure B-1 LOGO screen.

After loading, the program will display this screen. Once user has pressed any key, he goes to the second screen.

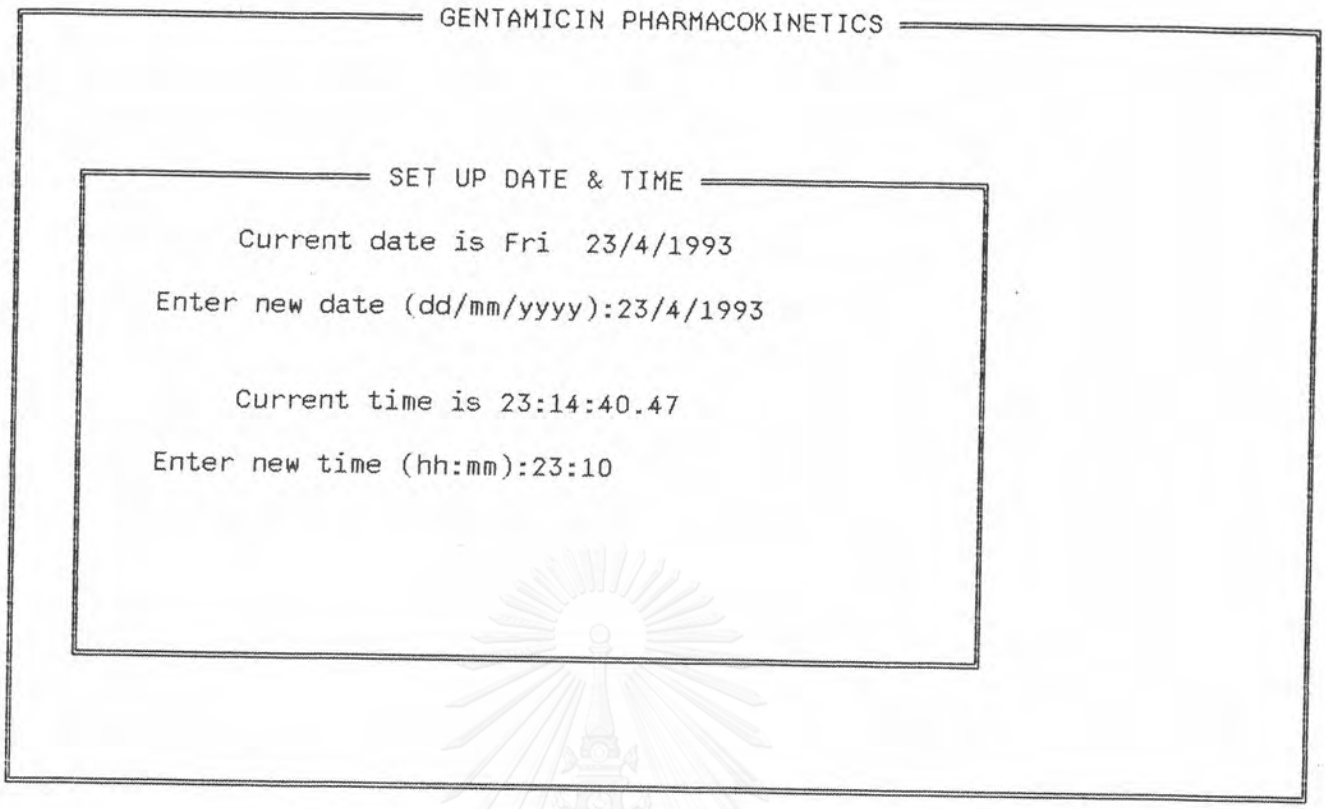


Figure B-2 SET UP DATE & TIME screen

The second screen allows the user to set up date & time to ensure that it is correct.

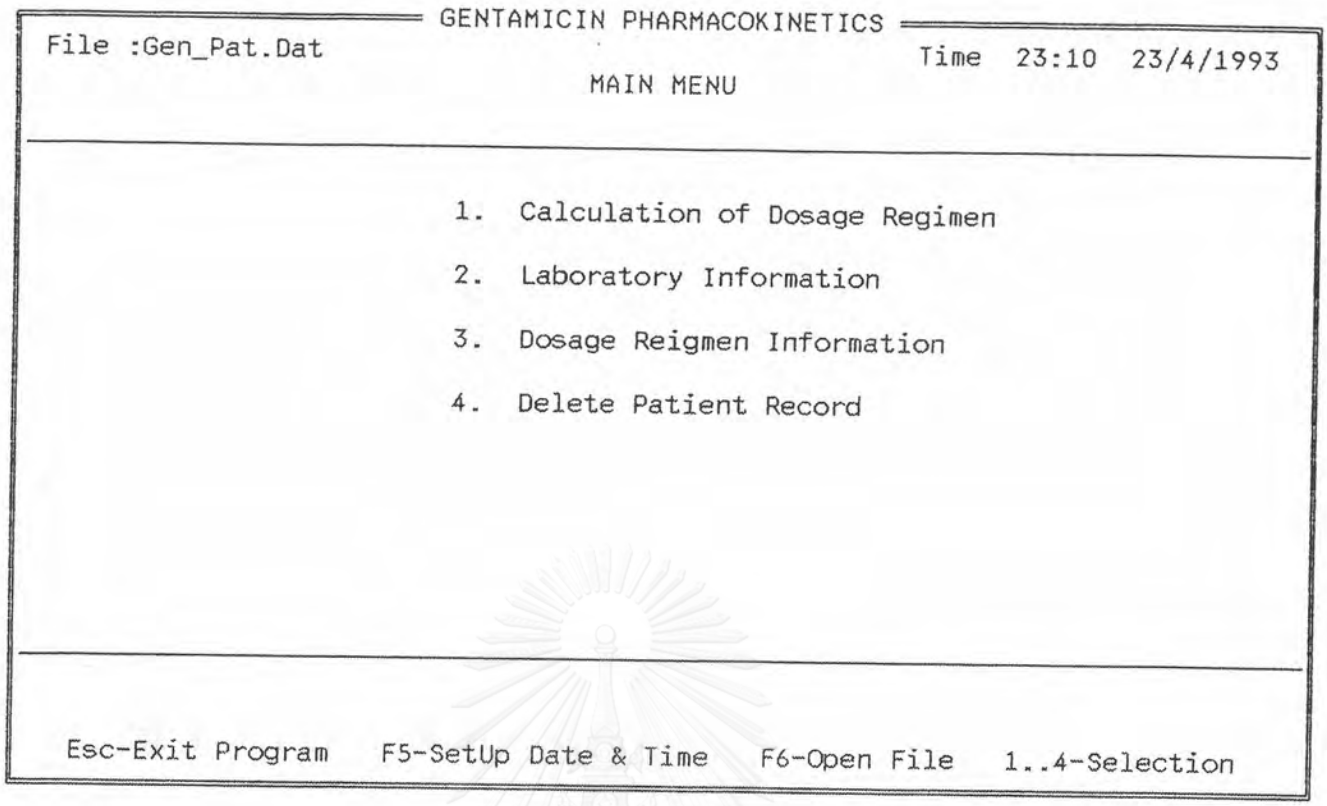


Figure B-3 MAIN MENU screen

From the SET UP DATE & TIME screen, the user is now at the MAIN MENU screen where he or she can select what to do.

```
                    GENTAMICIN PHARMACOKINETICS
File :Gen_Pat.Dat                                  Time  23:14  23/4/1993
                              REVIEW CHART         Hospital No. 1
        Consult #1                                 * New Patient *
-------------------------------------------------------------------------
      Demographic Data
 1) Name:                                    11) Diabetic? :
 2) Bed :                                    12) Abnormal liver Function? :
 3) Doctor  :                                13) Shock? :
      Physical Data                          14) Concurrent IV vancomycin or
 4) Age (year) :                                 amphotericin B? :
 5) Weight (kg):                             15) Hydration Status (N/D/E):N
 6) Height (cm):                                 Normal/Dehydrated/
 7) Sex (M/F)  :                                 /Edematous-Overhydrated
      Clinical Data                          16) Renal Function (N/C/E) :N
 8) Previous aminoglycoside therapy in           Normal/Chronic/End-Stage
    the last 10 days?(Y/N) :                17) Objective
 9) Recent Scr > 2 mg/dl? :
10) Recent Scr - Prior Scr >= 0.5 mg/dl?:
-------------------------------------------------------------------------

   PgDn-Next Screen    End-Save    F8-Print
```

Figure B-4 REVIEW CHART screen at the first consultation

If the entered hospital number is not already existed in file, the program will treat him as a new patient.

```
                    GENTAMICIN PHARMACOKINETICS
File :Gen_Pat.Dat                                  Time  23:17  23/4/1993
                              REVIEW CHART         Hospital No. 1
        Consult #1                                 * New Patient *
-------------------------------------------------------------------------
      Demographic Data
 1) Name: Alisa                          11) Diabetic? : N
 2) Bed : aaa                            12) Abnormal liver Function? :N
 3) Doctor  : ZZ                         13) Shock? : N
      Physical Data                      14) Concurrent IV vancomycin or
 4) Age (year) :   27.00                      amphotericin B? :N
 5) Weight (kg):   49.00                 15) Hydration Status (N/D/E):N
 6) Height (cm): 158.50                       Normal/Dehydrated/
 7) Sex (M/F)  :  F                           /Edematous-Overhydrated
      Clinical Data                      16) Renal Function (N/C/E) :N
 8) Previous aminoglycoside therapy in        Normal/Chronic/End-Stage
    the last 10 days?(Y/N) :N           17) Objective
 9) Recent Scr > 2 mg/dl? : N               sepsis
10) Recent Scr - Prior Scr >= 0.5 mg/dl?:N
-------------------------------------------------------------------------

  PgDn-Next Screen   End-Save   F8-Print
```

Patient Review Chart Information

```
Name          : Alisa
Hospital No.  : 1
Ward/Bed      : aaa
Doctor        : ZZ
Age (year)    :  27.00
Weight (kg)   :  49.00
Height (cm)   : 158.50
Sex           : Female
Previous aminoglycoside therapy in the last 10 days : N
Recent Scr > 2 mg/dl : N
Recent Scr - Prior Scr >= 0.5 mg/dl : N
Diabetic : N
Abnormal liver Function : N
Shock : N
Concurrent IV vancomycin or amphotericin B : N
Hydration Status : Normal
Renal Function : Normal
Objective : sepsis
```

Figure B-5 REVIEW CHART screen after finished filling new patient data (above) and printout (below) generated by pressing "F8" function key.

