Introduction

Choosing the best antimicrobial agent for a particular patient or infection can be a complicated process. Ideally, the best drug can be determined by comparing the properties of individual agents with each other. A favorable clinical profile (i.e., excellent efficacy, few adverse effects) is clearly the most important variable used for selection. However, this can be difficult when newer agents are being compared with older, established ones. Newer agents can show equivalent or superior clinical efficacy, yet their safety might not be established until they have been on the market for a couple of years or more.

In one study, half of all warnings by the U.S. Food and Drug Administration (FDA) were issued within seven years of a drug’s introduction to the market, and half of the drug withdrawals from the market occurred within two years of their introduction.1 The true efficacy and safety of a drug can be established only with extensive use.

It is difficult to choose an antibiotic from a group of two or more comparators because each drug within a class is likely to possess some favorable features. Few trials have directly compared the clinical efficacy of two drugs within a class, and studies that do so are usually underpowered and designed only to show equivalence. Generally, other drug characteristics must be used as means of comparison, for example:

- the agent’s clinical efficacy in FDA-approved and unapproved indications

PK/PD measures are drug characteristics that may be used to identify the best therapeutic agent for a particular indication. This article reviews the PK and the PD features of antibiotics that can be used to compare agents within a particular drug class.

Although clinical efficacy and safety remain the gold standards for comparing antibiotics, PK and PD measures have been employed with increasing frequency. Some PK and PD measures are more predictive of clinical efficacy than others. Throughout this article, the fluoroquinolones are used to illustrate the similarities and differences that can exist among agents within a single drug class.

Pharmacodynamic Measures

A PD measure characterizes the relationship between concentration and effect.2-5 For antibiotics, the most commonly measured effect is the inhibition of microbial growth. Bacterial killing (i.e., a 99.9% reduction of the initial number) can also be assessed; however, labor-intensive studies are necessary for this measure, in which numbers of bacteria are counted over time. As a result, this measure is rarely used. The most common concentration-related measure of antimicrobial effect is the minimum inhibitory concentration (MIC). For a given pathogen–antibiotic pairing, the MIC represents the minimum antimicrobial concentration that inhibits bacterial growth. The MIC is used extensively in the clinical laboratory to determine which antibiotics can be used to treat an infection that is caused by a specific pathogen that has been isolated.

Each MIC obtained in a clinical setting must be compared with a standard reference value, or breakpoint, for interpretation. Each antibiotic is assigned a breakpoint concentration value, which reflects, in part, the concentration of the antibiotic that can be achieved at the site of infection. Typically, organi-
zations such as the FDA and the National Committee on Clinical Laboratory Standards (NCCLS) determine and publish the breakpoint values for all antimicrobial agents.6 To be effective, an antibiotic should achieve concentrations at the site of infection in excess of the MIC. Thus, a pathogen is considered susceptible when the MIC is less than the breakpoint concentration and resistant when the MIC exceeds the breakpoint.

MIC50 and MIC90

Although individual MIC values can help to guide therapy in a specific patient, they are not useful in selecting an agent for the empirical treatment of infections caused by a specific bacterial species. Instead, decision-makers need a measure that reflects the drug’s activity against all isolates of a given pathogen. MIC50 and MIC90 values are generated by testing the susceptibility of multiple isolates of a particular pathogen against a drug.

As an example, we can suppose that the MICs of 60 isolates of Escherichia coli are determined for an agent. The MIC50 is an average (or median) estimate of activity; it is defined as the minimum concentration required to inhibit growth of half of the isolates (30 of 60 in this case). The MIC90 is a more conservative estimate, because it reflects the concentration required to inhibit the growth of 90% of the isolates (in this example, 54 of 60 isolates). MIC90 values are more commonly used because this value is more likely to reveal the presence of drug-resistant isolates in the population.

Although MIC90 (and MIC50) values are frequently used to compare antimicrobials directly, they have limitations. First, differences in MIC90 values between two drugs do not account for differences in concentrations achieved in vivo. A smaller MIC does not necessarily translate into a more active drug if the concentrations of that drug achieved in the body are also smaller. Such differences can be normalized in part by comparing the MIC90 with the aforementioned breakpoint value, which offers a crude estimate of drug concentrations in the body.

