Outreach:
A Tour of the Pharmaceutical Sciences

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ABSTRACT. The success of a college of pharmacy is dependent on the quality of its graduating professional students. Paramount to the quality of the graduating students is the talent of the college's new student applicant pool. To increase the exposure of students to pharmacy education and possible career options following graduation, many colleges of pharmacy have developed outreach programs with the intent of exposing high school and preprofessional students to a career in pharmacy. This interest in capturing the attention of younger students is not limited to the professional aspects of pharmacy but includes other career options such as working in the pharmaceutical industry. The American Association of Pharmaceutical Scientists has developed its own program called "Outreach: A Tour of the Pharmaceutical Sciences." The aim of the program is to introduce secondary school faculty and students to the pharmaceutical sciences as a possible career option. *[Article copies available for a fee from The Haworth Document Delivery Service: 1-800-342-9678. E-mail address: <getinfo@ haworthpressinc.com> Website: <http://www.HaworthPress.com>]*

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INTRODUCTION

Colleges of pharmacy have always sought to recruit the best students possible to train as pharmacists. This is especially true of those students with a gift for science and mathematics. Often times, students who apply to colleges of pharmacy have already had exposure to the profession through friends, family, or personal experience. In addition, students may make the choice to apply to a pharmacy program during their ''preprofessional'' undergraduate years based on interactions with other students or with instructors. Despite these experiences, students may not understand the multitude of options available to them once they have completed their professional training. Preprofessional students frequently do not know about the less traditional roles of pharmacists in the health care field, but focus on practice in either a retail or hospital setting as a career. Although professional pharmacy students are exposed to numerous career options, decisions about their prospective careers may have already been made based on their prior experience.

Pharmacy community outreach programs have proved to be an excellent means of disseminating information about the prospective roles of pharmacists in the health care field. These programs have also served as a means of attracting talented students to apply to pharmacy schools and colleges. In 1996, the Education Committee of the American Association of Pharmaceutical Scientists (AAPS) began a program directed at secondary school teachers and students to educate them about potential career options in the pharmaceutical sciences. The program, ''Outreach: A Tour of the Pharmaceutical Sciences,'' was developed to serve as a mechanism for colleges of pharmacy, in cooperation with the pharmaceutical industry, to show teachers of biology, chemistry, and the mathematical sciences how they could integrate the pharmaceutical sciences into their lesson plans. The purpose was not to have the teachers train their students to be pharmaceutical scientists, but rather to offer them a means of showing students how the science and math they are currently learning can be applied outside of the classroom. For example, teachers may educate their students on career options for chemists in a chemical manufacturing plant but may not be aware of or may neglect opportunities in a pharmaceutical company. Thus, the AAPS Outreach Program gives teachers and their students exposure to many of the careers that training in the pharmaceutical sciences may offer.

PROGRAM LOCATION

The annual AAPS Outreach Program is held on the weekend prior to the start of the AAPS annual meeting. The location of the AAPS Outreach

Program is a college of pharmacy in the same city where the AAPS holds its annual meeting. Thus the program is a cooperative project between the AAPS and the host city college of pharmacy. This cooperative arrangement between the AAPS and the host college of pharmacy allows for the greatest exposure of the participants to the profession of pharmacy and the pharmaceutical sciences. In addition, it offers the host college of pharmacy an excellent opportunity for recruiting future pharmacy students.

A part of the program that has been an overwhelming success is tours of laboratory and teaching facilities of the host city college of pharmacy.

PARTICIPANT RECRUITMENT

To offer the AAPS Outreach Program to the greatest number of participants, it is important to advertise the program as widely as possible, within budget constraints. Each year the organizers of the AAPS Outreach Program contact local school officials and provide them with information about the program, particularly emphasizing the professional development aspects of faculty involvement. In addition, the National Science Teachers Association is contacted to purchase a list of teachers in the area surrounding the host city. For example, for the 1998 AAPS Outreach Program, four zip codes in the greater San Francisco, CA, area were chosen, which resulted in a set of 792 names. These teachers were sent an announcement which included a brief description of the program, the proposed agenda, and registration information. This announcement was sent shortly after the beginning of the academic school year in September. The mailing was repeated approximately six weeks later. Secondary school faculty who were interested in attending were kept informed of the program, its location, and other pertinent information through e-mail. Faculty were encouraged to discuss the program with their students and to register students who were interested in the program.