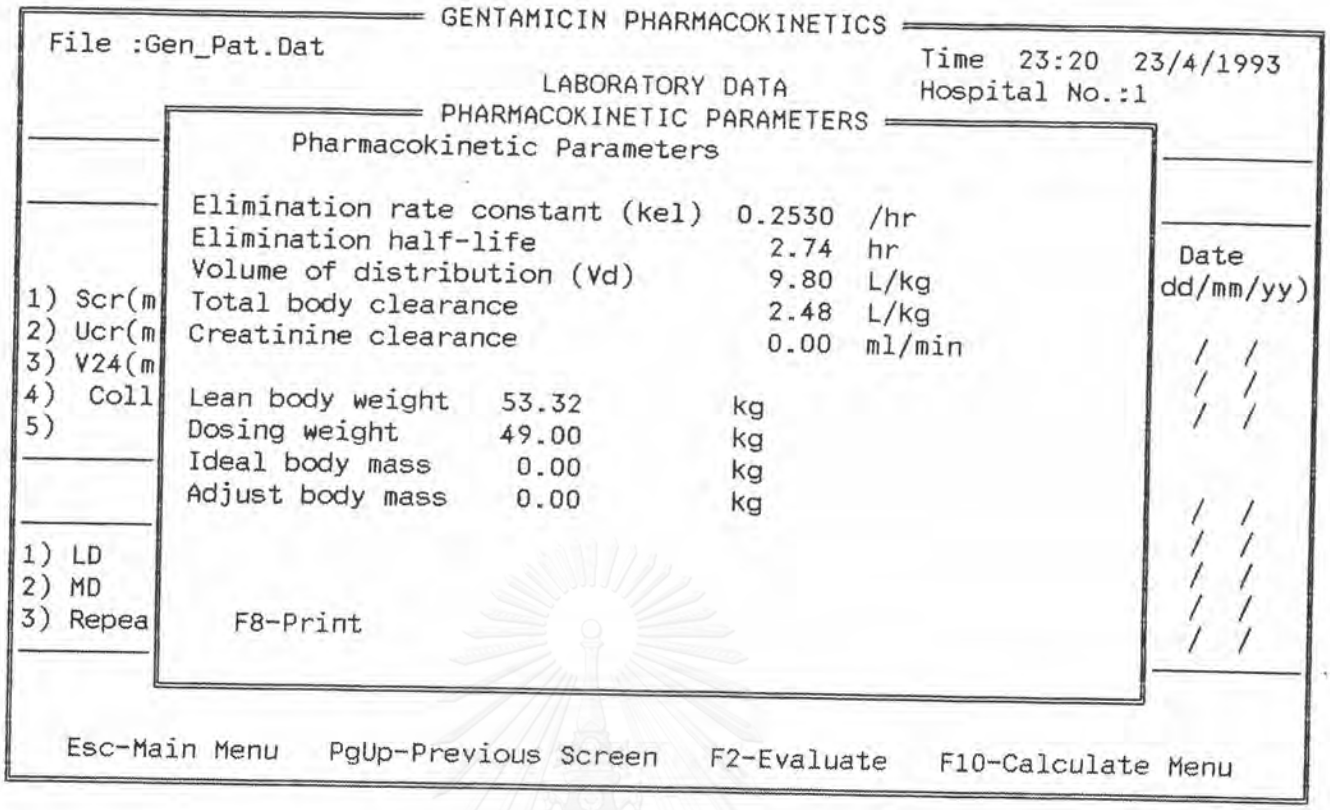
```
                    GENTAMICIN PHARMACOKINETICS
File :Gen_Pat.Dat                                   Time  23:12  23/4/1993
                          LABORATORY DATA           Hospital No.:1
                                                    Alisa
```

RENAL MONITORS			GENTAMICIN MONITORS		
	Time (hh:mm)	Date (dd/mm/yy)		Time (hh:mm)	Date (dd/mm/yy)
1) Scr(mg/dl):	:	/ /	1) Prior dose mg		
2) Ucr(mg/dl):			infused from	:	/ /
3) V24(ml) :			to	:	/ /
4) Collected From	:	/ /	2) Cmin(mg/L): at	:	/ /
5) To	:	/ /	3) Test dose mg		
TREATMENT DATA			infused from	:	/ /
			to	:	/ /
1) LD mg at	:	/ /	4) C1 (mg/L): at	:	/ /
2) MD mg at	:	/ /	5) C2 (mg/L): at	:	/ /
3) Repeat -hr infusion every hr			6) C3 (mg/L): at	:	/ /

```
  Esc-Main Menu   PgUp-Previous Screen   F2-Evaluate   F10-Calculate Menu
```

Figure B-6 LABORATORY DATA screen

This screen is designed to accept laboratory and treatment data.



Hospital No.: 1
NAME : Alisa
PHARMACOKINETIC PARAMETERS

Elimination rate constant (kel)	0.2530	/hr
Elimination half-life	2.74	hr
Volume of distribution (Vd)	9.80	L/kg
Total body clearance	2.48	L/kg
Creatinine clearance	0.00	ml/min
Lean body weight	53.32	kg
Dosing weight	49.00	kg
Ideal body mass	0.00	kg
Adjust body mass	0.00	kg

Figure B-7 PHARMACOKINETIC PARAMETERS screen (above) and printout (below)

Pharmacokinetic parameters can be shown as user pressed "F1" function key from within the LABORATORY DATA screen. Printout is generated by pressing "F8" from within the PHARMACOKINETIC PARAMETERS screen.

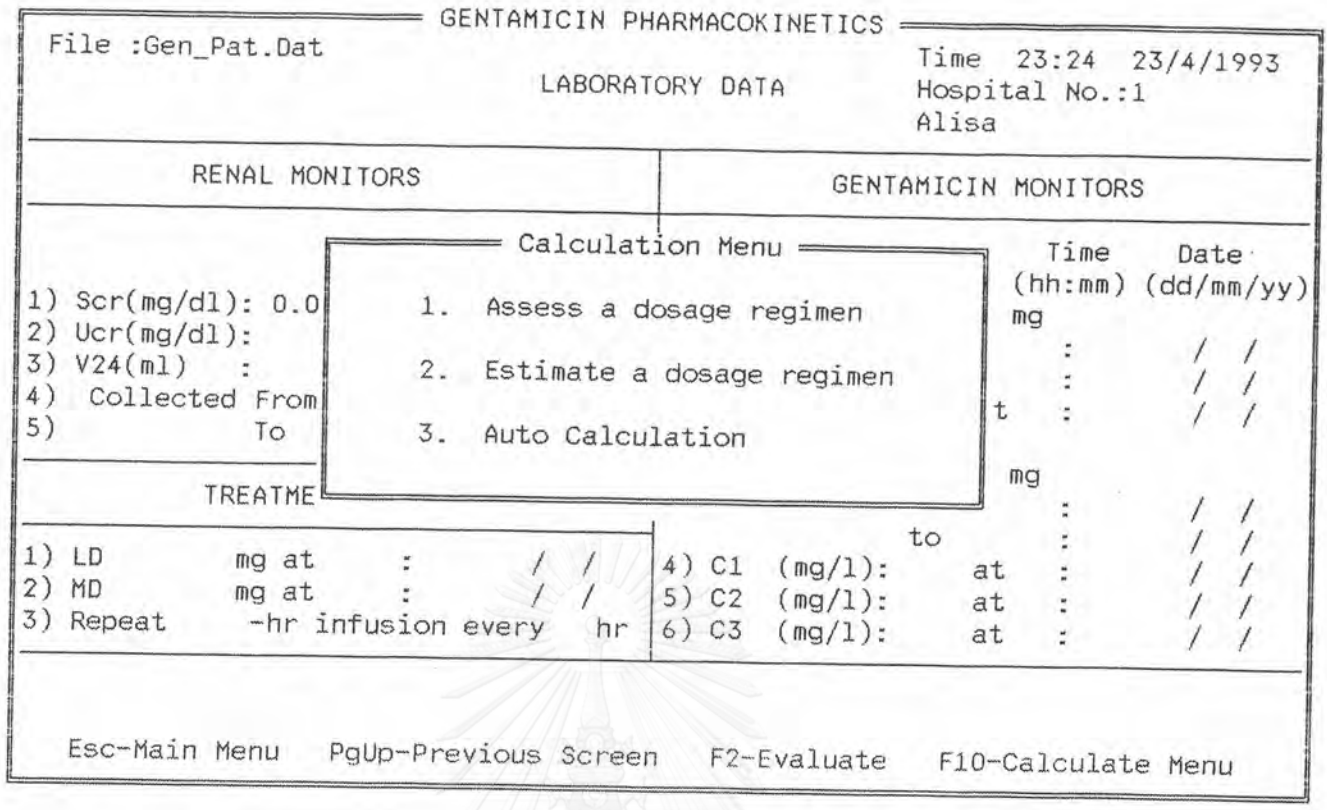


Figure B-8 CALCULATION MENU screen

If user pressed "F10" function key from within the LABORATORY DATA screen, the program will go to CALCULATION MENU. User will accomplish a desired dosage regimen in 3 alternative ways of calculation.