For a given pathogen, if the ratio of a drug’s MIC50 to breakpoint is 1 or less, at least 90% of the isolates will be susceptible; if the ratio is greater than 1, fewer than 90% of the isolates will be susceptible. For example, if the MIC90 of ciprofloxacin (Cipro®, Bayer) against 100 strains of Pseudomonas aeruginosa is 4 mcg/ml and the susceptibility breakpoint is 1 mcg/ml, we can conclude that fewer than 90% of those isolates are susceptible to ciprofloxacin.

Because the MIC90 is strictly drawn at the 90% level, it may exaggerate small differences or minimize large differences between agents. Therefore, if 89 of 100 isolates are susceptible to drug A and 91 of 100 isolates are susceptible to drug B, drug B will appear superior because its MIC90 will be less than the breakpoint, whereas the MIC90 will be greater than the breakpoint for drug A.

In another example, if 60 of 100 isolates are susceptible to drug A and 89 of 100 are susceptible to drug B, neither drug will appear highly active, based on the MIC90 or the ratio of MIC90 to breakpoint, although 29 more isolates are susceptible to drug B than to drug A.

Additional Measures

More recently, analyses of in vitro susceptibility studies have shifted away from point determinations (such as MIC50 or MIC90) and toward the use of methods that predict probability of activity with population models. The Monte Carlo simulation involves the creation of a large “population” of individuals or scenarios based on a statistical analysis of a smaller set of subjects.7–9

For example, susceptibility findings of a finite number (e.g., 50) of isolates against a given antibiotic can be analyzed via a gaussian distribution (mean and standard distribution). These variables can be used to generate a large hypothetical population of pathogens with different MICs. Curves can then be created showing the probability of observing a given MIC or the probability of observing a MIC that is less than or equal to the breakpoint concentration (Figure 1). Drug A consistently demonstrates lower MICs than drug B, but because the breakpoint for drug A (0.5 mcg/ml) is lower than for drug B (1.0 mcg/ml), the two drugs do not differ greatly in their net activity.

Pharmacokinetic Measures

Pharmacokinetics (PK) is the study of drug disposition in the

Figure 1  Relationship of drug potency to breakpoint. Each plot shows the cumulative probability of a bacterium exhibiting a given minimum inhibitory concentration (MIC) for drug A (dashed line) or drug B (solid line). Although drug A exhibits higher in vitro potency against the bacteria (illustrated by the lower MIC values), there is little difference in susceptibility at the breakpoint values.

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Steven C. Ebert, PharmD, BCPS
PK studies usually measure the time course of drug concentrations in the body or (especially with antibiotics) the delivery of a drug to extravascular sites where infection sometimes takes place. PK measures include the (1) minimum and maximum serum concentrations, (2) the elimination half-life, and (3) the area under the serum concentration-time curve.

**Standard Measures**

Traditional PK studies examine the time course of drug concentration in serum.\(^5\) Although drug concentrations should be measured at the site of infection, this can be difficult in practice for some sites. Therefore, serum concentrations are typically used because the drugs are distributed to tissues and tissue fluids through the bloodstream. Concentrations at the infection site should be considered if large differences in the PK properties exist between the blood and the infection site.

Typically, to measure the pharmacokinetics of a drug in a person, the clinician takes several samples (usually, six to 10) after the first dose or after multiple doses (for steady-state measurements) to determine the drug concentration over time as well as the rate of drug removal. Three primary PK measures are determined (Figure 2):

- the peak, or maximum, concentration (\(C_{\text{max}}\))
- the half-life (\(T_{1/2}\)), which is inversely proportional to the rate of elimination
- the area under the concentration–time curve (AUC), which is the product of serum concentration values and time

As a rule, population PK studies determine and report PK measures (\(C_{\text{max}}, \text{AUC}, T_{1/2}\)) for a given population. As a result, it is difficult to estimate the likelihood of a drug achieving a given target PK value in that population. Again, investigators have begun to incorporate Monte Carlo analysis into PK studies of populations. Drug clearance and volume of distribution measures can be varied independently to create a hypothetical population of patients with individual PK profiles. Population PK modeling can be extrapolated from published PK parameters to a population pool numbering in the thousands.

