

PHAR 7632 Chapter 23

Pharmacodynamic Models and Physiologically Based Pharmacokinetic Models

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Student Objectives for this Chapter

- To understand the different types of concentration - effect relationships
- To understand the mathematical relationships involved with direct reversible pharmacological effect kinetics
- To understand the development and use of physiologically based pharmacokinetic (PBPK) models

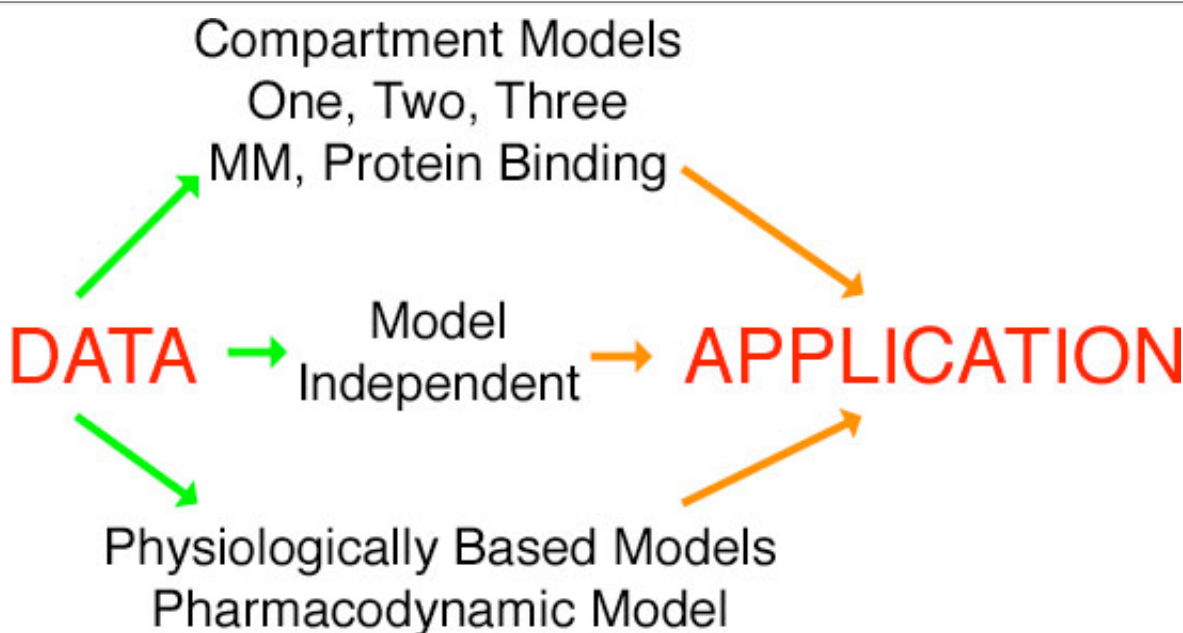


Figure 23.1.1 Diagram Representing Model Links between Data and Applications

The method of data analysis or modeling should match the data available and potential applications of the data and models. Compartmental models allow summarization of data and understanding of drug processes and the calculation of dose regimens and doses to effective drug concentrations. Model independent analysis allows summarization of data but reduced understanding of the time or dose dependent processes. Calculation of dosage regimens to an effective drug concentration is possible. Physiologically based and pharmacodynamic models require more data but allow increased understanding of drug distribution and response. These models allow dose adjustment to target tissue concentration or to a required drug response.