GENTAMICIN PHARMACOKINETICS

File :Gen_Pat.Dat

ASSESS A DOSAGE REGIMEN

Time 23:26 23/4/1993
Hospital No.:1
Alisa

DR No.	MD (mg)	q (hr)	Inf-T (hr)	Predicted SS Cmax(mg/L)	Predicted SS Cmin(mg/L)	Recommend
1.	80.00	8	0.50	8.84	1.32	Both Accept

Recommend

For this Dosage Regimen,
Both predicted steady-state peak and trough are acceptable.
Therefore, the patient should continue on this dosage regimen.

Esc-Exit F10-Calculate Menu

Figure B-9-1a ASSESS A DOSAGE REGIMEN screen at first run

This screen is shown immediately after user has pressed "1" (Assess a dosage regimen). With entry of a given or proposed dosage regimen, i.e. maintenance dose (MD), dosing interval (q), and infusion time (Inf time), this calculation module will assess a given dosage regimen by predicting the corresponding steady-state peak and trough levels and evaluating these values as displayed. In addition, the program gives a recommendation about how to adjust this dosage regimen.

GENTAMICIN PHARMACOKINETICS

File :Gen_Pat.Dat

Time 23:28 23/4/1993

ASSESS A DOSAGE REGIMEN

Hospital No.:1

Alisa

DR No.	MD (mg)	q (hr)	Inf-T (hr)	Predicted SS Cmax(mg/L)	Predicted SS Cmin(mg/L)	Recommend
1.	80.00	8	0.50	8.84	1.32	Both Accept
2.	70.00	8	0.50	7.73	1.16	Both Accept

Recommend

For this Dosage Regimen,
Both predicted steady-state peak and trough are acceptable.
Therefore, the patient should continue on this dosage regimen.

Esc-Exit F10-Calculate Menu

Figure B-9-1b ASSESS A DOSAGE REGIMEN screen at second run

User can try another one by entering a new input set.

GENTAMICIN PHARMACOKINETICS

File :Gen_Pat.Dat

ASSESS A DOSAGE REGIMEN

Time 23:33 23/4/1993
Hospital No.:1
Alisa

DR No.	MD (mg)	q (hr)	Inf-T (hr)	Predicted SS Cmax(mg/L)	Predicted SS Cmin(mg/L)	Recommend
1.	80.00	8	0.50	8.84	1.32	Both Accept
2.	70.00	8	0.50	7.73	1.16	Both Accept
3.	60.00	8	0.50	6.63	0.99	Both Accept
4.	56.00	8	0.50	6.18	0.93	Both Accept

Recommend

For this Dosage Regimen,
Both predicted steady-state peak and trough are acceptable.
Therefore, the patient should continue on this dosage regimen.

Esc-Exit F10-Calculate Menu

Figure B-9-1c ASSESS A DOSAGE REGIMEN screen at fourth run

User can try as many times as needed. The program provides up to 30 dosage regimens to be stored.

GENTAMICIN PHARMACOKINETICS

File :Gen_Pat.Dat

ASSESS A DOSAGE REGIMEN

Time 23:32 23/4/1993
Hospital No.:1
Alisa

DR No.	MD (mg)	q (hr)	Inf-T (hr)	Predicted SS Cmax(mg/L)	Cmin(mg/L)	Recommend
1.	80.00	8	0.50	8.84	1.32	Both Accept
2.	70.00	8	0.50	7.73	1.16	Both Accept
3.	60.00	8	0.50	6.63	0.99	Both Accept
4.	56.00	8	0.50	6.18	0.93	Both Accept

Select Dosage Regimen No :4

Esc-Exit F10-Calculate Menu

Figure B-9-1d ASSESS A DOSAGE REGIMEN screen at end run

After user has stopped calculation (by answering "N" to the question "Calculate another dosage regimen?"), he is asked by the program to select the dosage regimen he desired. In this example, he preferred the dosage regimen No. 4.

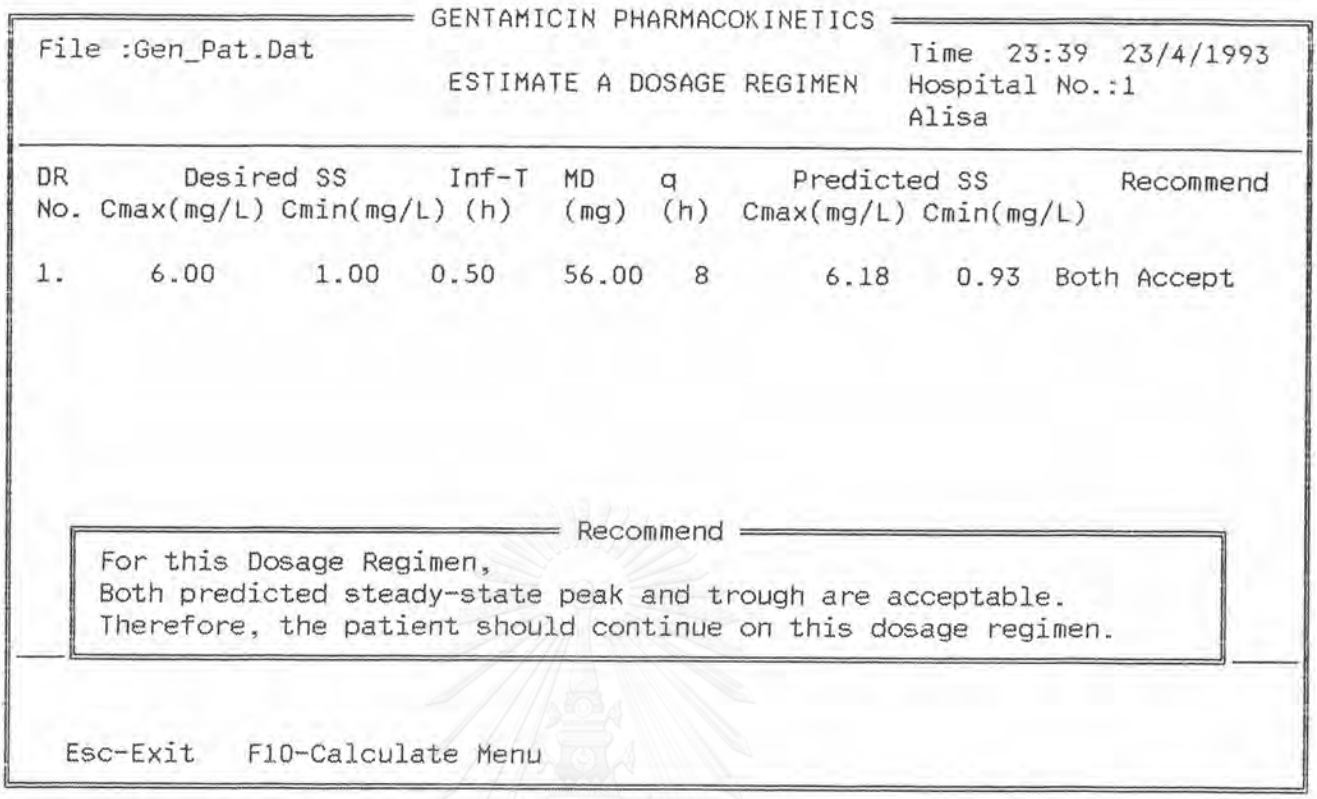


Figure B-9-2a ESTIMATE A DOSAGE REGIMEN screen at first run

This screen is shown immediately after user has pressed "2" (Estimate a dosage regimen). With entry of desired steady-state peak and trough levels including desired infusion time, this calculation module will estimate a dosage regimen, i.e. maintenance dose (MD) and dosing interval (q) which is rounded to the practical value. Furthermore, the program will assess this recommended dosage regimen by predicting the corresponding steady-state peak and trough levels and evaluating these values as displayed. In addition, the program also gives a recommendation about how to adjust this dosage regimen.

GENTAMICIN PHARMACOKINETICS

File :Gen_Pat.Dat

ESTIMATE A DOSAGE REGIMEN

Time 23:45 23/4/1993
Hospital No.:1
Alisa

DR No.	Desired SS Cmax(mg/L)	Cmin(mg/L)	Inf-T (h)	MD (mg)	q (h)	Predicted SS Cmax(mg/L)	Cmin(mg/L)	Recommend
1.	6.00	1.00	0.50	56.00	8	6.18	0.93	Both Accept
2.	6.00	1.00	1.00	56.00	8	5.82	0.99	Both Accept

Recommend

For this Dosage Regimen,
Both predicted steady-state peak and trough are acceptable.
Therefore, the patient should continue on this dosage regimen.

Esc-Exit F10-Calculate Menu

Figure B-9-2b ESTIMATE A DOSAGE REGIMEN screen at second run

User can try to another one by entering a new input set.