Eighty-seven faculty and students registered for the program, sixty-five of whom were present for the program. The faculty consisted of teachers with an emphasis in mathematics, general science, biology, chemistry, genetics, and statistics. They taught students who ranged from fifth to twelfth grade. The student participants were in the tenth to twelfth grade. In addition to individual faculty with their students, there were also science clubs with their faculty advisors. Thus, a great variety of faculty and students participated in the program.

PROGRAM COMPONENTS

When the AAPS Outreach Program began in 1996, participants were treated to short lectures on different pharmaceutical topics intermingled with

hands-on laboratory exercises. The purpose of this format was to give a brief discussion about a topic, such as the synthesis of a drug, and then have the participants go to the laboratory and perform a related experiment. The following year the AAPS Outreach Program was expanded to include additional topics with more time for discussion.

For the most recent AAPS Outreach Program, comments about the event from the participants and organizers over the past two years were reviewed. Based on the information received, the laboratory portion of the program was eliminated and the length of the program was decreased. The reason for the elimination of the laboratory sessions was that, while informative and educational, the laboratory sessions required a lot of time which may have been better spent in discussions with the presenters. Therefore, for the most recent AAPS Outreach Program held in San Francisco, the laboratories were not held and instead there was more time allotted for discussion. This change also decreased the total time for the program from six hours to four hours.

At the beginning of the Outreach Program, participants were given a booklet that had been prepared with notes and excerpts from the individual presentations. In addition, the booklet contained short biographies of the presenters, a list of registrants, and an evaluation form. Thus, the booklet could then serve as an informational source for the participants after the program was completed. Indeed, some faculty participants remained in contact with the presenters for several months to further discuss some of the ideas presented during the program.

The agenda for the 1998 program is given in Table 1. The topics were chosen based on suggestions from previous participants, education committee members, and colleagues. Although the topics were not covered in depth, the presentations do provide enough new information to keep the participants interested without overwhelming them with details.

The Appendix is an excerpt from the AAPS Outreach Program held in San Francisco in November 1998. The content is presented at a simple level to give the secondary school teachers and their students a rudimentary overview of the topic, which, in this case, is pharmacokinetics. The content is not meant to be technically advanced or to provide all possible explanations associated with pharmacokinetic principles. Instead, the program is designed such that the participants can read the material and have a general understanding of the topic prior to the start of the program and interact with the speaker during the presentation. The excerpt is provided here so those who wish to develop a similar program for their college of pharmacy can have an example of a topic and the level of sophistication at which it was presented.

TABLE 1. Agenda for Outreach '98: A Tour of the Pharmaceutical Sciences.

12:00 Noon   Welcome and Introductory Remarks

12:10 PM   Molecule to Market: The Drug Development Process

This lecture will discuss how drugs are discovered and the path that drugs must travel prior to being available in the marketplace. The discussion will also include how the Federal Food and Drug Administration approves new drugs.

Speaker: Seema Handu, Ph.D.

PharmaQuest, Inc.

1:00 PM   Novel Drug Delivery Systems

This lecture will discuss new and advanced methods that are used to administer drugs into the body. Some of these methods include sustained release tablets and skin patches, such as the nicotine patch.

Speaker: Nipun Davar, Ph.D.

Alza Corporation

1:30 PM   Pharmacokinetics: Why Medications Are Taken the Way They Are

This lecture will discuss how pharmacokinetics, which describes how drugs are absorbed and eliminated from the body, is important in determining the way in which medications are used. For example, why certain drugs can be taken only once a day and others have to be taken every four hours.

Speaker: Lane J. Brunner, Ph.D.

The University of Texas at Austin

2:00 PM   Code Blue Pharmacy

This lecture will discuss the role of the pharmacist in emergency medicine situations. While many people understand the role of the pharmacist in the community, the role of the pharmacist in the hospital is less clear. The discussion will focus on the important responsibilities of a pharmacist during a ''Code Blue,'' also known as a cardiac arrest.

