The USC Laboratory of Applied Pharmacokinetics presents a Workshop on

Population Pharmacokinetic/Dynamic Modeling: Basic Concepts and Building Blocks, with Clinical Applications to Optimally Individualized Drug Therapy.

Saturday, Sunday, and Monday, December 6, 7, and 8, 2003

This course is for physicians and pharmacists with an interest in population pharmacokinetic/dynamic modeling who have a grasp of the basic aspects of such work. **Day 1** will introduce and review **Basic PK/PD tools, building blocks, and concepts** of pharmacokinetic modeling, and will emphasize their application to optimal patient care. **Day 2** will discuss intermediate and advanced **PK/PD tools, and concepts,** including parametric and nonparametric population modeling. **Day 3 will continue advanced use of the software. Note:** if you would like to bring your own laptop computer to obtain and learn the relevant software (not included in the registration fee), you are encouraged to do so.

Preliminary Program

Faculty:
***Roger Jelliffe, M.D.**, Professor of Medicine, USC School of Medicine, USA*
***Ashutosh Gandhi, M.A.,** Laboratory of Applied Pharmacokinetics**,** USC School of Medicine, USA*

Saturday, December 6, 2003 – Concepts, Building Blocks, and Tools

8:30 AM – Registration
9:00 AM – Welcome – Dr. Kamal Matar.
9:15 AM - Review of Basic Pharmacokinetic Concepts
Compartmental Models
Cumulation and Elimination
T ½, Fraction lost, Doses sustained.
Changing T ½, changing dose, outcomes.
9:45 AM - Ways of fitting data for patients
Linear regression of logs of data
Must wait for steady state
Must wait for complete distribution after a dose
Nonlinear regression on the data itself
No wait for steady state
No wait for distribution
Bayesian fitting – the best
The MAP Bayesian scenario and feedback strategy

10:15 AM – Break

10:30 AM - Estimation of Creatinine Clearance without a urine specimen in unstable patients

10:45 AM - When to obtain serum data for Therapeutic Drug Monitoring –
- Not just the trough
- Capture the dynamics
- Some optimal strategies

11:15 AM - Modeling the assay error

11:45 AM - Parametric population models
- What "parametric" means here
- The iterative Bayesian (IT2B) modeling approach
  - Separating inter - from intra-individual variability (IIV)
  - Separating IIV from assay error
- Demonstration of the approach – an Amikacin data set

12:30 PM – Lunch

2:00 PM - Nonparametric population modeling approaches
- What "nonparametric means here
- The NPAG approach
- Using IIV, assay error, and stated ranges

2:45 PM - Using population modeling approaches optimally
- Get the assay error polynomial
- Use IT2B - get Gamma
- Then use NPEM, get the entire joint density, essentially resolving the population into up to one model for each subject studied.

3:15 PM - The separation principle: limitations to current dosage methods

3:30 PM - Break

3:45 PM - Introduction to multiple model (MM) dosage design
- Software for MM dosage regimens

4:15 PM - Getting MM Bayesian posterior joint densities
- MM Bayesian posteriors
- A new method – IMM – for detecting changing parameter values in patients

5:00 PM – Adjourn

Sunday, December 7, 2003 – Clinical Applications: Pharmacokinetics and Optimal Patient Care

9:00 AM – Review and Discussion - Dr. Kamal Matar.

9:15 AM –Modeling Drug Diffusion into Endocardial Vegetations

9:45 AM – "Concentration and Time – Dependent Drugs": Modeling Organism Growth and Kill by Antibiotics.

10:15 AM – Break

10:30 AM- How to Plan, Monitor, and Adjust Individualized Drug Dosage Regimens for Patients.

Set a target goal for each patient according to the need for the drug.
Aminoglycosides 10 and 1, or 20 and 0.5
Vancomycin trough 10
Digoxin – really a 2 compartment model
Clinical effect correlates better with tissue than serum concentrations
How to manage this problem clinically
Serum troughs usually 0.9 ng/ml
Peripheral peaks usually 7.0 ug/kg
Patients with atrial fibrillation need more

11:30 AM - Case studies in aminoglycoside therapy

Therapeutic drug monitoring
Making the individualized, Bayesian posterior, model
Analyzing the data
A patient on dialysis

12:30 PM – Lunch

2:00 PM - Cost-effectiveness of individualized therapy

Outcomes in Busulfan therapy for bone marrow transplants in children

2:30 PM – Hands-on session: Case studies in digoxin therapy

An initial regimen for a patient with atrial fibrillation
A case history: another patient with atrial fibrillation
A patient on digoxin and quinidine

3:00 PM – Hands-on session: Case studies in Aminoglycoside therapy

A Patient on Gentamicin
A dialysis patient on Gentamicin
A difficult patient on Tobramycin

3:30 PM – Break

3:45PM - Demo – Making an IT2B population model of Amikacin
4:15 PM - Demo – Making a NPAG population model of Amikacin
4:45 PM – Comparing results: parametric and Nonparametric models

5:00 PM – Adjourn

Monday, December 8, 2003 –Population Modeling and Hands-on Cases

9:00 AM – Review and Discussion - Dr. Kamal Matar.
9:15 AM - Summary: Strengths and Weaknesses of Parametric and Nonparametric methods
9:45 AM – Hands-on session – Determining the Assay Error Pattern
10:00 AM – Hands-on session - Estimating Creatinine Clearance without the Urine Specimen
10:15 AM - Hands-on session - Making an IT2B Model of Amikacin

10:45 AM – Break

11:00 AM – Hands-on session - Making an NPAG Model of Amikacin
11:30 AM - Modeling Antiepileptic Drugs
12:00 noon - Hands-on session - Using BOXES to make Large and Nonlinear PK/PD Models – Making a Michaelis-Menten Model of Phenytoin

12:30 PM – Lunch

2:00 PM – Hands-on session: Making a Michaelis-Menten IT2B Model of Phenytoin
2:30 PM - Hands-on session: Making a Michaelis-Menten NPAG Model of Phenytoin

3:15 PM – Break

3:30 PM – Hands-on session: Two Patients on Digoxin
4:00 PM – Hands-on session: Case Studies in Aminoglycoside Therapy
4:30 PM - Hands-on session: Case Studies in Vancomycin Therapy
5:00 PM - Adjourn