Nontraditional PharmD Program
PRDO 7700 Pharmacokinetics Review
Self-Assessment

Please consider the following questions. If you do not feel confident about the material being covered, then it is recommended that you take the ASHP module on Kinetics as a tutorial. This module can be taken concurrently, but would be much more beneficial if completed prior to beginning the units on kinetics. In PRDO 7700, kinetics will begin in unit 5 and continue through unit 12. Note that answers to these questions will not be provided until after Unit 5 completion of PRDO 7700.

Questions for Review

1. Define "therapeutic range."

2. TRUE OR FALSE?
   One goal of "clinical pharmacokinetics" is to optimize the probability of producing a favorable response and/or avoiding unacceptable toxicities.

3. Which of the following criteria is/are important in deciding which drugs should be routinely therapeutically monitored (i.e., have clinical pharmacokinetics performed)?

   I. Relatively well-defined therapeutic range.
   II. Wide therapeutic range.
   III. Low variability within individual patients.
   IV. Potential for significant toxicities at doses required for efficacy.
   V. Defined relationship between concentration and effect.

   A. I and IV only
   B. II and V only
   C. I, II, and V only
   D. III, IV, and V only
   E. I, IV, and V only

4. Which of the following statements is FALSE?

   A. Clinical pharmacokinetics (therapeutic monitoring) is based on the assumption that drug concentrations in the blood are directly related to the drug concentrations at the site of action.
   B. The therapeutic range is based on the probabilities of achieving the desired therapeutic response with minimal toxicities within a certain range of concentrations.
   C. Each individual patient may display his/her own individual therapeutic range for a certain drug.
   D. Clinical monitoring of drug concentrations may often be used independent of other aspects of patient monitoring, e.g. physical examination.
   E. In explaining an unusual response to a drug, distinction must be made between pharmacokinetic and pharmacodynamic causes.
5. TRUE OR FALSE?
   A drug which is 100% absorbed from the gastrointestinal tract has 100% bioavailability.

6. TRUE OR FALSE?
   Changes in gastric emptying time may affect either the rate of drug absorption or the extent of drug absorption, or both.

7. Aside from gastric emptying time, list and briefly explain four additional factors which may influence the rate or extent of absorption of drugs from the gastrointestinal tract.

8. TRUE OR FALSE?
   The molecular weight of a drug is the rate-limiting factor which governs the absorption of a drug from an extravascular site of administration (e.g., intramuscular).

9. The proportionality constant that relates the amount of drug in the body and concentration of drug in the body is which of the following?
   A. Clearance
   B. First order elimination rate constant
   C. Bioavailability
   D. Volume of distribution
   E. Half-life

10. TRUE OR FALSE?
    If two drugs have identical total systemic clearances, a drug which is highly tissue bound will usually have a longer half-life than a drug which is highly bound to plasma proteins.

11. TRUE OR FALSE?
    Drugs which are highly tissue bound tend to have large volumes of distribution.

12. TRUE OR FALSE?
    The rate of distribution of small, lipophilic, uncharged drugs is primarily limited by rates of blood flow to tissues.

13. TRUE OR FALSE?
    Clearance is defined as the amount of drug removed from the blood per unit of time.

14. List the three principal determinants of the rate and/or extent of hepatic clearance.

15. Define extraction ratio. How is the extraction ratio of a specific drug in a specific organ calculated/determined? What is the significance of the extraction ratio?
16. TRUE OR FALSE?
The elimination of a drug with a hepatic extraction ratio of 1.0 is highly subject to alterations in blood flow and protein binding.

17. Which of the following are assumptions that are required to appropriately use the one compartment pharmacokinetic model?

I. Bioavailability does not change over time
II. Drug elimination is zero order
III. Distribution equilibrium is reached instantaneously
IV. All of the dose is metabolized by the liver
V. Drug elimination is first order

A. II and IV only  
B. III and V only  
C. I and V only  
D. I and IV only  
E. II and III only

18. TRUE OR FALSE?
In a first-order one-compartment model, the fraction of an administered dose eliminated within a given time is independent of the size of the dose.

19. Which of the following statements is TRUE?

A. Changes in clearance may occur independently of changes in volume of distribution.
B. Changes in the elimination rate constant may occur independently of changes in clearance.
C. Changes in the elimination rate constant may occur independently of changes in volume of distribution.
D. Change in volume of distribution are dependent on changes in bioavailability.
E. Changes in half-life may occur independently of changes in either volume of distribution or clearance.

20. TRUE OR FALSE?
Changes in drug elimination through changes in hepatic metabolism may result in alterations in both the volume of distribution and area under the concentration-time curve (AUC).