Figure 3 demonstrates how the pharmacokinetics of two drugs can be compared through Monte Carlo simulation. The probability of achieving a given magnitude of PK measure (in this case, AUC) can be estimated with this analysis. Population modeling allows comparisons between drugs in the probability of achieving a PK parameter over a large population pool.

Comparisons of \(C_{\text{max}}\) and AUC by themselves are not particularly useful for evaluating two or more antibiotics because they do not relate the serum level of the drug with the drug’s in vitro potency against a particular pathogen. In other words, drug A might achieve higher concentrations in the serum, but drug B might have higher potency against a particular pathogen. Therefore, we cannot determine which drug will be more effective in eradicating an infection if only the PK values are known.

The value for \(T_{1/2}\) does provide useful information for comparison of drugs. Drugs with a longer half-life remain in the serum longer and therefore may be given less frequently. Ciprofloxacin, for instance, has a half-life of 3.5 hours and must be administered twice daily, whereas levofloxacin (Levaquin\(^\text{®}\), Ortho-McNeil) has a longer half-life (6.9 hours) and is administered only once a day. Drugs that need to be given less frequently have some advantages, including convenience of dosing administration for inpatients, especially with the intravenous route, and greater treatment compliance by outpatients.\(^10\)

**Protein Binding**

Although most drugs are reversibly bound to serum proteins such as albumin and alpha\(_1\)-acid glycoprotein, they vary considerably in the extent of their binding. Only 10% to 30% of the total serum concentration of the aminoglycoside gentamicin (Garamycin\(^\text{®}\), Schering) is bound to serum proteins, compared with 90% to 95% for the carbapenem ertapenem (Invanz\(^\text{®}\), Merck).\(^11-13\) Serum protein binding is considered an important means of comparing antibiotics, for three reasons:

- Only the unbound drug is thought to exert an antibiotic effect.
- Only the unbound drug is thought to diffuse into extravascular sites.
- Protein binding may slow the rate of drug elimination, increasing the half-life and thereby allowing a longer dosing interval.

![Important Pharmacokinetic Measures](image-url)
Clinicians who compare the serum PK profiles of two drugs may correct for protein binding and may calculate the unbound drug concentrations. For example, gatifloxacin (Tequin®, Bristol-Myers Squibb) yields a C_{max} of 3.9 mcg/ml and is 20% bound to serum proteins, which results in an unbound C_{max} of 3.1 mcg/ml (Table 1).

Moxifloxacin (Avelox®, Bayer) achieves a C_{max} of 3.3 mcg/ml, but nearly 50% of the drug is protein-bound, which results in an unbound C_{max} of 1.65 mcg/ml. Therefore, although the original C_{max} of the two drugs is nearly equivalent, a large difference exists when only the unbound drug concentration is considered. If a dose of moxifloxacin results in a serum AUC of 34 mcg x hour/ml, the unbound AUC will be approximately 17 mcg x hour/ml. In fact, the true impact of protein binding is probably less than theory would suggest. Numerous studies of antibiotic activity in serum have shown that protein binding does not begin to reduce antibiotic activity until it exceeds 80%. Therefore, a drug with serum protein binding of 60% is probably no worse than one that is 20% bound. Corrections for protein binding probably need to be done only for highly bound (more than 80%) drugs. However, as noted in the previous example, corrections for protein binding across the board are commonly performed to level the playing field when two or more drugs are being compared. More research is clearly needed to support this practice.

Bioavailability

A drug’s oral bioavailability can play an important role in determining proper dosing. Some drugs are not as readily absorbed through the gastrointestinal system as other drugs, or a proportion of the drug can become inactivated before it is absorbed. This can result in a significant decrease in drug exposure for a given dose and must be considered particularly when patients are in transition while switching from IV to oral therapy with the same drug. The dosages of drugs that have significantly decreased bioavailability must be adjusted to facilitate the transition switch. For the currently available fluoroquinolones, ciprofloxacin must be administered at a dose that is 25% higher during the IV-to-oral switch because only 70% of the drug is bioavailable (Table 1).