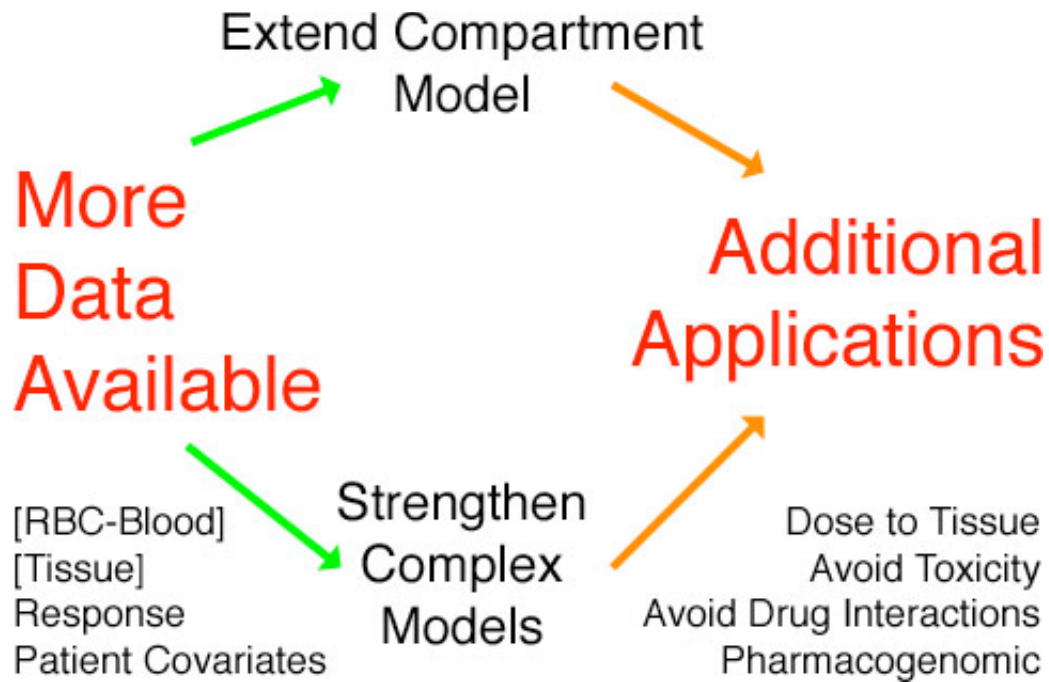


Figure 23.1.2 Diagram Representing Model Extension with More Data

With more data, more samples or sampling sites, the models can be expanded or extended. Drug concentrations in various tissues allows the understanding and quantitation of drug distribution in more detail. Drug response, either therapeutic or toxic, can be incorporated into useful models. Patient covariate information provides information for customizing dosing regimens to a particular patient.

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Pharmacodynamic Models

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Pharmacologic Models

Ref: Text book pp 61-64

- Sigmoid E_{max} Model (Hill Equation)

$$Effect = \frac{E_{max} \bullet Cp_{ss}^{\gamma}}{Cp_{ss50}^{\gamma} + Cp_{ss}^{\gamma}}$$

Equation 23.2.1 Sigmoid E_{max} Response versus Concentration (Hill Equation)

- E_{max} Model
- Linear Model
- Logarithmic Model

Pharmacodynamics - Link between Pharmacokinetics and Pharmacology

Ref: Textbook pp 66-75

- Direct Effects - Reversible
 - Rapid response - Central compartment
 - Rapid response - Peripheral compartment
 - Rapid response - Effect compartment
 - Delayed response - Drug/Receptor binding
- Indirect Effects
- Irreversible Effects

[Want more explore this type of model!](#)

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Physiologically Based Pharmacokinetic Models

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Physiologically Based Pharmacokinetic Models

