A GUIDE TO ANTIBIOTIC THERAPY

HENRY WELCH, Ph.D.

MEDICAL ENCYCLOPEDIA

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INTRODUCTION

In this brief text an attempt has been made to condense for the physician's ready reference the important information concerning each of 31 antibiotics. General indications, side effects, major dosage form(s), average daily dose, and the blood and urine concentrations to be anticipated are included. In addition, the in vitro susceptibility of each group of important pathogenic microorganisms to each antibiotic is given. Much of the material has been obtained from the published literature; however, our own experience with each drug is also included.

Behind the imposing array of laboratory data contained in this guide lies a simple, practical tool of great clinical importance for the practicing physician.

Cognizance should be taken of the fact that the susceptibility of an organism to an antibiotic may vary considerably from strain to strain and also that various investigators report different susceptibility results on even the same strain. Thus, representative susceptibility data on strains of each organism are given in three categories as reported in the literature: (1) the lowest inhibitory concentration, (2) the highest, and (3) the concentration of antibiotic to which at least half the strains are susceptible.

When interpreting the data included in this text, the reader should keep in mind that there is a general relationship between the blood concentration obtainable with a given dose of the antibiotic, the degree of susceptibility of the organism, and the expected therapeutic effect. An antibiotic can, nevertheless, give poor results in the test tube (an apparent "in vitro failure") and still be an "in vivo success." Furthermore, an antibiotic may give relatively low blood concentrations yet, because the organisms against which it is directed are highly susceptible, produce excellent therapeutic results. In addition, there are listed antibiotics that produce very high blood concentrations and these are still found to be effective in infections even though the organism involved is moderately resistant when tested in vitro. By contrast, an antibiotic may give excellent in vitro data yet fail to give the desired therapeutic result even though the blood concentrations obtainable appear adequate, e.g., penicillin in certain staphylococcal infections.

On occasion, more than one antibiotic may appear to be applicable based on sensitivity tests and blood concentrations attainable with the usual doses. In such cases, obviously, the physician's "drug of choice" may be related to several factors, such as comparative toxicity of the antibiotics in question, their mode of administration, their rate of excretion, the nature of the disease, and the allergic history of the patient.

The total antibiotic production estimated for 1958 is more than 2.7 million pounds.

There are 28 antibiotics and more than 400 preparations of them now available for human and/or animal use in the United States. In addition, three other basic antibiotics in use abroad are under clinical trial here (leucomycin, colimycin, and spiramycin) and may well be available in the United States by the time this text is in print. An alphabetical list of the available basic antibiotics is given below. In addition to the generic names, trade names are also included, except for bacitracin, neomycin, penicillin, streptomycin, dihydrostreptomycin, and tyrothricin, which are used in so many dosage forms as to make listing impractical, and except for amphomycin, candicidin, leucomycin, and hygromycin B for which no trade names have been designated.

GENERIC NAME	TRADE NAME
Amphomycin	
Amphotericin B	Fungizone
Bacitracin	
Candicidin	
Carbomycin	Magnamycin
Chloramphenicol	Chloromycetin
Chlortetracycline	Aureomycin
*Colimycin**	Colistin
Cycloserine	Oxamycin, Seromycin
Dihydrostreptomycin (*See streptomycin*)	
Erythromycin	Erythrocin, Ilosone
Framycetin	Soframycin
Fumagillin	Fumidil
Griseofulvin	Grifulvin; Fulvicin
Hygromycin B	
Kanamycin	Kantrex
*Leucomycin**	
Neomycin	
Novobiocin	Albamycin, Cathomycin

* Now in use in Japan. Not yet available in the United States.

GENERIC NAME	TRADE NAME
Nystatin	Mycostatin
Oleandomycin (*See triacetyloleandomycin*)	Matromycin
Oxytetracycline	Cosa-Terramycin
Penicillin	
Polymyxin	Aerosporin
Ristocetin	Spontin
Spiramycin†	Rovamycin
Streptomycin	
Tetracycline	Achromycin, Panmycin, Polycycline, Steclin, Cosa-Tetracyn
Thiostrepton	Microthion
Triacetyloleandomycin	Cyclamycin, Tao
Tyrothricin	
Vancomycin	Vancocin
Viomycin	Viocin

† Now in use in Europe. Not yet available in the United States.