GENTAMICIN PHARMACOKINETICS

File :Gen_Pat.Dat

ESTIMATE A DOSAGE REGIMEN

Time 23:46 23/4/1993
Hospital No.:1
Alisa

DR No.	Desired SS Cmax(mg/L)	Cmin(mg/L)	Inf-T (h)	MD (mg)	q (h)	Predicted SS Cmax(mg/L)	Cmin(mg/L)	Recommend
1.	6.00	1.00	0.50	56.00	8	6.18	0.93	Both Accept
2.	6.00	1.00	1.00	56.00	8	5.82	0.99	Both Accept
3.	5.90	1.00	0.50	52.00	8	5.74	0.86	Both Accept
4.	6.20	0.90	0.50	56.00	8	6.18	0.93	Both Accept

Recommend

For this Dosage Regimen,
Both predicted steady-state peak and trough are acceptable.
Therefore, the patient should continue on this dosage regimen.

Esc-Exit F10-Calculate Menu

Figure B-9-2c ESTIMATE A DOSAGE REGIMEN screen at fourth run

User can try as many times as needed. The program provides up to 30 dosage regimens to be stored.

GENTAMICIN PHARMACOKINETICS

File :Gen_Pat.Dat

ESTIMATE A DOSAGE REGIMEN

Time 23:52 23/4/1993
Hospital No.:1
Alisa

DR No.	Desired SS Cmax(mg/L)	Cmin(mg/L)	Inf-T (h)	MD (mg)	q (h)	Predicted SS Cmax(mg/L)	Cmin(mg/L)	Recommend
1.	6.00	1.00	0.50	56.00	8	6.18	0.93	Both Accept
2.	6.00	1.00	1.00	56.00	8	5.82	0.99	Both Accept
3.	5.90	1.00	0.50	52.00	8	5.74	0.86	Both Accept
4.	6.20	0.90	0.50	56.00	8	6.18	0.93	Both Accept

Selective Dosage Regimen No :1

Esc-Exit F10-Calculate Menu

Figure B-9-2d ESTIMATE A DOSAGE REGIMEN screen at end run

By pressing "N" to answer the question "Calculate another dosage regimen?", the calculation is stopped. Then the user is asked by the program to select the dosage regimen he desired. In this example, he preferred the dosage regimen No. 1.

GENTAMICIN PHARMACOKINETICS

File :Gen_Pat.Dat — Time 23:58 23/4/1993

AUTO-CALCULATION — Hospital No.:1

Alisa

DR No.	Desired SS Cmax(mg/L)	Desired SS Cmin(mg/L)	Inf-T (h)	MD (mg)	q (h)	Predicted SS Cmax(mg/L)	Predicted SS Cmin(mg/L)	Recommend
1)	4.0-10.0	0.5- 2.0	0.5	36.0	6	4.42	1.10	Both Accept
2)			1.0	36.0	6	4.16	1.17	Both Accept
3)			0.5	37.0	6	4.54	1.13	Both Accept
4)			1.0	37.0	6	4.27	1.21	Both Accept
5)			1.5	37.0	6	4.02	1.29	Both Accept
6)			0.5	37.0	8	4.09	0.61	Both Accept
7)			0.5	38.0	6	4.66	1.16	Both Accept
8)			1.0	38.0	6	4.39	1.24	Both Accept
9)			1.5	38.0	6	4.13	1.32	Both Accept
10)			0.5	38.0	8	4.20	0.63	Both Accept

Select DR No.

Esc-Exit PgDn-Next PgUp-Previous F10-Calculate Menu

Figure B-9-3a AUTO-CALCULATION screen

If user chose the third menu item of the CALCULATION MENU or pressed "3", the program will generate up to 30 dosage regimens that meet the set up criteria automatically. In this screen, only the first 10 dosage regimens are displayed. The remainder will be shown by pressing the function key "PgDn".

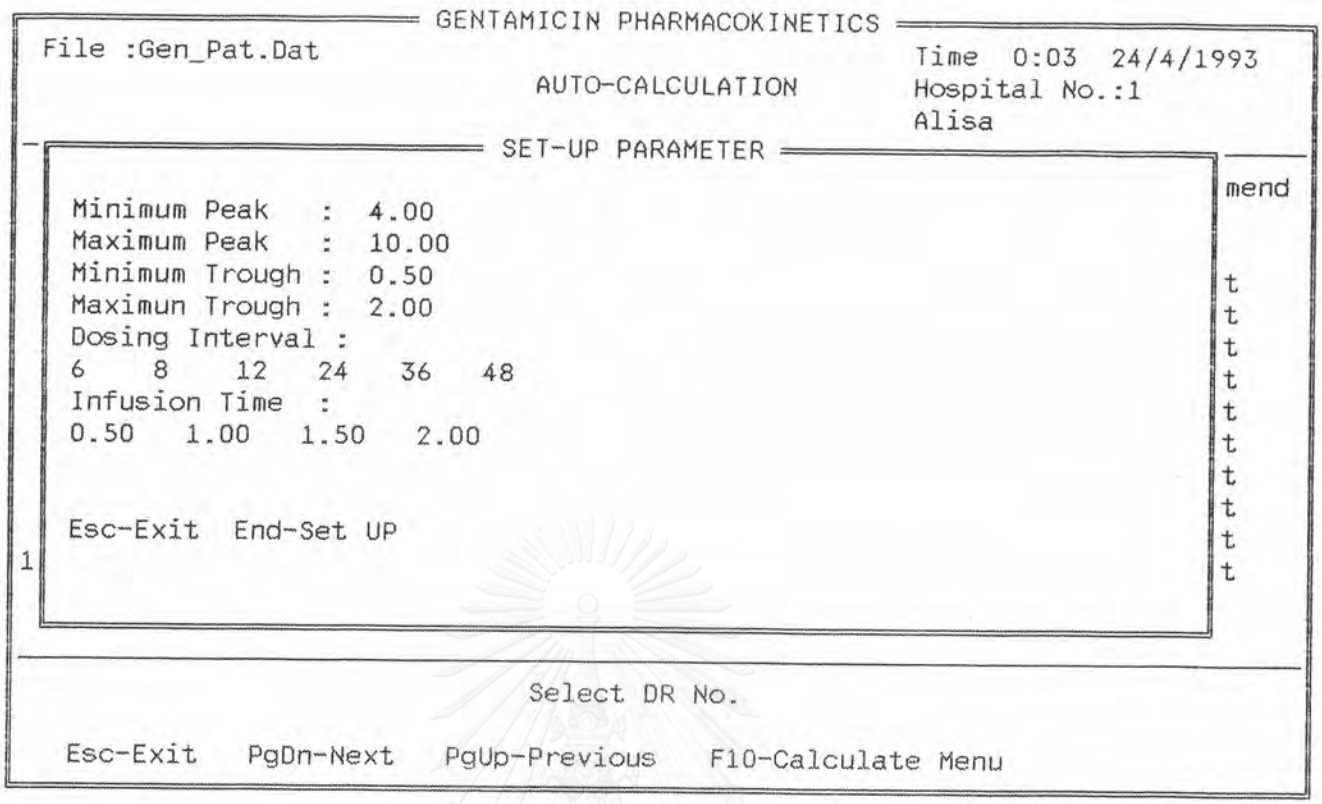


Figure B-9-3b SET UP PARAMETER screen, showing default values

Set up parameters or criteria to be used in auto-calculation module are demonstrated here. Values shown in this figure are default or set by the program to be used unless the user specifies otherwise.

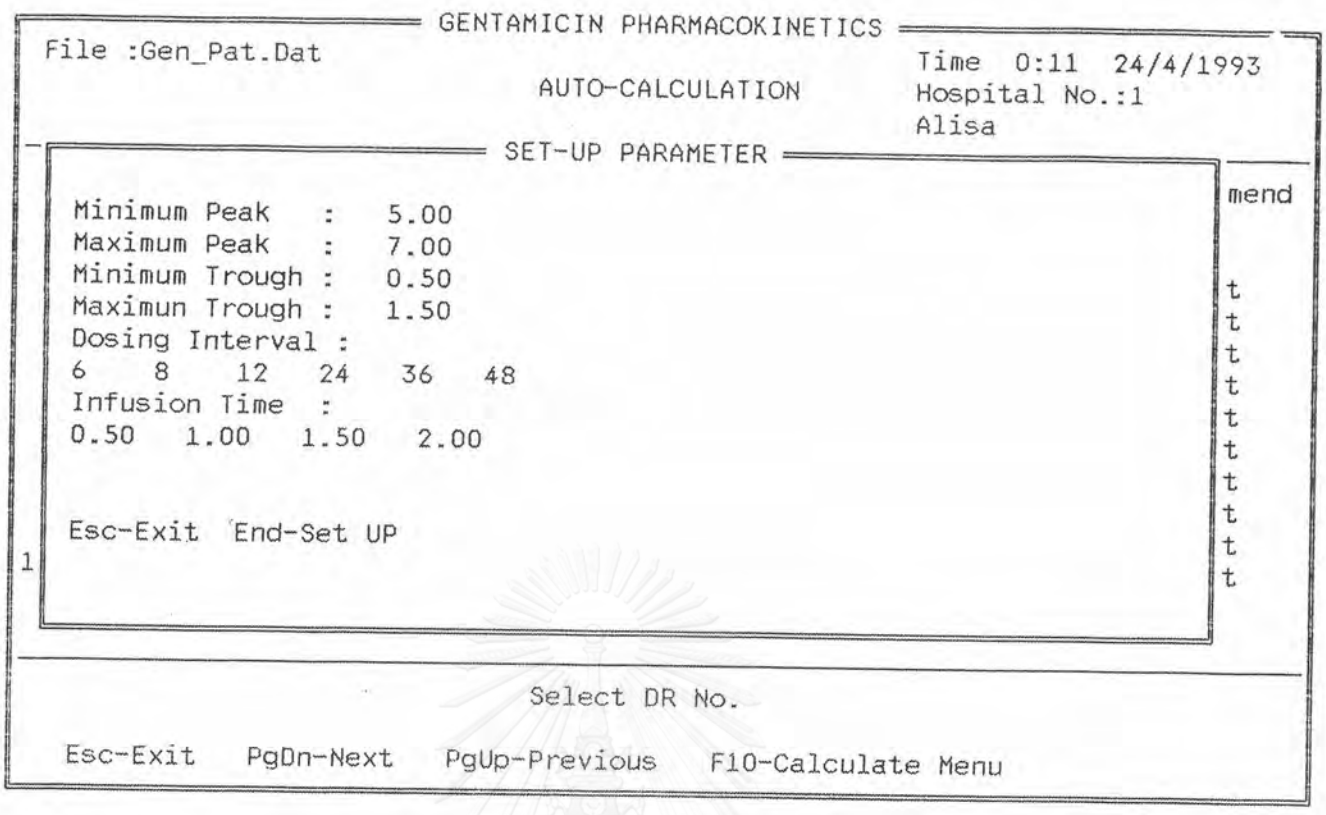


Figure B-9-3c SET UP PARAMETER screen, showing user-defined values The default values could be changed as the user specified.