Speaker: Steven R. Kayser, Pharm.D.

University of California at San Francisco Medical Center

2:30 PM   Refreshment Break

2:50 PM   Tour of UCSF School of Pharmacy Laboratories

The tour will be conducted by pharmacy graduate students and faculty and will consist of a brief overview of the laboratory's research and possible demonstrations. The UCSF School of Pharmacy is internationally recognized for its excellence in research and training pharmaceutical scientists.

3:50 PM   Concluding Remarks

4:00 PM   Session Ends

PROGRAM EVALUATION

To improve the program and to determine what changes could be made to better address the participants' expectations, an evaluation form was included with the AAPS Outreach booklet (Table 2). Participants were asked to complete this evaluation during the break prior to the laboratory tours. Of the 87 registrants, approximately 65 people participated in the program. Forty-five of these completed the evaluations. The results are included in Table 2. Participants were also asked to provide written comments regarding the strengths of the program and how they would like to see the program improved. Many of the written comments complimented the approach that the speakers used and reported that the depth at which the material was presented was appropriate for the audience. In addition, many of the faculty participants appreciated the use of examples and applications that demonstrated the knowledge that their students were currently learning. Constructive criticism included the need for more breaks, a suggestion to shorten some of the

TABLE 2. Program Evaluation and Corresponding Results.

The program organizers would be grateful if you would please take a few moments of your time to evaluate your experience with the program. Your evaluations and suggestions are a vital part of our continuing effort to make this program the best possible introduction to the pharmaceutical sciences. Please circle the number that best represents your opinion.

	SA[a] (1	2	U 3	4	SD 5)	Mean
1. I believe the program met my expectations.	6/6[b]	4/17	2/7	1/2	0/0	1.8/2.2
2. The program increased my knowledge of the pharmaceutical sciences.	6/23	4/4	2/2	1/3	0/0	1.8/1.5
3. The speakers' approach to presenting the material was informative and easy to follow.	6/5	5/19	2/5	0/3	0/0	1.7/2.2
4. (Students only) The program has helped me to consider a career in the pharmaceutical sciences.	5	14	9	3	0	2.3[c]
5. (Faculty only) The program has increased my interest to introduce the pharmaceutical sciences to my students as a career option.	4	7	0	2	0	2.0
6. I would recommend this program to other students and faculty.	5/7	4/15	3/7	1/2	0/0	2.0/2.1[c]

[a]SA = strongly agree, U = undecided, and SD = strongly disagree
[b]Ratio indicates number of faculty responding/number of students responding.
[c]One student did not respond.

presentations, and a desire for more in-class demonstrations and hands-on activities.

SUMMARY

Colleges of pharmacy are constantly developing new methods to recruit quality students into their programs. Included in these methods are community outreach programs directed at high school and preprofessional college students to show students the critical role pharmacists play in the health care field. Similarly, organizations such as the American Association of Pharmaceutical Scientists are actively seeking to increase the number of talented students in professional and basic science programs with the intent of having these students train for a career in the pharmaceutical sciences. One such program, ''Outreach: A Tour of the Pharmaceutical Sciences,'' helps secondary school teachers and their students understand the possible career choices offered by training in the pharmaceutical sciences and how their current academic lessons can be applied outside of the classroom.

The AAPS Outreach Program has gone through its third iteration. Each year the program is refined and attempts to address the shortcomings of the previous offerings. The program is expanding through the individual college of pharmacy chapters of the AAPS. These graduate student driven chapters have begun developing similar outreach programs for secondary schools in their own cities. Thus, in addition to the annual AAPS Outreach Program, these programs will help local secondary school faculty with their professional development and recruit talented students into the pharmaceutical sciences.

APPENDIX

Pharmacokinetics: Why Medications Are Taken the Way They Are

Objective. The objective of this lecture is to discuss the processes of drug delivery into and distribution throughout the body, using the principles of pharmacokinetics. At the end of the lecture, the participants will have a better understanding of how a drug substance moves in and out of the body and how this may relate to the effectiveness of a drug.