In addition, drugs that are not totally absorbed may pass through unchanged in the intestinal tract. This event can have unintended significant consequences on the normal gut flora, especially if the drug is active against anaerobes, such as Bacteroides fragilis. In some studies, agents with anaerobic activity resulted in increased colonization of vancomycin-resistant enterococci and in a higher incidence of diarrhea caused by Clostridium difficile. Moxifloxacin and gatifloxacin have higher activity against anaerobes, whereas ciprofloxacin and levofloxacin have less activity. Approximately 25% of moxifloxacin and 20% to 35% of ciprofloxacin are excreted unchanged in the feces; in contrast, approximately 5% or less of gatifloxacin and levofloxacin are eliminated in this way.

Extravascular Fluid Concentrations

Because most infections originate in extravascular sites rather than in the bloodstream, antibiotics must be able to...
penetrate into these sites. Accordingly, numerous studies have been performed to quantify the extravascular delivery of antibiotics. Sites for extravascular delivery may be broadly classified into four categories:

- extracellular sites reached via diffusion from the blood
- intracellular fluid
- extracellular sites with restrictive barriers
- urine

The clinical and physiological significance of antibiotic delivery to some of these extravascular sites is relatively straightforward. Hydrophilic and polar drugs are excreted into the urine, which is necessary for the effective treatment of urinary tract infections (UTIs). The minimum fractional excretion into the urine of the drug dose necessary to treat UTIs has not been established. For example, ciprofloxacin is commonly used to treat UTIs, even though only 30% of a dose is excreted into the urine (Table 1).14 Only 20% of a dose of moxifloxacin is excreted unchanged into the urine, and the drug is not indicated for UTIs. Levofloxacin and gatifloxacin, however, are excreted primarily into the urine and are minimally metabolized.

Concentrations of antibiotics in extracellular sites reached via diffusion (muscle, peritoneal fluid, and other soft tissues) can be approximated by the concentrations in plasma, although the rate of equilibration is sometimes slow. The most important data concerning extravascular drug delivery involve penetration to extracellular sites with restrictive barriers and intracellular fluid. Drug delivery into these sites is not predictable according to serum pharmacokinetics. Notable sites with restrictive barriers include cerebrospinal fluid (CSF), ocular fluid, and lung epithelial lining fluid. Differences in the extent of delivery for antibiotics within a particular class have occurred.

For example, a 500-mg oral dose of ciprofloxacin results in a $C_{max}$ of 1.9 mcg/ml in the lung epithelial lining fluid, whereas a 500-mg oral dose of levofloxacin attains a $C_{max}$ of 9.9 mcg/ml.21 Intracellular delivery of antibiotics (e.g., penetration into the alveolar macrophages) is necessary in order to treat atypical pathogens such as Chlamydia and Legionella species. Again, marked variability between drugs within an antibiotic class may be observed (e.g., maximal concentrations of 34.9 mcg/ml for ciprofloxacin vs. 97.9 mcg/ml for levofloxacin in the alveolar macrophages).21

In summary, PK comparisons between antibiotics should include the extent and magnitude of their delivery into less accessible areas, such as CSF, lung epithelial lining fluid, intracellular fluid, and urine. The extent of delivery into other sites is less important, but it might be of benefit when the antibiotic is being considered in the case of an indication for which clinical data are limited. For example, if PK studies show excellent delivery of an antibiotic into the sinus fluid, that agent may be effective in treating acute bacterial sinusitis if it has adequate activity against common sinusitis pathogens.

### Pharmacokinetic/Pharmacodynamic Measures

PK/PD measures can provide additional information from the individual PK and PD values because they simultaneously account for the time course of antimicrobial concentrations in the body and the drug’s intrinsic activity against a particular bacterium.5,22 This allows direct comparisons between drugs with different PK profiles and different activity against pathogens in vitro.