GENTAMICIN PHARMACOKINETICS

File :Gen_Pat.Dat

AUTO-CALCULATION

Time 0:13 24/4/1993
Hospital No.:1
Alisa

DR No.	Desired SS Cmax(mg/L)	Desired SS Cmin(mg/L)	Inf-T (h)	MD (mg)	q (h)	Predicted SS Cmax(mg/L)	Predicted SS Cmin(mg/L)	Recommend
1)	5.0- 7.0	0.5- 1.5	0.5	44.0	6	5.40	1.34	Both Accept
2)			1.0	44.0	6	5.08	1.43	Both Accept
3)			0.5	48.0	6	5.89	1.47	Both Accept
4)			0.5	48.0	8	5.30	0.79	Both Accept
5)			0.5	52.0	8	5.74	0.86	Both Accept
6)			1.0	52.0	8	5.40	0.92	Both Accept
7)			1.5	52.0	8	5.09	0.98	Both Accept
8)			0.5	56.0	8	6.18	0.93	Both Accept
9)			1.0	56.0	8	5.82	0.99	Both Accept
10)			1.5	56.0	8	5.48	1.06	Both Accept

Select DR No.

Esc-Exit PgDn-Next PgUp-Previous F10-Calculate Menu

Figure B-9-3d AUTO-CALCULATION screen, showing up to 30 dosage regimens that meet the user-defined or new criteria.

GENTAMICIN PHARMACOKINETICS

File :Gen_Pat.Dat

AUTO-CALCULATION

Time 0:17 24/4/1993
Hospital No.:1
Alisa

DR No.	Desired SS Cmax(mg/L)	Desired SS Cmin(mg/L)	Inf-T (h)	MD (mg)	q (h)	Predicted SS Cmax(mg/L)	Predicted SS Cmin(mg/L)	Recommend
11)	5.0- 7.0	0.5- 1.5	2.0	56.0	8	5.17	1.13	Both Accept
12)			0.5	60.0	8	6.63	0.99	Both Accept
13)			1.0	60.0	8	6.23	1.06	Both Accept
14)			1.5	60.0	8	5.87	1.13	Both Accept
15)			2.0	60.0	8	5.54	1.21	Both Accept
16)			1.0	64.0	8	6.65	1.13	Both Accept
17)			1.5	64.0	8	6.26	1.21	Both Accept
18)			2.0	64.0	8	5.91	1.29	Both Accept
19)			1.5	68.0	8	6.65	1.28	Both Accept
20)			2.0	68.0	8	6.27	1.38	Both Accept

Select DR No.

Esc-Exit PgDn-Next PgUp-Previous F10-Calculate Menu

Figure B-9-3d AUTO-CALCULATION screen, showing up to 30 dosage regimens that meet the user-defined or new criteria. (Continued...)

GENTAMICIN PHARMACOKINETICS

File :Gen_Pat.Dat

AUTO-CALCULATION

Time 0:18 24/4/1993
Hospital No.:1
Alisa

DR No.	Desired SS Cmax(mg/L)	Desired SS Cmin(mg/L)	Inf-T (h)	MD (mg)	q (h)	Predicted SS Cmax(mg/L)	Predicted SS Cmin(mg/L)	Recommend
21)	5.0- 7.0	0.5- 1.5	2.0	72.0	8	6.64	1.46	Both Accept
22)			2.0	76.0	12	6.39	0.51	Both Accept
23)			2.0	80.0	12	6.73	0.54	Both Accept

Select DR No.

Esc-Exit PgDn-Next PgUp-Previous F10-Calculate Menu

Figure B-9-3d AUTO-CALCULATION screen, showing up to 30 dosage regimens that meet the user-defined or new criteria. (Continued...)

GENTAMICIN PHARMACOKINETICS

File :Gen_Pat.Dat

AUTO-CALCULATION

Time 0:15 24/4/1993
Hospital No.:1
Alisa

DR No.	Desired SS Cmax(mg/L)	Desired SS Cmin(mg/L)	Inf-T (h)	MD (mg)	q (h)	Predicted SS Cmax(mg/L)	Predicted SS Cmin(mg/L)	Recommend
1)	5.0- 7.0	0.5- 1.5	0.5	44.0	6	5.40	1.34	Both Accept
2)			1.0	44.0	6	5.08	1.43	Both Accept
3)			0.5	48.0	6	5.89	1.47	Both Accept
4)			0.5	48.0	8	5.30	0.79	Both Accept
5)			0.5	52.0	8	5.74	0.86	Both Accept
6)			1.0	52.0	8	5.40	0.92	Both Accept
7)			1.5	52.0	8	5.09	0.98	Both Accept
8)			0.5	56.0	8	6.18	0.93	Both Accept
9)			1.0	56.0	8	5.82	0.99	Both Accept
10)			1.5	56.0	8	5.48	1.06	Both Accept

Select DR No. 8

Esc-Exit PgDn-Next PgUp-Previous F10-Calculate Menu

Figure B-9-3e AUTO-CALCULATION screen at end run

By pressing "Esc" function key, the calculation is stopped. Then the user is asked by the program to select the one he desired. In this example, he preferred the dosage regimen No. 8.

```
                    GENTAMICIN PHARMACOKINETICS
File :Gen_Pat.Dat                                   Time  0:18  24/4/1993
                         CONSULTANT
      Consultant Current Dosage Regimen
LD 64.00   mg ( 1.60 ml of 80 mg/2ml vial)
MD 56.00   mg ( 1.40 ml of 80 mg/2ml vial)
Repeat 0.50 -hr infusion every 8  hr
With Peak : 6.18      Trough :0.93
For this Dosage Regimen,
Both predicted steady-state peak and trough are acceptable.
Therefore, the patient should continue on this dosage regimen.



     Recommend Blood Sampling times
Sampling Gentamicin level :
Test Dose  => C1 = 0.5 ,C2 = 1 and C3 = 2 hour after end of infusion
draw on the dose close to the next scheduled batch day

Sampling Creatinine level :every 3 days

    Esc-Exit  Q-Main Menu  End-Save & Main Menu  F8-Print
```

```
Hospital No.: 1
NAME : Alisa
Consultant Current Dosage Regimen
LD       64.00 mg (  1.60 ml of 80 mg/2ml vial)
MD       56.00 mg (  1.40 ml of 80 mg/2ml vial)
Repeat  0.50  -hr infusion every 8  hr
With Peak :  6.18  Trough :0.93
 Recommend :
For this Dosage Regimen,
Both predicted steady-state peak and trough are acceptable.
Therefore, the patient should continue on this dosage regimen.
Recommend Blood sampling times
Sampling Gentamicin level :
Test Dose  => C1 = 0.5 ,C2 = 1 and C3 = 2 hour after end of infusion
draw on the dose close to the next scheduled batch day

Sampling Creatinine level : every 3 days
```

Figure B-10 CONSULTANT screen (above) and printout (below)

Regardless of which way to find the desired dosage regimen. After entering of the chosen number, the CONSULTANT screen is displayed automatically.