Introduction. *Pharmacokinetics* is a field of study that examines the time course of drug substances through the body. This time course includes how a drug is introduced into the body, where the drug goes once it is in the body, and how a drug is removed from the body. While these concepts are fairly simple to understand on a qualitative basis, the purpose of pharmacokinetics is to quantitate these concepts. Definitions of commonly used terms are given in Table 2.

Pharmacokinetics asks very specific questions which are concerned with how much drug is in the body at a particular point in time. These questions are important, since their answers are the basis for how medications are taken. For example, two nonprescription pain medications, Advil® (ibuprofen) and Aleve® (naproxen), are commonly taken for the relief of mild pain. While both drugs are from the same therapeutic class and have similar effectiveness, Advil® can be safely taken every four hours while Aleve® should not be taken more often than every eight hours. This difference in how often each of the pain medications can be taken is based on pharmacokinetic principles. In essence, the Advil® is removed from the body more rapidly than the Aleve® and thus to continue pain relief, the Advil® should be taken more often. Therefore, the principles of pharmacokinetics are used to determine how often drugs are to be taken so that they remain effective.

Another important use of pharmacokinetic principles is to decrease or eliminate unwanted effects while maintaining the usefulness of the drug. Using the example of Advil® again, a number of studies have shown that an effective dose of Advil® for the relief of mild, short-term pain is 200 mg to 400 mg given every four to six hours. These doses were determined based on how much of the Advil® gets into the body after the tablets are taken by mouth. The principles of pharmacokinetics are used to determine that, following a dose of 200 mg to 400 mg every four to six hours, a safe and effective amount of Advil® in the body is reached. If more than this amount gets into the body, then there is a greater chance of unwanted effects, also called side-effects. If less than this amount gets into the body, then the drug is not effective as a medicine.

Based on pharmacokinetic principles, some drugs are available as both a prescription and nonprescription drug. Anaprox DS® is a prescription coun-

## TABLE 2. Definitions of Some Commonly Used Pharmacokinetic Terms.

Absorption .... the process a drug must undergo in order to get into the bloodstream. A drug can be *absorbed* from the stomach, intestines, or from the muscle.

Apparent Volume
of Distribution ...... a theoretical volume to which the drug appears to distribute in the body. The *apparent volume of distribution* is a reflection of the dose of the drug given and the plasma concentration of the drug.

Clearance .... a more specific definition of elimination and refers to the rate at which a drug is removed form the body. The *clearance* of a drug from the body usually reflects the removal of the drug from the body by a particular organ, such as the liver or kidneys.

Concentration-Time
Profile .... a graphical representation of the time course of a drug in the body. A *concentration-time profile*, also known as a concentration vs. time curve, is used to examine the plasma concentrations of a drug over the time that the drug is in the body.

Disposition .... a description of where a drug goes throughout the body and how the body removes the drug. The *disposition* of a drug is a combination of the absorption, distribution, metabolism, and removal from the body.

Distribution .... the process where a drug disperses throughout the body after it has reached the bloodstream. A drug must *distribute* to the part of the body in which it works.

Elimination .... the process which the body uses to remove the drug. A drug can be *eliminated* from the body by the liver or kidneys.

Metabolism .... the process in which the liver chemically changes a drug to another compound. *Metabolism* by the liver is one of the reasons why the concentration of a drug in the plasma decreases.

Metabolite .... the by-product that occurs when the liver chemically changes a drug. A *metabolite* is often the harmless compound that is made after a drug passes through the liver.

Pharmacokinetic
Model .... a visual representation of the progress of a drug into and out of the body. A *pharmacokinetic model* is used as the initial step in pharmacokinetic analysis.

Pharmacokinetics .. the mathematical description of the processes of drug absorption, distribution, and elimination from the body. *Pharmacokinetics* examines the time course of a drug in the body.