ACKNOWLEDGMENTS

The preparation of the tables of susceptibility of the various organisms to the 31 antibiotics included in the text required an extensive review of the literature. The author gratefully acknowledges the time and effort of Julian Kramer and William W. Wright, who were mainly instrumental in gathering and documenting this material. The assistance of Mary Ann Garth, Robert Harlow, Elizabeth Sanchez, and Elsie Tarcza is also deeply appreciated. Grateful acknowledgment is extended to Howard I. Weinstein, M.D., who kindly reviewed all of the clinical material.

FOREWORD

The word "guide" is defined in the dictionary as "one who shows others the way," and also as "a handbook or manual of information . . . ." Both definitions could be combined to describe this book, as slim in format as it is wide in range, in which a distinguished authority on antibiotic medicine offers physicians an admirably systematized arrangement of invaluable scientific data on which they may rely for accurate and unerring treatment of infectious diseases.

At the beginning of the century, clinicians still regarded the laboratory with a timorous respect equaled only by the awe felt by physiks four hundred years ago at the sight of the alchemist's weird workshop. For many physicians, the laboratory was still a *terra incognita* into which only a select minority dared venture. At that time it might have seemed unwise to advise the physician to use the cryptic and dehumanized laboratory report in contending with the immediate problem of the patient in need of urgent and lifesaving treatment.

Even as clinical practice and surgery—which, in a great historic mistake of medicine, were kept apart for several centuries—registered portentous progress only when they were integrated in the professional training of the physician, similarly the present integration of laboratory and clinic has been the golden key that opened the door to many admirable advances in the art of healing

The laboratory today has a threefold function in helping the physician: First, as a center of scientific research where problems are scrutinized that, in spite of their apparent initial vagueness, lead to the solution of other eminently practical problems in the clinical field; second, as an instrument of diagnostic investigation, since laboratory reports, with their figures, charts, and tables, often solve the mysteries encountered by the clinician at the patient's bedside; and third, as a powerful tool in deciding the correct therapy for a patient, since it can not only determine the causal agent of a disease but also guide the physician in choosing the right drug, the right dose, and the right way to administer it so as to ensure its maximum curative efficacy.

This *Guide to Antibiotic Therapy* exemplifies the third of the three great missions of the laboratory. This is the first time an investigator of the caliber of Dr. Henry Welch, whose long professional life has run parallel with the historic development of antibiotics, has provided a book that embodies everything the practicing physician ought to know about antibiotic therapy. This, furthermore, he has done in a clear, concise, and, above all, elegantly instructive manner, for the author is a born educator, a fact well demonstrated by his vast scientific output as investigator, writer, and lecturer.

In this book disease as a nosologic entity, its etiologic agent, and its therapy are integrated within a single picture of great scientific luminosity, proving that if medicine was "made" in the Middle Ages in the medical libraries of monasteries, and in the last century in hospitals, today it is made in the laboratory.

With this work, Dr. Welch adds to his proud harvest in the field of antibiotic medicine not only a therapeutic instrument of tremendous value to the practicing physician, since it invites him to refine and speed up as far as possible the specific character of his diagnosis, but also a document of immense scientific value.

As a conch shell applied to the ear will bring the distant voice of the sea, so this book will bring the harassed physician, on whose swift and effective action the life of an infectious patient depends, the voice of the laboratory advising him how best to fulfill his noble Samaritan mission.

Félix Martí-Ibáñez, M.D.

New York
May 14, 1959

	INHIBITORY CONCENTRATIONS μg./ml. LOW	HIGH	MAJORITY
ACTINOMYCETES			
A. bovis			
A. israelii			
Nocardia asteroides			
AEROBACTER			
A. aerogenes			>50
BACILLI			
B. anthracis			0.5
BRUCELLA			
Br. sp.			>100
CLOSTRIDIA			
Cl. botulinum			
Cl. tetani			
Cl. perfringens			
CORYNEBACTERIA			
C. diphtheriae			0.39
ESCHERICHIA			
E. coli			>100
HEMOPHILUS			
H. ducreyi			
H. influenzae			
H. parainfluenzae			
H. pertussis			
KLEBSIELLA			
K. pneumoniae			>100
MYCOBACTERIA			
Myco. tuberculosis			
NEISSERIA			
N. gonorrhoeae			
N. meningitidis			
PASTEURELLA			
Past. pestis			
Past. tularensis			
PROTEUS			
P. sp.			>100
PSEUDOMONAS			
Ps. sp.			>100
SALMONELLA			
Sal. typhosa			>100
Sal. sp.			>100

AMPHOMYCIN

GENERAL INDICATIONS

For topical use in the treatment of lesions infected by staphylococci, streptococci, and other gram-positive organisms.