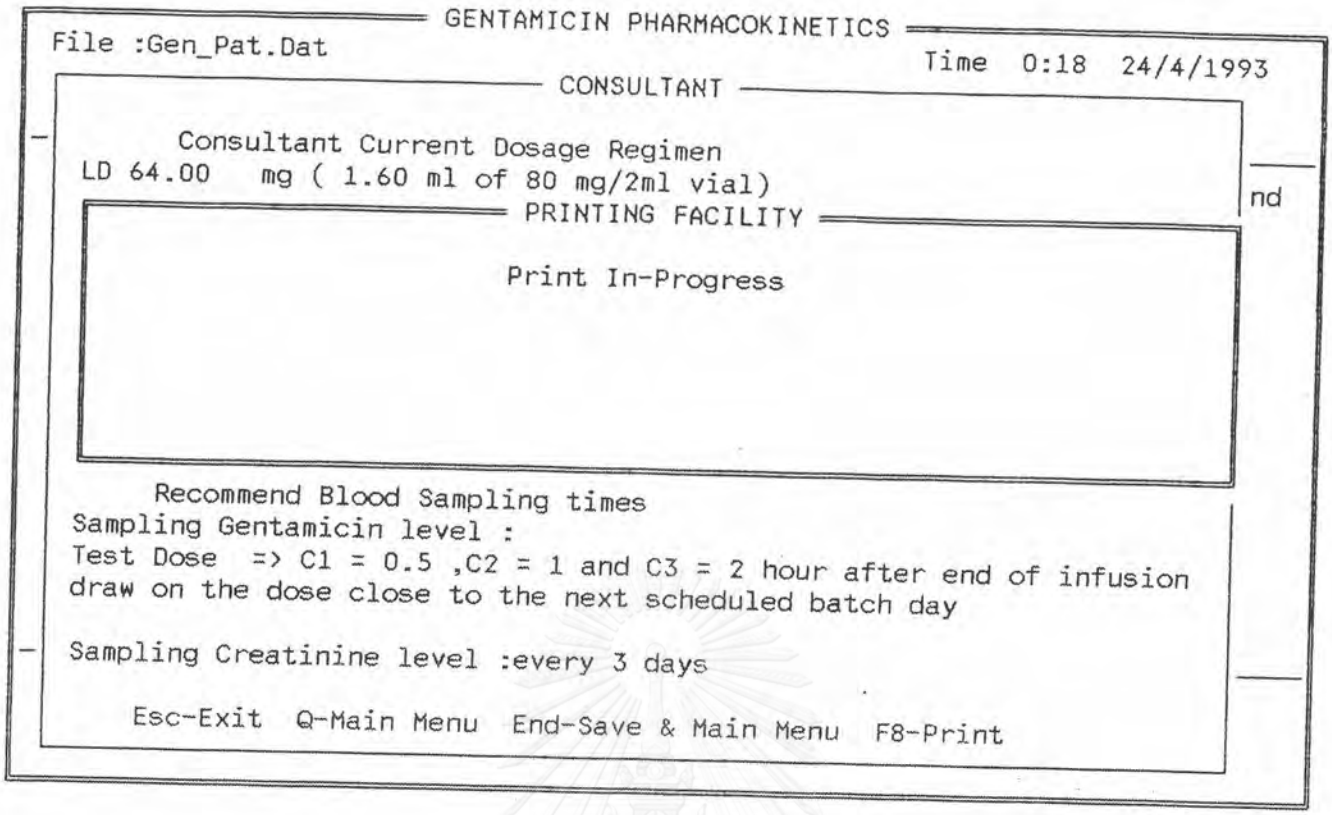


Figure B-11 PRINTING FACILITY screen

Printing facility is provided in every information screen. User can use this facility by pressing "F8" function key.

```
                    GENTAMICIN PHARMACOKINETICS
File :Gen_Pat.Dat                                  Time  10:31  25/4/1993
                              REVIEW CHART         Hospital No. 1
                                                   * Current Patient *
-------------------------------------------------------------------------
      Demographic Data
 1) Name: Alisa
 2) Bed : aaa
 3) Doctor  : ZZ
      Physical Data
 4) Age (year) :  27.00
 5) Weight (kg):  49.00
 6) Height (cm): 158.50
 7) Sex (M/F)  :  F
      Clinical Data
 8) Previous aminoglycoside therapy in
    the last 10 days?(Y/N) :N
 9) Recent Scr > 2 mg/dl? : N
10) Recent Scr - Prior Scr >= 0.5 mg/dl?:N
11) Diabetic? : N
12) Abnormal liver Function? :N
13) Shock? : N
14) Concurrent IV vancomycin or
     amphotericin B? :N
15) Hydration Status (N/D/E):N
     Normal/Dehydrated/
     /Edematous-Overhydrated
16) Renal Function (N/C/E) :N
     Normal/Chronic/End-Stage
17) Objective
    sepsis

-------------------------------------------------------------------------
  PgDn-Next Screen    End-Save    F8-Print
```

Figure B-11 REVIEW CHART screen at subsequent consultation

If the entered hospital number is already existed in file, the program will show patient record promptly.

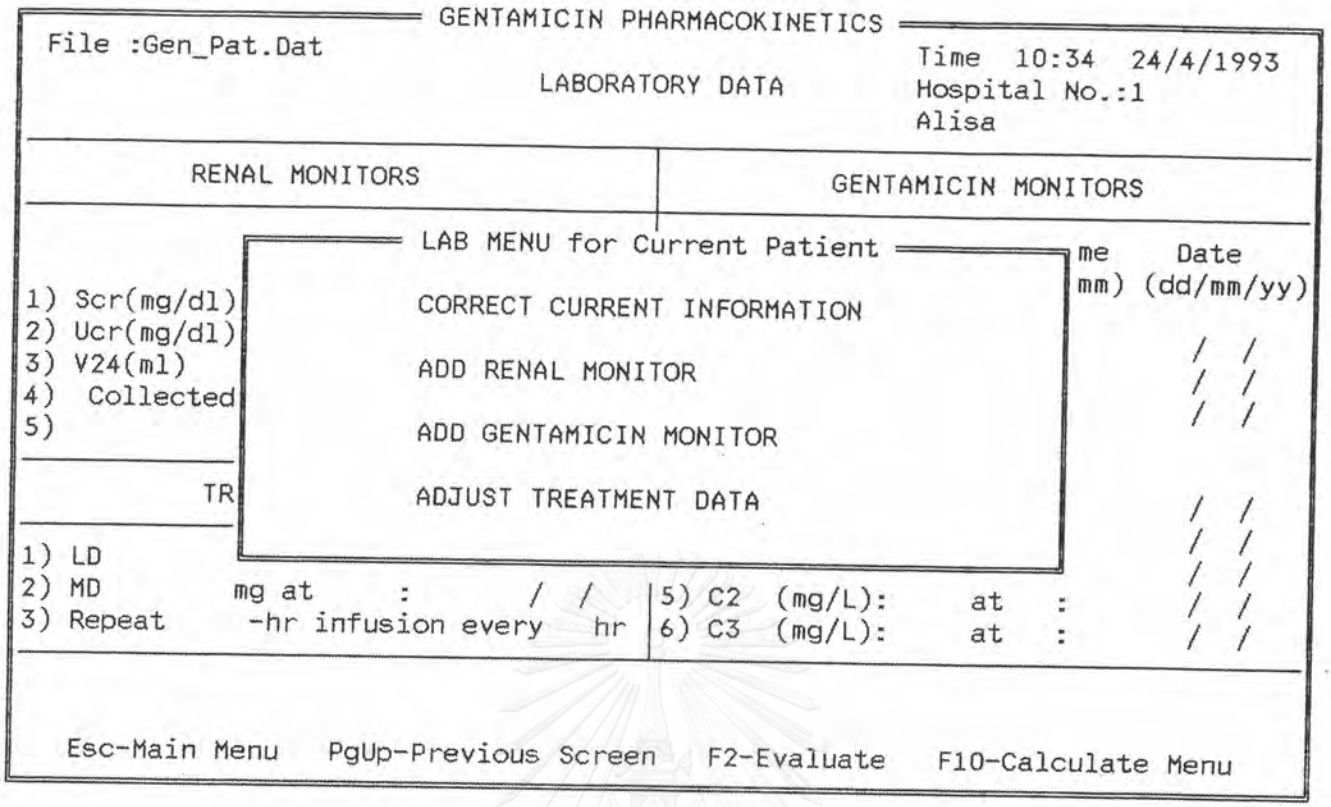


Figure B-12 LAB MENU for Current Patient screen

User can choose the items on this menu to correct or add laboratory or treatment data as they occured.

GENTAMICIN PHARMACOKINETICS

File :Gen_Pat.Dat

LABORATORY DATA

Time 10:17 25/4/1993
Hospital No.:1
Alisa

RENAL MONITORS

	Time (hh:mm)	Date (dd/mm/yy)
1) Scr(mg/dl):0.90	8 :00	24/4 /93
2) Ucr(mg/dl): 30.50		
3) V24(ml) : 3600		
4) Collected From	20:00	23/4 /93
5) To	20:00	24/4 /93

TREATMENT DATA

1) LD 64.00 mg at	10:00	24/4 /93
2) MD 56.00 mg at	18:00	24/4 /93
3) Repeat 0.50-hr infusion every 8 hr		

GENTAMICIN MONITORS

	Time (hh:mm)	Date (dd/mm/yy)
1) Prior dose 64.00 mg		
infused from	10:00	24/4 /93
to	10:30	24/4 /93
2) Cmin(mg/L):1.04 at	18:00	24/4 /93
3) Test dose 56.00 mg		
infused from	18:00	24/4 /93
to	18:30	24/4 /93
4) C1 (mg/L):5.25 at	19:00	24/4 /93
5) C2 (mg/L):4.60 at	19:30	24/4 /93
6) C3 (mg/L): at	:	/ /

Esc-Main Menu PgUp-Previous Screen F2-Evaluate F10-Calculate Menu

Hospital No.: 1
NAME : Alisa

RENAL MONITORS

Serum creatinine concentration (mg/dl) : 0.90 at 8:00 24/4/93
Urine creatinine concentration (mg/dl) : 30.50
24-hour urine volume (ml) : 3600 collected from 20:00 23/4/93 to 20:00 24/4/93