Steady-State ...... a constant plasma concentration of the drug following the drug being administered by a constant rate intravenous infusion. The *steady-state* plasma concentration of a drug occurs when the infusion rate is equal to the body's clearance rate of the drug.

terpart to Aleve[®]. Although both drugs contain the same active ingredient, Anaprox DS[®] tablets have over twice the amount of this active ingredient. Thus, when taking Anaprox DS[®], over twice the amount of the drug will get into the body as compared with Aleve[®]. This larger amount will increase the chance of side-effects and thus is the reason why physician and pharmacist supervision is needed when taking Anaprox DS[®]. This principle is true for all prescription medications. It is not to say that these drugs are extremely dangerous, it is just that the amount of the drug necessary for the effect is greater than that considered safe for self-medication. This is just one example of how pharmacokinetic principles may directly affect the use of drugs.

The Pharmacokinetic Model. The purpose of a *pharmacokinetic model* is to represent the progress of a drug through a biological system, such as the human body. An example of a pharmacokinetic model is given in Figure 1. Integral to the use of pharmacokinetics is the ability to measure drug concentrations and therefore be able to determine the amount of drug in the body at any point in time. Since it is impossible to measure the concentration of drug everywhere in the body, a representative sample has to be taken. For pharmacokinetic analysis, this representative sample usually comes from the plasma. The plasma is the part of the blood that is obtained after the red and white blood cells have been removed. The amount of drug in the plasma is representative of the amount of drug in the entire body. Of course, the underlying assumption is that the amount or concentration of drug measured in the plasma is related to the concentration of drug in the part of the body where the drug works. For our purposes, we will accept that this assumption is valid.

In a pharmacokinetic model, such as in Figure 1, the boxes represent distinct ''compartments'' in which a drug can exist. The ''arrows'' represent the progression of time. In Figure 1, the 'A' compartment represents the drug in a dosage form, such as a capsule or tablet. The drug is ingested and then, in the stomach and intestines, it breaks up and dissolves. Once dissolved, the drug can be taken up into the body. This process is called drug *absorption*. After the drug is absorbed, it *distributes* throughout the body. The 'B' compartment represents the drug in the body. Since it is impractical to sample

FIGURE 1. An example of a pharmacokinetic model of a drug taken as a tablet. After circulating through the body, the drug is removed through the urine.
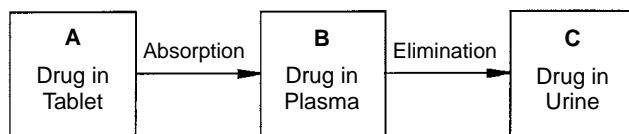
every possible tissue in the body for the presence of a drug, the plasma concentration of the drug is used as being representative of the drug in the body. The 'C' compartment represents drug that has been removed or *eliminated* from the body. This elimination can be from the body chemically breaking down the drug, which is known as drug *metabolism*. Or, the body can eliminate the drug without metabolism through the urine. Either way, the drug is permanently removed from the body.

Drug Concentration in the Body over Time. The pharmacokinetic model in Figure 1 has its origins from observations of how drug concentrations in the plasma decrease over time. After a drug has been ingested, the absorption process begins. This absorption process continues until the drug has been absorbed from the stomach or intestines into the bloodstream. While the drug is being absorbed, the drug that was previously absorbed is also being distributed, and then eliminated. In other words, a single drug molecule will be absorbed, distributed throughout the body, and then be eliminated from the body. These processes happen to each of the individual drug molecules and are independent of the other drug molecules. This principle allows us to construct a time-course of the drug in the body. Obviously we cannot examine each individual molecule in the body, but we are able to examine a representative sample of molecules which will give us an idea of the disposition of the drug.

If we were to take plasma samples over the time that the drug was absorbing, distributing, and being eliminated, then we would be able to create a graphical representation of these processes. This graphic representation is called a *concentration-time profile*, or *concentration vs. time curve*. An example of such a curve is given in Figure 2. The graph in Figure 2 shows that as the drug is being absorbed, the plasma concentration is increasing. The drug concentration then reaches a peak which indicates that most, if not all, of the drug has been absorbed. Then, the drug concentration in the plasma decreases indicating that the drug is being eliminated. We can use this information to estimate the rates of absorption and elimination so that we can predict how much of the drug will be in the body at a particular point in time. Rate estimation is a common type of analysis in pharmacokinetic studies.

