Manual of Antibiotics and Infectious Diseases

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Sixth Edition

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Preface

This manual is designed for students, housestaff, practicing physicians, and other health professionals involved in the day-to-day care of patients with infectious diseases. An attempt has been made to incorporate into one book a variety of important source materials that ordinarily can be found in many different locations:

The manual is divided into eight sections:

Section I. Antibiotics

Clinically important information is presented for each antibiotic. In some instances, two or three antibiotics that are similar are discussed together. This section includes the availability and trade names of each drug, its clinical use, administration and dosage, dosage in renal insufficiency, pharmacology, adverse reactions, and drug interactions. Further reading lists are also supplied.

Section II. Empiric Antibiotic Therapy

Recommendations are made for drugs of choice, alternative therapy, appropriate dosages, and routes of administration for various clinical situations in which infection is suspected.

Section III. Therapy of Established Infection

Empiric antibiotic therapy is continued until Gram stains and cultures from the laboratory reveal one or more specific agents. At this point, specific therapy is begun; this section summarizes antibiotic choices, doses, route of administration, and duration of therapy.

Section IV. Antibiotic Susceptibilities

Section V. Prophylactic Antibiotics

This section provides guidelines for the use of prophylactic antibiotics; general principles; American Heart Association recommendations for the prevention of endocarditis during various surgical procedures; American Heart Association recommendations for the

prevention of rheumatic fever; tuberculosis; and meningococcal infection.

Section VI. Availability and Clinical Use of Immunobiologic Agents and Antiparasitic Drugs

These agents are available by request from the Immunobiologics, Biologic Products Division, Bureau of Laboratories, of the Center for Disease Control. Guidelines are given for the use of BCG; immune serum globulin and hepatitis B immune globulin; influenza vaccine; pneumococcal vaccine; polio vaccine; rabies immune globulin; tetanus prophylaxis; immunobiologic agents and drugs distributed by the CDC and drugs for the treatment of parasitic infections, including malaria.

Section VII. Sexually Transmitted Diseases—Treatment Guidelines

United States Public Health Service recommendations for the treatment of syphilis and gonorrhea are provided.

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Acknowledgments

We would like to dedicate this manual to our wives, Michelle and Joan, without whose patience and understanding this manual would not have been possible.

We would like to thank Karen Mah-Hing for her patient secretarial assistance.

Abbreviations

AIDS	acquired immunodeficiency syndrome
bid	twice a day
BUN	blood urea nitrogen
cc	cubic centimeter
CDC	Center for Disease Control
CNS	central nervous system
Cl_{CR}	creatinine clearance
C_p	plasma concentration
Cr_S	serum creatinine
CSF	cerebrospinal fluid
dl	deciliter(s)
FTA-ABS	fluorescent treponemal antibody absorption (test)
GI	gastrointestinal
g	gram(s)
G6PD	glucose-6-phosphate dehydrogenase (deficiency)
HIV	human immunodeficiency virus
hr	hour(s)
ID	intradermal
IM	intramuscular
IT	intrathecal
IU	international unit(s)
IV	intravenous
kg	kilogram(s)
L	Liter
LD	loading dose

LP	lumbar puncture
M	molar
MBC	minimum bactericidal concentration
mcg	microgram(s)
MD	maintenance dose
meq	milliequivalent
mg	milligram(s)
MIC	minimum inhibitory concentration
MLC	minimum lethal concentration
ml	milliliter(s)
MU	million units
PO	by mouth
PPD	purified protein derivative (of tuberculin)
qd	daily, once a day
qid	4 times a day
qod	every other day
q2h	every 2 hours
q4h	every 4 hours
q6h	every 6 hours
q8h	every 8 hours
q12h	every 12 hours
RBC	red blood cell
RPR	rapid protein reagin
SIADH	syndrome of inappropriate antidiuretic hormone secretion
$t_{1/2}$	half-life
TB	tuberculosis
TGC	third-generation cephalosporin
tid	3 times a day
U	unit(s)
UTI	urinary tract infection
V_D	volume of distribution
VDRL	Venereal Disease Research Laboratories

Contents

Section I

ANTIBIOTICS

The summaries of antibiotics that follow are designed to provide the clinician with an overview of the clinical use of each agent, along with pertinent facts concerning comparative efficacy and toxicity, if similar agents are available. Each section provides information on appropriate dosage and administration in patients with normal and impaired renal function and other important clinical pharmacologic parameters. Sections on adverse reactions and significant drug interactions are provided, and a few references are listed to allow the reader to review each agent in more depth or to investigate more controversial points.