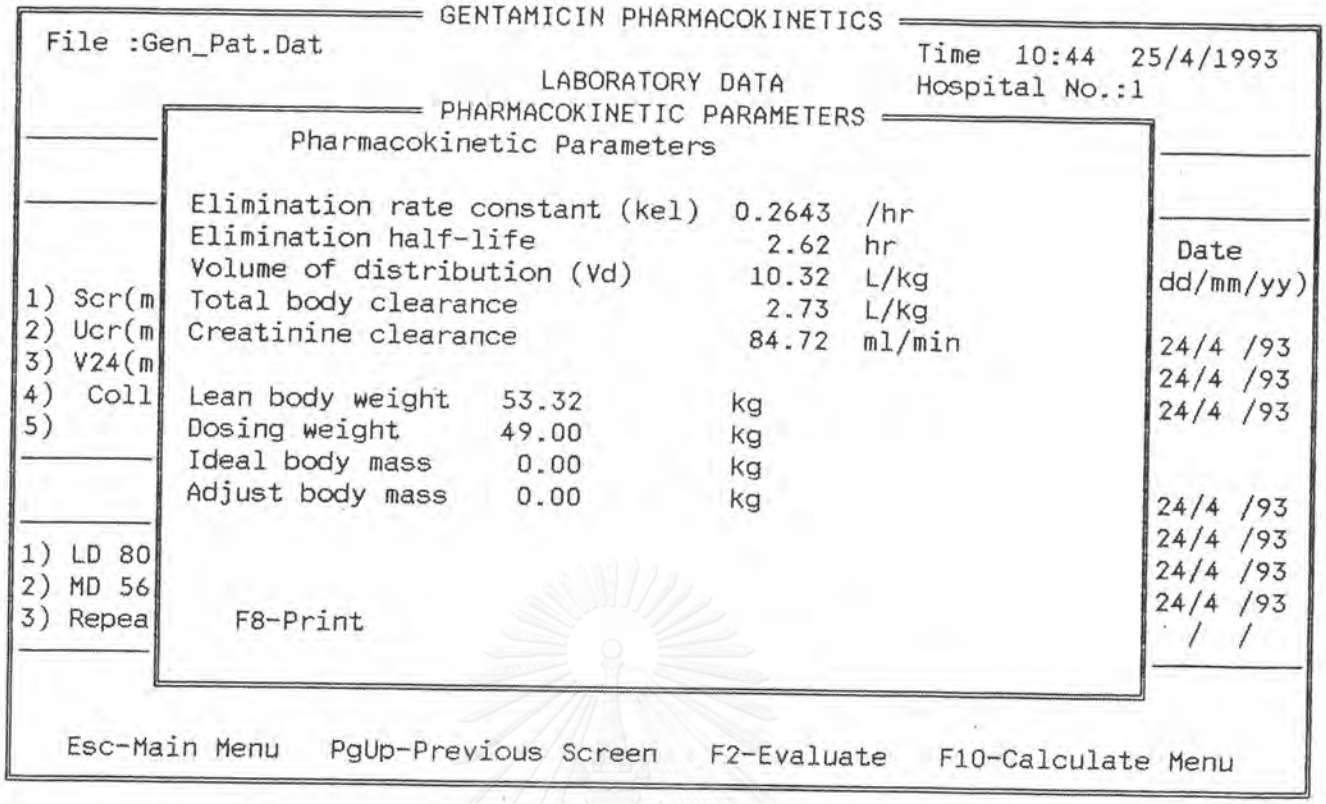
TREATMENT DATA

Loading dose (mg) : 64.00 at 10:00 24/4/93
Maintenance dose (mg) : 56.00 at 18:00 24/4/93
Repeat 0.50-hour infusion every 8 hours

GENTAMICIN MONITOR

Prior dose : 64.00 mg Infused from 10:00 24/4/93 to 10:30 24/4/93
Cmin (mg/L): 1.04 at 18:00 24/4/93
Test dose : 56.00 mg Infused from 18:00 24/4/93 to 18:30 24/4/93
C1 (mg/L): 5.25 at 19:00 24/4/93
C2 (mg/L): 4.60 at 19:30 24/4/93
C3 (mg/L): 0.00

Figure B-13 LABORATORY DATA screen (above) and printout (below) after finished entering data.



Hospital No.: 1
NAME : Alisa
PHARMACOKINETIC PARAMETERS

Elimination rate constant (kel)	0.2643	/hr
Elimination half-life	2.62	hr
Volume of distribution (Vd)	10.32	L/kg
Total body clearance	2.73	L/kg
Creatinine clearance	84.72	ml/min
Lean body weight	53.32	kg
Dosing weight	49.00	kg
Ideal body mass	0.00	kg
Adjust body mass	0.00	kg

Figure B-14 PHARMACOKINETIC PARAMETERS screen (above) and printout (below) according to recently input data in figure B-13.

```
                    GENTAMICIN PHARMACOKINETICS
File :Gen_Pat.Dat                                  Time  10:47  25/4/1993
                          CONSULTANT

        Evaluate  Current Dosage Regimen
    LD 64.00    mg ( 1.60 ml of 80 mg/2ml vial)
    MD 56.00    mg ( 1.40 ml of 80 mg/2ml vial)
    Repeat 0.50 -hr infusion every 8  hr
    With Peak : 5.78       Trough :0.80
    For this Dosage Regimen,
    Both predicted steady-state peak and trough are acceptable.
    Therefore, the patient should continue on this dosage regimen.



        Recommend Blood Sampling times
    Sampling Gentamicin level :Previous Dose => Cmin
    Test Dose  => C1 = 0.5 ,C2 = 1 and C3 = 2 hour after end of infusion
    draw on the dose after reaching steady-state
    ( 13.11 hr from the beginning of this dosage regimen)
    Sampling Creatinine level :every 3 days

       Esc-Exit  Q-Main Menu  End-Save & Main Menu  F8-Print
```

```
Hospital No.: 1
NAME : Alisa
Evaluate Current Dosage Regimen
LD        64.00 mg (  1.60 ml of 80 mg/2ml vial)
MD        56.00 mg (  1.40 ml of 80 mg/2ml vial)
Repeat  0.50  -hr infusion every 8  hr
With Peak :  5.78  Trough :0.80
 Recommend :
For this Dosage Regimen,
Both predicted steady-state peak and trough are acceptable.
Therefore, the patient should continue on this dosage regimen.
Recommend Blood sampling times
Sampling Gentamicin level : Previous Dose => Cmin
Test Dose  => C1 = 0.5 ,C2 = 1 and C3 = 2 hour after end of infusion
draw on the dose after reaching steady-state
( 13.11 hr from the beginning of this dosage regimen)
Sampling Creatinine level : every 3 days
```

Figure B-15 CONSULTANT screen (above) and printout (below) representing an evaluation of current dosage regimen. Calculations are based on pharmacokinetic parameters recently estimated.

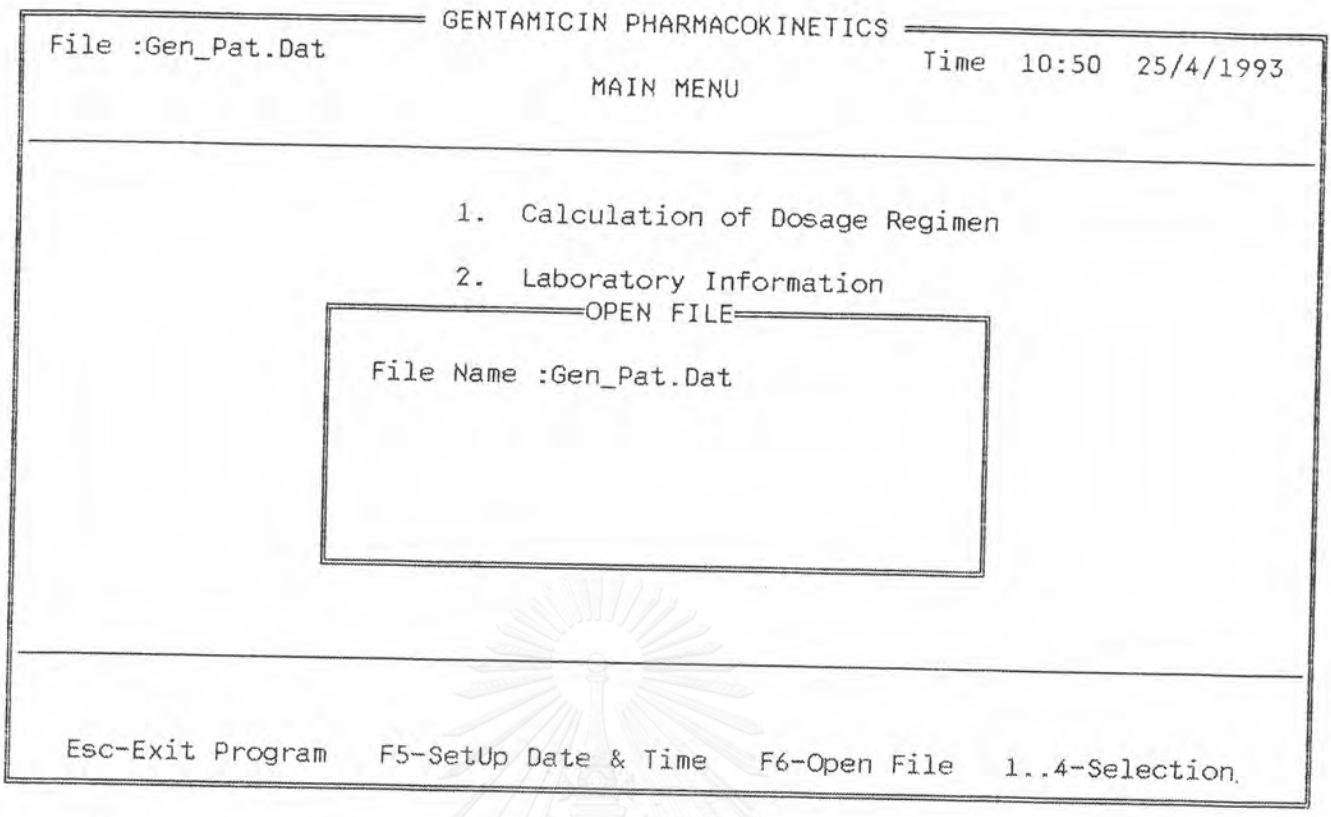


Figure B-16 OPEN FILE window

User can press "F6" from within the MAIN MENU to open a file as needed.