Apparent Volume of Distribution. To make the pharmacokinetic model in Figure 1 and the concentration vs. time curve in Figure 2 appear to be more like the body, we must incorporate some additional concepts. The first concept is that of distribution, which we briefly discussed earlier. Distribution refers to the process where after a drug is absorbed and circulates through the body, it will disperse to different parts of the body. This is important since the drug usually needs to distribute out of the plasma and into the body tissues in order to be an effective medication. The degree as to which a drug disperses in the body is determined by estimating the *apparent volume of distribution*.

FIGURE 2. An example of a concentration vs. time curve for a drug in the body. The curve shows how the processes of absorption and elimination are dependent on the time after a drug has been taken.
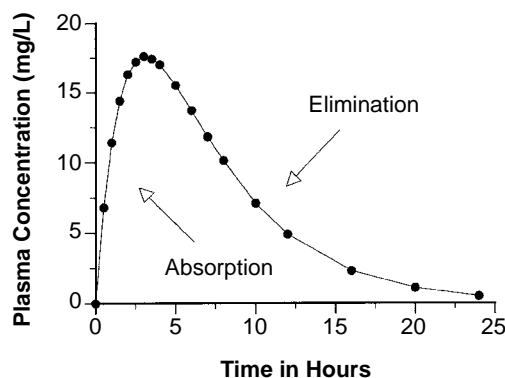

This is a volume that the drug would theoretically disperse into, provided the entire body was large enough, and each part of the body was composed of the same type of fluid material. It is important to understand that the apparent volume of distribution does not represent any real volume in the body, but is simply a theoretical estimate of how much the drug distributes throughout the body. For example, Garamycin® (gentamicin) and Fungizone® (amphotericin B) are drugs used to treat serious infections in hospitalized patients. Garamycin® does not distribute throughout the body very well, whereas Fungizone® is extensively distributed throughout the body. The differences in the apparent volume of distribution for Garamycin® and Fungizone® are dependent on their differences in chemical structure and how each drug interacts with tissues in the body.

The apparent volume of distribution is one of the most important pharmacokinetic parameters. This volume is used when we need to estimate how much drug to give so that we can reach an effective drug concentration in the plasma. In pharmacokinetics, the definition of the apparent volume of distribution is that it is a proportionality constant that relates the dose of the drug administered and the concentration of the drug in the plasma. In other words, the greater the apparent volume of distribution for a given dose, the lower the concentration of drug in the plasma. This point is illustrated in Figure 3.

The illustration in Figure 3 shows that if the same amount of a charcoal powder was dispersed into two different containers of water, one with a larger volume than the other, that the resulting "concentration" of charcoal in the larger volume container would be less than the smaller container. In other words, there is more charcoal per unit volume in the smaller container. Thus,

FIGURE 3. An illustration of the concept of volume of distribution. An equal amount of charcoal is added to containers of different volumes of water. After the charcoal in water is well mixed, a sample is taken from each of the containers. The darker the shade of gray, the greater the concentration of charcoal in the container.
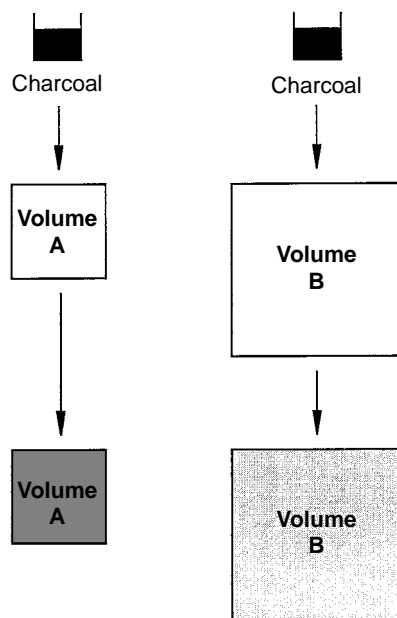
if one takes a sample of the charcoal in water mixture from each container, the sample from the smaller container will have a higher concentration. Therefore, if we knew the amount of charcoal that was placed into the container and we could measure the concentration of the charcoal in water mixture, then we would be able to calculate the volume of that container. For example, suppose we added 100 mg of charcoal to the container and found that the resulting concentration of the charcoal in water solution was 2 mg/mL. An amount divided by a concentration is a volume (i.e., mg ÷ mg/mL = mL). Thus, 100 mg of charcoal divided by a concentration of 2 mg/mL would give a volume of 50 mL. While it is easy to directly measure the volume of a solution in a laboratory container, it is nearly impossible to directly measure the volume of fluids in the body. This is why for drug therapy, we estimate the apparent volume of distribution using pharmacokinetic principles.