An attempt is made to provide information on all currently useful antibiotics. Older drugs that have fallen into relative disuse are not included. For example, semisynthetic penicillins such as phenethicillin or hetacillin, cephalosporins such as cephaloridine or cephaloglycin, aminoglycosides such as neomycin, or agents such as triacetyloleandomycin have little to no role in current clinical medicine and are either less effective or more toxic than new agents. Our experience and other clinical data document the relative lack of interstitial nephritis secondary to nafcillin. Since methicillin is associated with a significant incidence of nephritis, and since oxacillin may be hepatotoxic, recommendations in the manual are for the use of nafcillin in the treatment of staphylococcal infection. Over the past 5 years there have been an increasing number of reports of infections with methicillin (or nafcillin)-resistant *Staphylococcus aureus* in US hospitals. In some medical centers, 20 to 50% of all *S. aureus* isolates and up to two-thirds of *S. epidermidis* isolates are resistant to methicillin. In these settings, vancomycin is the empiric treatment of choice for serious staphylococcal infections. Although methicillin-resistant *S. aureus* isolates may appear to be sensitive to other agents by routine disc testing, these antibiotics (e.g., cephalosporins) are either ineffective or unproven in methicillin-resistant *S. aureus* infection.

Several tetracycline and sulfonamide derivatives are deliberately ex-

cluded, since these analogs offer no advantage over tetracycline or sulfisoxazole in the treatment of infectious diseases. Exceptions are noted in the summaries of each drug. It must be emphasized that although the summaries reflect the majority of opinions on clinical use, they also contain our opinions and interpretation of the available data, as well as our experiences.

Several "third-generation" cephalosporins and "fourth-generation" penicillins have become available for clinical use, and these are included in the summaries. Cinoxacin (a nalidixic-acid analog), acyclovir, ketoconazole, and netilmicin are included as well. Data are also supplied on agents which are investigational at the time of this writing, but which we expect to soon be available.

DEFINITIONS

Serum Concentrations. The values provided are the expected maximal concentrations achieved after administration of the listed dose.

Urinary Concentrations. The values provided are the range of maximal concentrations achievable after administration of the listed dose in a patient with normal renal function.

Volume of Distribution (V_D). The apparent volume of distribution is that volume of fluid into which the drug appears to distribute through body fluid compartments and by its uptake into tissues. It is a relationship between the total amount of drug in the body and the serum concentration $\left(\frac{\text{Amount of drug in the body}}{\text{Serum concentration}} = V_D\right)$, and is expressed as volume (L) or volume per unit weight (L/kg).

Half-Life ($t_{1/2}$). When absorption and distribution are complete, the plasma concentrations for most antibiotics decline exponentially; thus drug elimination follows first-order kinetics. The slope of the curve obtained during this phase is equal to the elimination rate constant (k). Half-life is related to the slope k by the equation:

$$t_{1/2} = \frac{\text{Ln } 2}{k} = \frac{0.693}{k}$$

The slope of the curve and half-life can be estimated by a plot of drug concentration (log scale) versus time (linear scale) (see Fig. 1–1).

PROTEIN BINDING

The values listed are the average reported for percent of drug bound to plasma proteins. These data are potentially important since highly protein bound drugs are generally not cleared by hemodialysis. Additionally, the protein-bound drug is not antibacterially active and the bound drug is not diffusible.