Figure 4 illustrates the most common PK/PD measures of antimicrobial activity, including the ratio of peak concentration to MIC ($C_{max}$/MIC), the duration of time the serum concentration exceeds the MIC ($T > MIC$), and the ratio of the area under the curve to MIC (AUC:MIC).

Determining which PK/PD measure is most applicable for any given antimicrobial class has been studied via animal and in vitro models of infection. The most applicable measure for each class is consistent with the pharmacological properties of that antibiotic class, namely, the relationship between the magnitude of concentration and bactericidal rate and the presence or absence of persistent antimicrobial effects (post-antibiotic effect) after the drug has been removed from the environment.

Table 2 lists pertinent PK/PD measures for various antibiotic classes. For drugs that demonstrate a linear relationship between concentration and bactericidal rate (e.g., aminoglycosides and fluoroquinolones) or for those that exhibit...
For drugs that demonstrate saturable, concentration-independent bactericidal rates and little to no persistent effect (e.g., beta-lactams and macrolides), the amount of time above the MIC is most predictive of efficacy.22

Knowing the appropriate PK/PD measure for antibiotics allows direct comparisons between agents. However, as with MIC data, we must know the magnitude of the variable required for efficacy (i.e., a PK/PD breakpoint). Studies in humans have begun to delineate the threshold values required to achieve efficacy (Table 3).22–25 For beta-lactams, maintaining serum concentrations in excess of the MIC for at least 50% of the dosing interval has been linked to efficacy in otitis media and sinusitis.25 For concentration-dependent antibiotics, such as the fluoroquinolones, the 24-hour AUC:MIC ratio should exceed 100 to 125 to maximize the chance of eradicating gram-negative bacteria in respiratory infections, particularly *P. aeruginosa*.24 For *Streptococcus pneumoniae* treatment of pneumococcal pneumonia, the 24-hour AUC:MIC ratio should exceed 30 to 40 to maximize the probability of a successful outcome.23

Achieving the recommended PK/PD targets not only ensures the likelihood of clinical success but also increases the chance of bacterial eradication and limits the emergence of resistance. Table 4 shows AUC:MIC ratios for various fluoroquinolones against various bacterial pathogens.14

It is tempting to assume that concentration-dependent drugs that achieve higher AUC:MIC ratios are more clinically effective than drugs that just surpass the PK/PD target. However, evidence with the fluoroquinolones suggests that the use of doses that approximate the PK/PD breakpoint achieve bacterial killing effects similar to doses that far exceed the breakpoint.23,26,27

One study used an *in vitro* PD model to test killing by moxifloxacin, sparfloxacin (Zagam®, Bertek), and levofloxacin of 10 strains of *S. pneumoniae* with varying susceptibilities.26 The AUC:MIC ratios ranged from 108 to 900 for moxifloxacin, 16 to 128 for levofloxacin, and 20 to 160 for sparfloxacin. There was little difference between regimens in the level of killing after 36 hours. A separate *in vitro* PD study of these drugs also showed no differences in the overall selection of resistant isolates of *S. pneumoniae*.27

Using clinical data with levofloxacin and gatifloxacin for patients with community-acquired pneumonia, Ambrose et al. found that microbiological cures achieved 100% once the AUC:MIC ratio exceeded 33.7.23 Thus, reaching the PK/PD target may be sufficient for achieving maximal efficacy and eradicating pathogens.

As noted previously, Monte Carlo simulation is emerging as a practical tool that accounts for individual variability and increases the probability of achieving a given endpoint rather than an all-or-none estimate. If the variation in the PK disposition of a drug is co-modeled with the variation of *in vitro* activity, we can estimate the likelihood of achieving a target PK/PD measure for various drugs. Furthermore, by combin-

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**Table 2** Pertinent Pharmacokinetic and Pharmacodynamic (PK/PD) Measures for Various Antibiotics or Antibiotic Classes