Another important use of the apparent volume of distribution is to estimate

the total amount of drug in the body. Analogous to our discussion above regarding the dose of drug, we can estimate the amount of a drug in the body at a particular time provided we know the apparent volume of distribution and the plasma concentration. This relationship is described by the equation:

$$X = Vd \cdot C_p$$

where X represents the amount of the drug in the body, Vd is the apparent volume of distribution, and C_P is the concentration of drug in the plasma. This pharmacokinetic equation is often used when it is necessary to know the total amount of drug in the body.

Clearance Concepts. Previously in our discussion we introduced the idea of drug elimination. Now we can provide a more complete explanation of the elimination process. Essentially, when a drug molecule passes through the body it will come in contact with numerous tissues and organs. Two of these organs, the kidney and liver, are primarily responsible for removing the drug from the body. This is the process of *detoxification*. The kidney removes the drug by filtering the drug into the urine. This process is passive and usually does not involve any chemical change to the drug molecules. The liver takes a more active role in drug elimination. As mentioned earlier, drug metabolism is the process where the body chemically changes the drug to another compound, or by-product, known as a *metabolite*. The liver is the organ in the body in which most of the metabolism occurs.

Both of the processes of filtering by the kidney and metabolism by the liver are part of the concept of *clearance*. A schematic representation of clearance by the liver is given in Figure 4. Drug molecules in the blood enter the liver and flow through in one direction. As the drug molecules pass through the liver, enzymes located in the liver tissue chemically change the drug molecule to metabolites. Thus, if we were to measure the concentration of drug in the plasma immediately before the liver and immediately after the liver, then the difference would be the clearance of the drug by the liver. The clearance by the liver is different for each drug. As you might guess, drugs

FIGURE 4. A schematic representation of metabolism of drug molecules as they pass through the liver. This process is termed clearance.
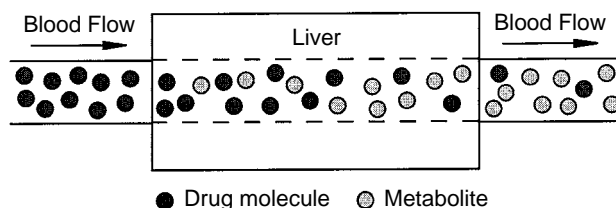
that are cleared by the liver more rapidly tend to have their plasma concentrations decrease more rapidly. Thus, in order to remain effective as medications, the drugs would have to be given more often. For instance, let us return to the Advil® and Aleve® example. As we discussed earlier, Advil® is usually taken every four hours and Aleve® is usually taken every eight hours. These differences are due to the difference rates of clearance for each drug. Advil® is cleared more rapidly than Aleve® and therefore needs to be taken more often than Aleve® in order to have the same plasma concentrations. Thus, we now can use a pharmacokinetic explanation to account for the different ways in which these two similar medications are to be taken safely.

Steady-State Conditions. When people are treated medically in the hospital, they are often administered drugs directly into the bloodstream. This is known as intravenous administration. Many drugs are very potent and will cause unwanted side-effects if they are given as an immediate injection into the bloodstream. Therefore, drugs are often given by a slow infusion into the bloodstream over a long period of time. This type of administration is known as an intravenous infusion. Since the rate of the intravenous infusion can vary, so can the amount of the drug that is administered to the patient. If the rate of the infusion remains constant while the drug is being given, we can easily calculate the total amount of the drug that the patient received. For example, Xylocaine® (lidocaine) is a heart medication that is given by intravenous infusion to seriously ill patients in the hospital. A common dose of Xylocaine® is 1 g dissolved in a 1000 mL sugar solution, which would give a concentration of Xylocaine® in the solution of 1 mg/mL. This solution is then infused at a particular rate. Suppose that the Xylocaine® was infused at a rate of 2 mL per minute and the infusion was stopped after 60 minutes. We can calculate that the patient received 120 mg of Xylocaine® by knowing that the total volume of the Xylocaine® infused was 120 mL, the infusion was given over 60 minutes, and that the concentration of the Xylocaine® solution was 1 mg/mL.