SIDE EFFECTS

Because of its polypeptide structure, allergic sensitization is rare.

DOSAGE FORM

TOPICAL APPLICATION ONLY

AMPHOMYCIN CALCIUM OINTMENT

AMPHOMYCIN

	INHIBITORY CONCENTRATIONS μg./ml.		
	LOW	HIGH	MAJORITY
SHIGELLA			
Sh. sp.			>100
SPIROCHETES			
Borrelia sp.			
Leptospira icterohaemorrhagiae			
Spirillium minus			
Treponema pallidum			
T. pertenue			
T. carateum			
STAPHYLOCOCCI			
Staph. aureus	1.56	6.25	6.25
Staph. epidermitis			
STREPTOCOCCI-PNEUMOCOCCI			
D. pneumoniae	0.78	2.5	1.56
Str. sp. (pyogenic group)	0.39	2.5	0.78
Str. sp. (viridans group)			2.5
Str. sp. (enterococcus group)			6.25
VIBRIO			
V. comma			
MISCELLANEOUS			
Bacteroides funduliformes			
YEASTS AND MOLDS			
Asperigillus fumigatus			
Blastomyces dermatiditis			
Candida albicans (monilia)			>100
Coccidioides immitis			
Crytococcus neoformans			
Epidermophyton inguinale			
Histoplasma capsulatum			
Trichophyton rubrum			
RICKETTSIA			
R. akari			
R. prowazekii			
R. typhi			
R. rickettsii			
R. tsutsugamushi			
R. burneti			
VIRUSES			
Lymphogranuloma			
Psittacosis-lymphogranuloma group			
PROTOZOA			
Endamoeba histolytica			
Trichomonas sp.			

	INHIBITORY CONCENTRATIONS μg./ml. LOW	HIGH	MAJORITY
ACTINOMYCETES			
A. bovis			
A. israelii			
Nocardia asteroides			CE*
AEROBACTER			
A. aerogenes			
BACILLI			
B. anthracis			
BRUCELLA			
Br. sp.			
CLOSTRIDIA			
Cl. botulinum			
Cl. tetani			
Cl. perfringens			
CORYNEBACTERIA			
C. diphtheriae			
ESCHERICHIA			
E. coli			
HEMOPHILUS			
H. ducreyi			
H. influenzae			
H. parainfluenzae			
H. pertussis			
KLEBSIELLA			
K. pneumoniae			
MYCOBACTERIA			
Myco. tuberculosis			
NEISSERIA			
N. gonorrhoeae			
N. meningitidis			
PASTEURELLA			
Past. pestis			
Past. tularensis			
PROTEUS			
P. sp.			
PSEUDOMONAS			
Ps. sp.			
SALMONELLA			
Sal. typhosa			
Sal. sp.			

AMPHOTERICIN B

GENERAL INDICATIONS

For the treatment, in the hospital, of disseminated deep mycotic infections including coccidioidomycosis, cryptococcosis, disseminated moniliasis, histoplamosis, and North American blastomycosis.

SIDE EFFECTS

Transient anorexia, chills, and fever may occur during first few days of treatment. Headache, nausea, and vomiting are early toxic manifestations requiring a reduction in the dosage. Blood urea nitrogen and nonprotein nitrogen should be checked routinely during treatment. If these values become elevated, treatment is contraindicated until they become normal. In patients on prolonged therapy, liver, kidney, and bone marrow studies should be done at appropriate intervals. Maximum daily dosage should not exceed 1.5 mg./Kg.

DOSAGE FORMS

INTRAVENOUS ADMINISTRATION ONLY

STERILE AMPHOTERICIN B

Dosage: 50 mg. each day or every other day by slow intravenous infusion of a solution of 0.1 mg./ml. of amphotericin B in 5% dextrose solution over a period of 6 hours.

Serum concentrations expected:

1.5 μg./ml. (peak)
0 μg./ml. (24 hours)

Urinary concentration expected:

1.5 μg./ml. (peak)

* CE = Clinically effective.