GENTAMICIN PHARMACOKINETICS

File :Gen_Pat.Dat

LABORATORY INFORMATION

Time 10:52 25/4/1993
Hospital No. 1
Alisa

RENAL MONITOR					GENTAMICIN MONITOR					
Scr	Draw at	Ucr	V24	Clcr	P-dose	Cmin	T-dose	C1	C2	C3
0.90	8:0 24/4/93	30.50	3600	84.72	64.00	1.04	56.00	5.25	4.60	0.00
0.80	8:0 23/4/93	27.50	3800	90.71						

Figure B-17 LABORATORY INFORMATION screen

This screen is displayed after user has selected the menu item "2" from within the MAIN MENU. And, by entering a hospital number, it shows all laboratory data input.

GENTAMICIN PHARMACOKINETICS

File :Gen_Pat.Dat

DOSAGE REGIMEN INFORMATION

Time 10:55 25/4/1993
Hospital No. 1 1
Alisa

Pharmacokinetic Parameter				Recommend Dosage Rigemen				
Clcr	LBW	kel	Vd	MD	inf-T	q	p-Cmax	p-Cmin
84.72	53.32	0.2643	10.32	56.00	0.50	8	5.78	0.80
90.71	53.32	0.2309	9.80	56.00	0.50	8	6.41	1.13
0.00	53.32	0.2530	9.80	56.00	0.50	8	6.18	0.93

Figure B-18 DOSAGE REGIMEN INFORMATION screen

This screen is displayed after user has selected the menu item "3" from within the MAIN MENU. And, by entering a hospital number, it shows pharmacokinetic parameters together with evaluation of dosage regimen.

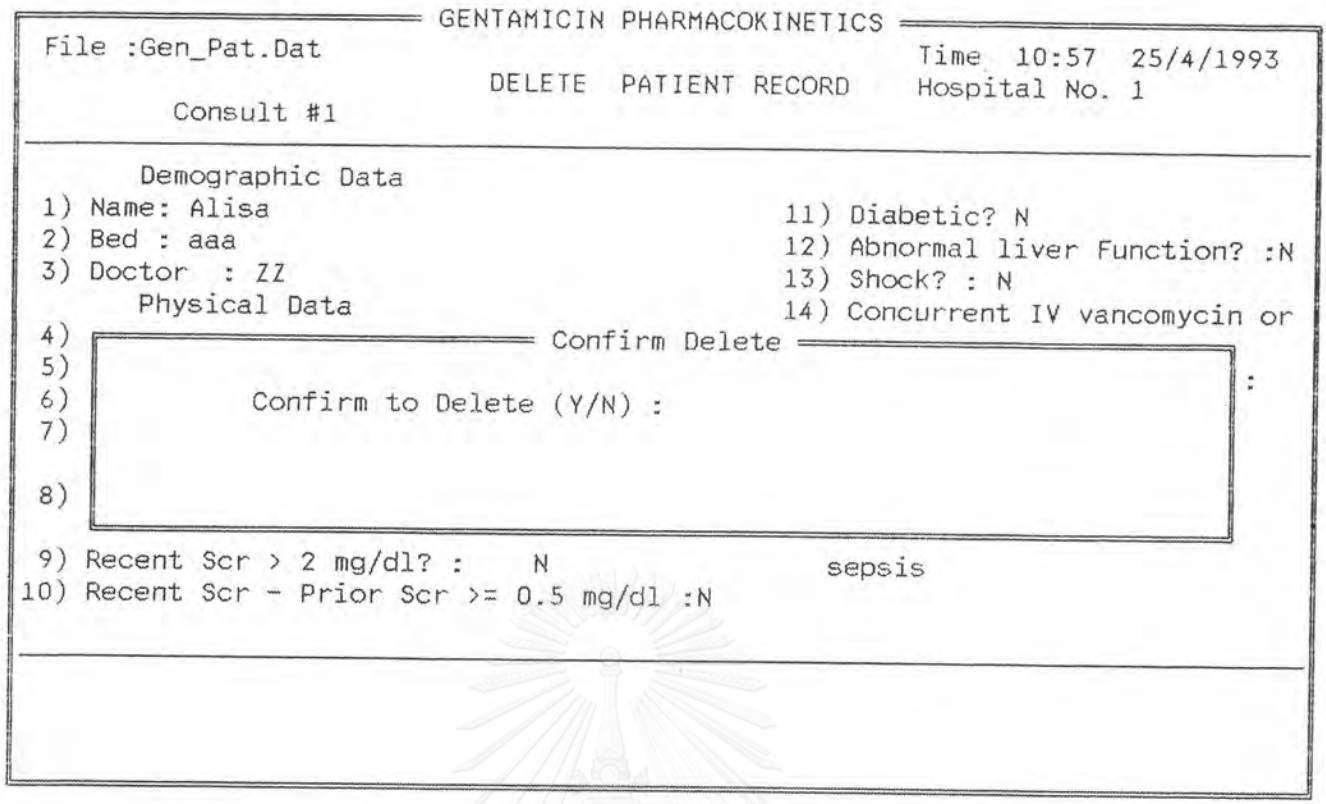


Figure B-19 DELETE PATIENT RECORD screen

This screen is displayed after user has selected the menu item "4" from within the MAIN MENU. And, by entering a hospital number, it shows a patient record to be deleted and ask the user to confirm his desire.

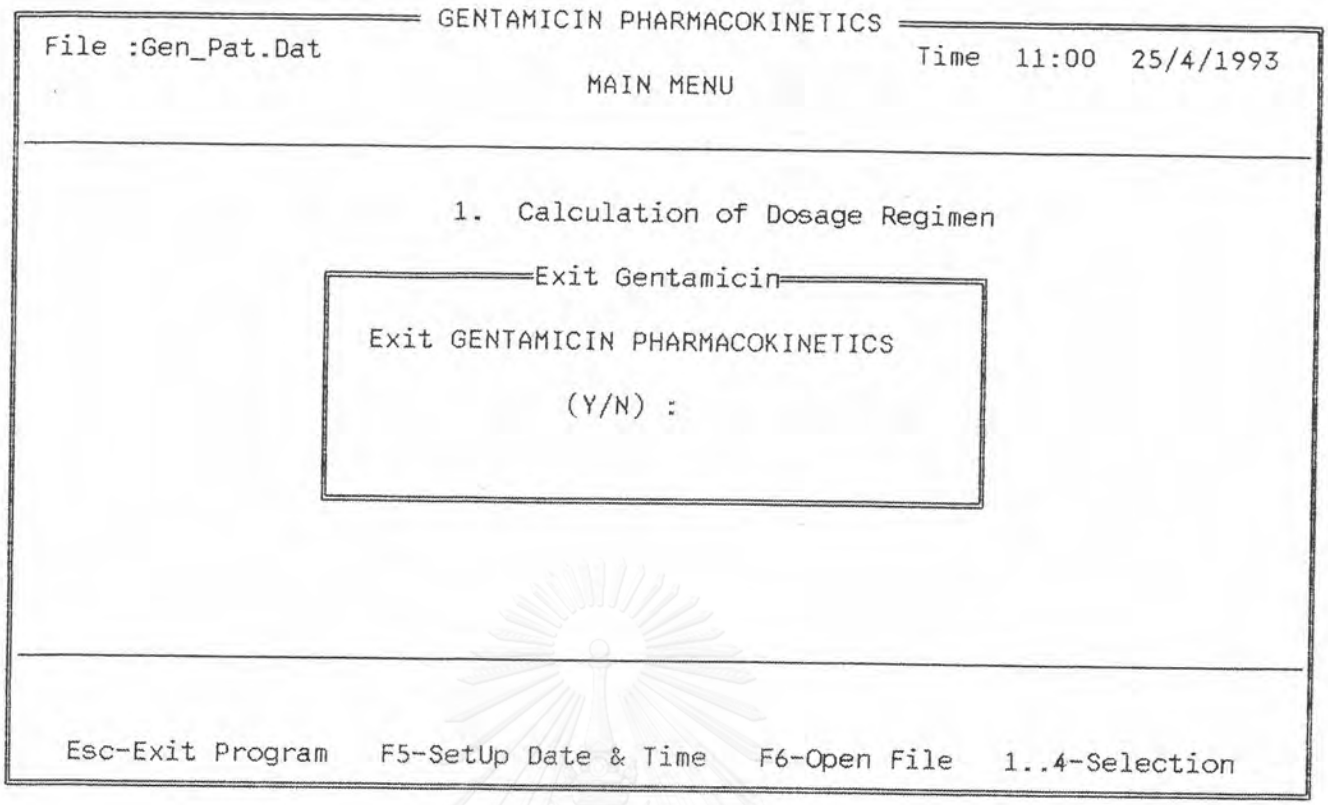


Figure B-20 EXIT program screen

This screen is displayed after user has pressed "Esc" from within the MAIN MENU to ask the user to confirm his desire.

BIOGRAPHY

Miss Surassawadee Suntharasaj was born on January, 15th, 1966, in Chachoengsao, Thailand. She graduated with a Bachelor Degree in 1988 from the Faculty of Pharmaceutical Science, Chulalongkorn University, Bangkok, Thailand.