Sometimes patients are given intravenous infusions over a very long period of time, such as many days or even weeks. For these patients, in addition to how much drug they have received, we are also interested in the concentration of drug in the body. When a drug is administered by intravenous infusion for a long period of time, a constant amount of drug is maintained in the plasma. This is termed the *steady-state* concentration. This is a very important concept concerning the administration of drugs for patients in the hospital. Previously, we discussed that the amount or concentration of drug in the plasma needs to be at a certain level in order for the drug to be effective. To achieve this plasma concentration for a long period of time, people need to keep retaking oral medications. Such is the case for Advil® and Aleve®. In the hospital, patients who need to maintain a constant plasma drug concentration are often administered drugs by an intravenous infusion, delivered at a constant rate, for however long it is necessary.

If one were to measure the drug concentration in the plasma following the start of an intravenous infusion, then there would be an initial increase, followed by a plateau of the concentration of drug in the plasma. This plateau is called the steady-state plasma concentration (Figure 5). Just as in the case of oral administration, there is an initial increase in plasma drug concentrations. However, in the case of intravenous administration, the initial increase is not due to absorption, but rather distribution into the body. Absorption is not a factor, since the drug is being administered directly into the bloodstream. But, the drug still must follow the other principles discussed earlier, such as distribution and elimination. As soon as the drug enters the bloodstream, it undergoes both distribution and elimination. The process that determines the steady-state plasma concentration is how rapidly the drug is eliminated, or cleared, from the body. The steady-state plasma concentration is reached when the rate of drug infusion equals the rate of drug elimination. In other words, when the rate of drug elimination from the body equals the rate at which the drug is being infused into the body, a constant plasma drug concentration is reached. Hence the term, steady-state.

It is important to understand that if either the infusion rate or clearance rate changes, then a new steady-state would be reached. This change in steady-state plasma concentration is proportional to the change in infusion or clearance rates. For example, suppose that a drug is infUsed at a certain rate and then that rate is doubled. Provided there is no change in the body's clearance rate, then the new steady-state plasma concentration would be twice the previous concentration. This relationship can be seen by the equation:

$$C_{P,SS} = \frac{K_0}{Cl}$$

FIGURE 5. An example of an intravenous infusion and the resulting plasma concentrations.
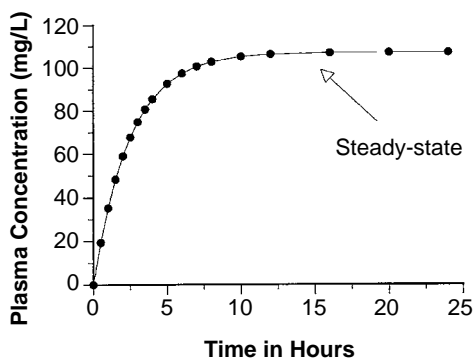
where $C_{P,SS}$ is the steady-state plasma drug concentration, K_o is the intravenous infusion rate, and Cl is the clearance rate. This pharmacokinetic equation is routinely used to estimate the clearance rate of drugs in patients who are in the hospital.

Summary. We have discussed some of the fundamental concepts of pharmacokinetics and how these concepts help explain the usefulness of medications. Although there are many subtleties in pharmacokinetics that were not discussed, we were able to examine many of the fundamental principles. We have examined the reasoning behind why some drugs are taken more often than others. We have also used a pharmacokinetic model to discuss how a drug is absorbed into the body, distributed throughout the body, and then eliminated from the body. We next discussed how to graphically represent drug concentration in the plasma over time and how this graph is used to describe the processes of absorption and elimination. And finally, we introduced three fundamental concepts of pharmacokinetics: apparent volume of distribution, clearance, and steady-state. In all, we have discussed most of the principles of pharmacokinetics without having to delve into the mathematical theory surrounding the topic.