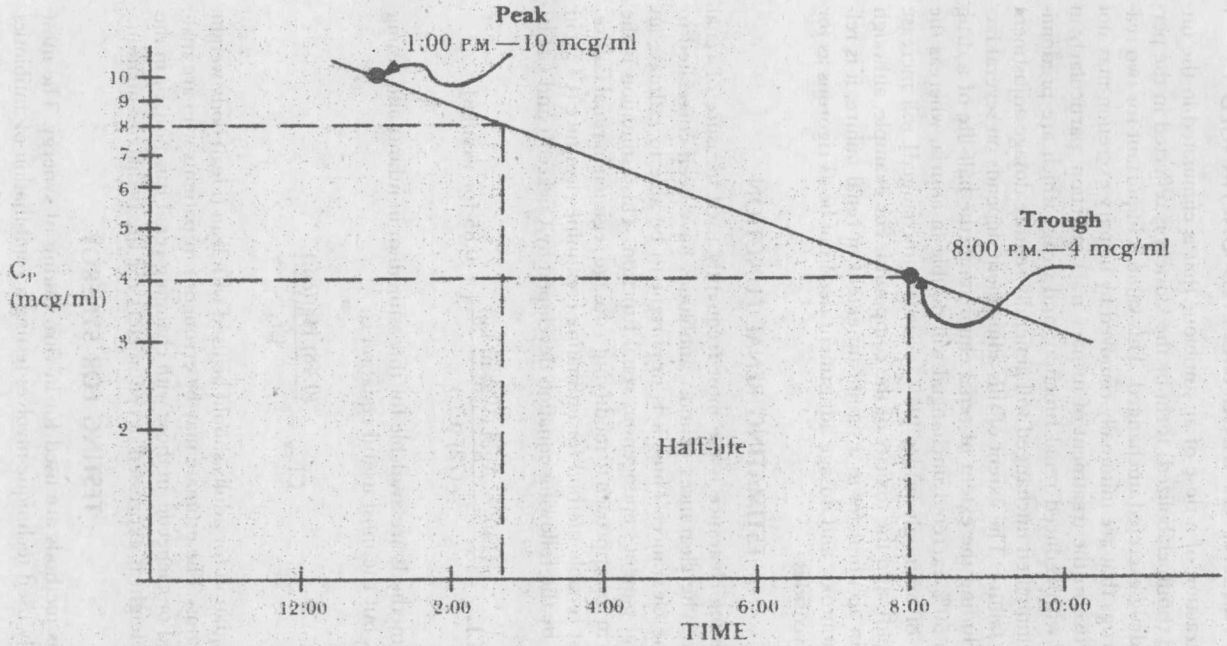

Fig. I–1. In order to estimate the half-life of a drug, one should (1) draw a straight line connecting the two measured plasma levels at the appropriate time, and then (2) choose two points along the line, the first of which is half the concentration of the second. The time it takes for the C_p to decline by half (8 to 4 mcg/ml) is 5½ hours.

PERCENT OF DRUG EXCRETED UNCHANGED

The fraction of a dose of an antibiotic that is eliminated in the unchanged (nonmetabolized) form by the kidneys is reflected in the percent of drug excreted unchanged. This value is important for two reasons: Drugs that are minimally removed by urinary excretion may not be effective in the treatment of urinary tract infection, particularly in patients with reduced renal function; and drugs which are predominantly eliminated unchanged will generally require dosage adjustment in renal failure. The extent of this adjustment depends on several factors, including the extent of renal elimination (the half-life of a drug which is 50% excreted unchanged will double in anuria, whereas the half-life of aminoglycosides [95% excreted unchanged] will increase twentyfold), and the toxicity of the compound. For example, although ampicillin accumulates to a significant extent in renal failure, it is relatively nontoxic and dosage adjustment need not be as rigorous as for aminoglycosides.

ESTIMATING RENAL FUNCTION

Creatinine clearance is the most frequently used measure of renal function. The clearances of most antibiotics have been correlated to creatinine clearance. Thus, it is important to be able to estimate an individual patient's endogenous renal function. This estimation is the first step in the approach to modifying a dosage regimen in renal failure. The most reliable method for estimating creatinine clearance (CL_{CR}) in adults is by the following equation developed by Cockcroft and Gault:

$$CL_{CR} = \frac{(140 - \text{Age})\ (\text{Wgt in kg})}{(72)\ (Cr_S)}\ [\times\ 0.85 \text{ for women}]$$

Various methods are available for this estimation in infants and young children, but the most useful equation is:

$$CL_{CR} = \frac{(0.48)\ \text{Hgt(cm)}}{Cr_S}$$

The equation for adults should be used with lean (ideal) body weight in kilograms. The estimate may be erroneous in patients who are malnourished or cachectic, in those with changing renal function, or in the elderly. Height is expressed in centimeters for the pediatric equation.

TESTING FOR SYNERGY

Various methods are used for in-vitro testing of synergy. The most commonly used technique involves testing a combination of antibiotics