21. The drug concentration immediately after a drug is administered intravenously is 15 mg/L; 6 hours later, the concentration is 3 mg/L. What are the elimination rate constant and half-life of this drug?

What is the predicted tobramycin concentration 8 hours after a peak concentration of 8 mg/L is observed if the elimination rate constant is known to be 0.15/hr?

22. TRUE OR FALSE?
All drugs having the same clearance reach the same steady-state concentration when given at the same intravenous infusion rate.
23. An intravenous anticonvulsant agent is to be administered to a patient in status epilepticus. The drug has a plasma half-life of 8 hours and a volume of distribution of 225 L. Calculate an appropriate loading dose and continuous infusion rate to quickly reach and maintain a steady-state concentration of 10 mg/L.

24. A patient is started on a continuous intravenous infusion of theophylline at a rate of 50 mg/hour. Theophylline is known to have a volume of distribution of 35 liters and a half-life of 4 hours in this patient. What is the expected steady-state concentration of theophylline if the current infusion rate is continued, and how long will it take to achieve?

25. Which of the following statements is TRUE?

A. A steady-state plasma concentration is achieved when the continuous infusion of drug has been given for at least seven half-lives of the drug.
B. A doubling of the rate of continuous infusion should result in a four-fold increase in the drug's steady-state concentration.
C. Plasma steady-state concentrations resulting from a continuous infusion are dependent on the relationship between a drug's infusion rate and the volume of distribution.
D. When an intravenous infusion rate is changed, it will take approximately four half-lives to reach a new steady-state.

26. TRUE OR FALSE?
The "uphill" portion of the plasma concentration versus time curve following an oral drug dose demonstrates the effects of absorption only.

27. TRUE OR FALSE?
Decreases in the rate of absorption (ka) of a drug result in a decreased Cmax and increased tmax, assuming that all other variables are held constant.

28. TRUE OR FALSE?
Drug-drug or drug-food interactions which result in decreased rate of drug absorption are usually much more clinically significant than those resulting in decreased extent of absorption.

29. The following information was obtained after administration of three different dosage forms of the same drug to the same group of patients:

Drug A: AUC = 34 mg*hr/L after a 50 mg oral dose
Drug B: AUC = 85 mg*hr/L after a 75 mg intravenous dose
Drug C: AUC = 60 mg*hr/L after a 100 mg oral dose

What is the absolute bioavailability of Drug A? What is the relative bioavailability of drug A compared to Drug C?
30. TRUE OR FALSE?
Changes in either drug dose or bioavailability will cause direct changes in Cmax but will not change the time to maximum serum concentrations.

31. TRUE OR FALSE?
Drugs with the same clearance generally reach steady-state concentration at the same time.

32. TRUE OR FALSE?
The larger the volume of distribution, the lower the average steady-state concentration of a drug.

33. TRUE OR FALSE?
The extent of drug accumulation with multiple dosing regimens is dependent only on the half-life of the drug and the frequency of drug administration.

34. TRUE OR FALSE?
The extent of drug accumulation increases when a drug is given less frequently.

35. The primary purpose in administering a loading dose of a drug at the initiation of therapy is to:
   A. Achieve steady-state more rapidly.
   B. Avoid drug toxicity seen at higher concentrations.
   C. Maximize drug accumulation with subsequent doses.
   D. Determine the most effective concentrations of drug in any given patient.
   E. Achieve therapeutic concentrations of drug more rapidly.

36. Which of the following statements regarding multiple-dosing regimens are TRUE?
   I. The rate and extent of drug accumulation depend on the drug's elimination half-life and dosing frequency.
   II. The same daily dose of a drug will produce the same average concentration at steady state, regardless of how it's divided (e.g. Fishmanide 200 mg every 8 hours or 300 mg every 12 hours).
   III. The same daily dose of a drug will produce the same maximum and minimum concentrations at steady state, regardless of how it's divided (e.g. Fishmanide 200 mg every 8 hours or 300 mg every 12 hours).
   IV. Changes in the clearance of a drug (e.g. renal dysfunction) do not significantly affect drug accumulation.
   V. Changes in the volume of distribution of a drug do not significantly affect drug accumulation.

   A. I and II only
   B. II and III only
   C. I and V only
   D. III and IV only
   E. II, IV and V only

37. Which of the following dosage adjustments will increase the steady-state concentration?
   A. Increasing the dose but keeping the same dosing interval.
   B. Keeping the same dose but decreasing the dosing interval.
   C. Keeping the same dose but increasing the dosing interval.
   D. A and B only.