<table>
<thead>
<tr>
<th>Drug/Drug Class</th>
<th>Bactericidal Activity/Duration of Persistent Effects</th>
<th>Pertinent PK/PD Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminoglycosides</td>
<td>Concentration-dependent/prolonged</td>
<td>AUC:MIC (C&lt;sub&gt;max&lt;/sub&gt;:MIC)</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>Concentration-dependent/moderate</td>
<td>AUC:MIC</td>
</tr>
<tr>
<td>Beta-lactams</td>
<td>Concentration-independent/minimal</td>
<td>Time &gt; MIC</td>
</tr>
<tr>
<td>Macrolides</td>
<td>Concentration-independent/moderate</td>
<td>Time &gt; MIC</td>
</tr>
<tr>
<td>Azalides</td>
<td>Concentration-independent/prolonged</td>
<td>AUC:MIC</td>
</tr>
<tr>
<td>Ketolides</td>
<td>Concentration-independent/moderate</td>
<td>AUC:MIC</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Concentration-independent/prolonged</td>
<td>AUC:MIC (Time &gt; MIC)</td>
</tr>
</tbody>
</table>

AUC = area under the concentration–time curve; C<sub>max</sub> = maximum concentration; MIC = minimum inhibitory concentration.

Data from Ebert SC, Craig WA. *Infect Control Hosp Epidemiol* 1990;11:319–326.2

**Table 3** Magnitude of Pharmacokinetic and Pharmacodynamic (PK/PD) Measures Predictive of Efficacy for Select Antibiotic Classes Versus Some Pathogens

<table>
<thead>
<tr>
<th>Drug/Drug Class</th>
<th>Pertinent PK/PD Variable</th>
<th>Magnitude of Variable Correlated with Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-lactams</td>
<td>Time &gt; MIC</td>
<td>≥40%–50% of dosing interval</td>
</tr>
<tr>
<td>Fluoroquinolones vs. gram-negative bacteria</td>
<td>24-hour AUC:MIC</td>
<td>≥90–125</td>
</tr>
<tr>
<td>Fluoroquinolones vs. <em>Streptococcus pneumonia</em></td>
<td>24-hour AUC:MIC</td>
<td>≥30–40</td>
</tr>
</tbody>
</table>

AUC = area under the concentration–time curve; MIC = minimum inhibitory concentration.

being the likelihood of achieving a target PK/PD with that of success for a particular PK/PD measure, we may be able to compare the probability of success for two drugs.

**Conclusion**

PK/PD measures of antibiotics are being used increasingly as a surrogate means of comparing the *in vivo* activity of antimicrobial agents. However, when antibiotics are being compared, PK/PD measures should be used only as an addition to important considerations such as clinical efficacy and safety, drug interactions, costs, dosing convenience, and the breadth of possible indications. Models that project estimates of clinical outcomes (efficacy, emergence of resistance, or both), based on clinical and experimental data, can also assist clinicians and P&T committee members as they try to select the most appropriate antimicrobial agents to use in the clinical setting.

**References**


**Disclosure**

Dr. Ebert has disclosed that he received an honorarium from DesignWrite in Princeton, New Jersey, relating to this article and that he also serves as a consultant for Ortho-McNeil.
Continuing Education for Physicians and Pharmacists

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Expiration Date: April 30, 2005

TOPIC: Application of Pharmacokinetics and Pharmacodynamics to Antibiotic Selection

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Multiple Choice
Select the one correct answer.

1. Which term characterizes the relationship between the concentration and effect of a drug on the body?
   a. pharmacokinetics
   b. pharmacodynamics
   c. half-life
   d. bioavailability

2. An antibiotic is considered effective when:
   a. its concentration at the site of infection is less than the minimum inhibitory concentration (MIC).
   b. it causes no side effects.
   c. its concentration at the site of infection is greater than the MIC.
   d. the MIC exceeds its breakpoint value.

3. Which pharmacokinetics measurement would be more useful in comparing two drugs?
   a. Cmax
   b. MIC50
   c. T1/2
   d. AUC

4. Serum protein binding is considered an important means of comparing antibiotics for the following reasons except:
   a. Only the bound drug is thought to exert an antibiotic effect.
   b. Only the unbound drug is thought to diffuse into extravascular sites.
   c. Protein binding may slow the rate of drug elimination, thereby allowing a longer dosing interval.
   d. Only the unbound drug is thought to exert the antibiotic effect.