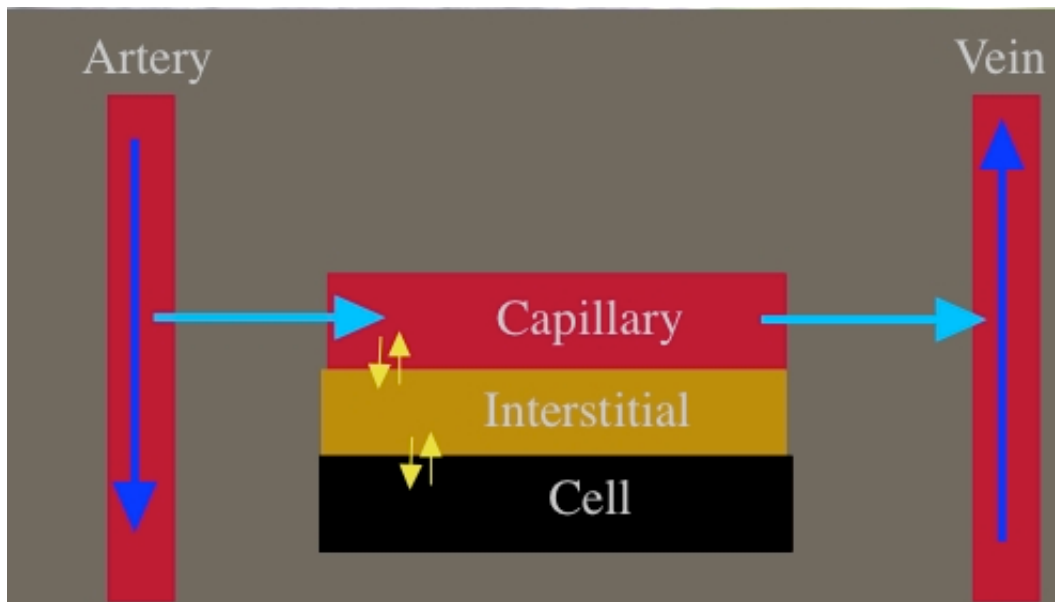


Figure 23.3.1 Drug Transport within the Organ/Tissue

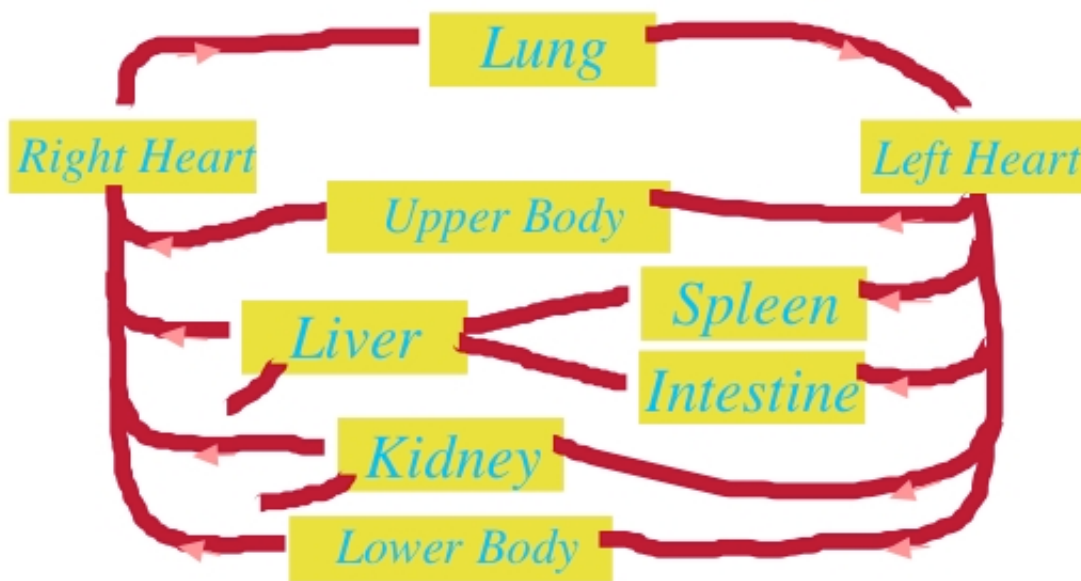


Figure 23.3.2 Drug Distribution throughout the Body

Plasma - Blood

$$V_P \cdot \frac{dC_P}{dt} = (\text{Injection}) + Q_L \cdot \frac{C_L}{R_L} + Q_K \cdot \frac{C_K}{R_K} + \dots - (Q_L + Q_K + \dots) \cdot C_P$$

Muscle

$$V_M \cdot \frac{dC_M}{dt} = Q_M \cdot \left(C_P - \frac{C_M}{R_M} \right)$$

Figure 23.3.3 Some of the Equations - Plasma, Muscle

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