5. The following statements regarding pharmacokinetics are true except:
   a. Considerations of infection site concentrations should be done if large differences exist in the PK properties between blood and infection site.
   b. Population modeling can allow comparisons between drugs in terms of the probability of achieving a PK parameter over a large population pool.
   c. Comparisons of effectiveness between two drugs can be determined by using PK values alone.
   d. Most drugs are reversibly bound to serum proteins and vary considerably in the extent of their binding.

6. Which statement is false with regard to the oral bioavailability of antibiotics?
   a. Some drugs are not as readily absorbed through the gastrointestinal tract.
   b. A portion of the drug may be inactivated as a result of absorption.
   c. Making a transition from the intravenous to the oral route does not need to account for bioavailability changes.
   d. None of the above.

7. Incomplete absorption of antibiotics from the intestinal tract may result in:
   a. a higher incidence of diarrhea caused by Clostridium difficile.
   b. increased colonization of vancomycin-resistant enterococci.
   c. unintended consequences on the normal gut flora.
   d. all of the above.

8. With regard to the treatment of urinary tract infections (UTIs) with antibiotics, which statement is true?
   a. Nonpolar or hydrophobic drugs are excreted into the urine, which is necessary to treat UTIs.
   b. Minimal fractional excretion into the urine to treat UTIs has been established at 30%.
   c. Fluoroquinolones are not indicated for the treatment of UTIs.
   d. None of the above.

9. Which of the following statements is true?
   a. Drug delivery into sites with restrictive barriers does not affect the antibiotic serum concentration.
   b. The antibiotic concentration in extracellular fluid cannot be approximated by plasma concentration.
   c. The extent of drug delivery does not differ according to drug class.
   d. Penetration into extracellular sites is the most important factor influencing extravascular drug delivery.

10. According to Table 4, which of the following statement is incorrect?
    a. AUC:MIC is a pertinent pharmacokinetic/pharmacodynamic (PK/PD) measure for aminoglycosides, fluoroquinolones, and macrolides.
    b. AUC:MIC is a pertinent PK/PD measure for aminoglycosides and fluoroquinolones but not for macrolides.
    c. Time > MIC is an adequate PK/PD measure for macrolides and beta-lactams.
    d. AUC:MIC is an appropriate PK/PD measure for azalides and ketolides.
CE Registration and Evaluation Form

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Title: Application of Pharmacokinetics and Pharmacodynamics to Antibiotic Selection
Authors: Steven C. Ebert, PharmD, BCPS
Submission deadline: April 30, 2005
ACPE Program #079-999-04-016-H01

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Please fill in the box next to the letter corresponding to the correct answer

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3. a  b  c  d
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9. a  b  c  d
10. a  b  c  d

Evaluation

Rate the extent to which: 

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<tr>
<th>Very High</th>
<th>High</th>
<th>Moderate</th>
<th>Low</th>
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1. Objectives of this activity were met
2. You were satisfied with the overall quality of this activity
3. Content was relevant to your practice needs
4. Participation in this activity changed your
   knowledge/attitudes
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   of participation in this activity
6. This activity presented scientifically rigorous,
   unbiased, and balanced information
7. Individual presentations were free of commercial bias
8. Adequate time was available for Q&A
9. Which ONE of the following best describes the impact of this activity on your performance:
   [ ] This program will not change my behavior because my current practice is consistent with what was taught.
   [ ] This activity will not change my behavior because I do not agree with the information presented.
   [ ] I need more information before I can change my practice behavior.
   [ ] I will immediately implement the information into my practice.
10. Will you take any of the following actions as a result of participating in this educational activity (check all that apply)
    [ ] Discuss new information with other professionals
    [ ] Consult the literature
    [ ] Discuss with industry representative(s)
    [ ] Participate in another educational activity
    [ ] Other ________________________
    [ ] None

Send the completed form and $10 payment (make checks payable to P&T) to: Department of Health Policy, Thomas Jefferson
University, Attn: Continuing Education Credit, 1015 Walnut Street, Suite 115, Philadelphia, PA 19107.