AMPHOTERICIN B

	INHIBITORY CONCENTRATIONS μg./ml. LOW	HIGH	MAJORITY
SHIGELLA			
Sh. sp.			
SPIROCHETES			
Borrelia sp.			
Leptospira icterohaemorrhagiae			
Spirillum minus			
Treponema pallidum			
T. pertenue			
T. carateum			
STAPHYLOCOCCI			
Staph. aureus			
Staph. epidermitis			
STREPTOCOCCI-PNEUMOCOCCI			
D. pneumoniae			
Str. sp. (pyogenic group)			
Str. sp. (viridans group)			
Str. sp. (enterococcus group)			
VIBRIO			
V. comma			
MISCELLANEOUS			
Bacteroides funduliformes			
YEASTS AND MOLDS			
Asperigillus fumigatus	1.9	>40	>40
Blastomyces dermatiditis	0.5	3.7	3.7
Candida albicans (monilia)	0.5	1.0	1.0
Coccidioides immitis			0.2
Crytococcus neoformans			CE
Epidermophyton inguinale			
Histoplasma capsulatum	0.04	0.1	0.1
Trichophyton rubrum	7.3	14.7	14.7
RICKETTSIA			
R. akari			
R. prowazekii			
R. typhi			
R. rickettsii			
R. tsutsugamushi			
R. burneti			
VIRUSES			
Lymphogranuloma			
Psittacosis-lymphogranuloma group			
PROTOZOA			
Endamoeba histolytica			
Trichomonas sp.			

	INHIBITORY CONCENTRATIONS units/ml.		
	LOW	HIGH	MAJORITY
ACTINOMYCETES			
A. bovis			
A. israelii	0.005	0.075	0.03
Nocardia asteroides			
AEROBACTER			
A. aerogenes	10	10^4	5000
BACILLI			
B. anthracis	4.0	12.5	6.0
BRUCELLA			
Br. sp.			
CLOSTRIDIA			
Cl. botulinum	0.006	15.6	3.0
Cl. tetani	0.006	15.6	5.0
Cl. perfringens	0.002	62.5	5.0
CORYNEBACTERIA			
C. diphtheriae	0.004	0.015	0.01
ESCHERICHIA			
E. coli	125	10^4	5000
HEMOPHILUS			
H. ducreyi			
H. influenzae	0.06	0.63	0.6
H. parainfluenzae			
H. pertussis	0.002	5.0	5.0
KLEBSIELLA			
K. pneumoniae	625	10^4	10^4
MYCOBACTERIA			
Myco. tuberculosis			
NEISSERIA			
N. gonorrhoeae	0.006	0.008	0.007
N. meningitidis			
PASTEURELLA			
Past. pestis			
Past. tularensis			
PROTEUS			
P. sp.	125	$>10^4$	10^4
PSEUDOMONAS			
Ps. sp.			
SALMONELLA			
Sal. typhosa			
Sal. sp.	>10	400	400

BACITRACIN

GENERAL INDICATIONS

For use in infections that have proved resistant to penicillin and other antibiotics and that are due to bacitracin-susceptible organisms, such as cellulitis, abscesses, wound infections, chronic osteomyelitis, gangrene, bacterial endocarditis, and staphylococcal meningitis.

The oral form is used in the treatment of amebiasis and other intestinal infections due to susceptible organisms and (in conjunction with other drugs) for bowel sterilization prior to surgery. The topical form is used for the treatment of superficial infections due to susceptible organisms.

SIDE EFFECTS

If the blood urea nitrogen or nonprotein nitrogen is elevated, intramuscular bacitracin is contraindicated. If during treatment the blood urea nitrogen or nonprotein nitrogen becomes elevated, bacitracin should be discontinued. The fluid intake should be kept higher than 2000 ml./day. If necessary, administer sodium bicarbonate orally to maintain the urinary *p*H over 6.0. Urinary output should not fall below 800 ml./24 hour period. Albumin and cellular elements (rarely red blood cells) may appear in the urine during treatment. Anorexia, nausea, and vomiting alone are not indications for discontinuing bacitracin. This drug is poorly absorbed from the gastrointestinal tract.

DOSAGE FORMS

INTRAMUSCULAR ADMINISTRATION

STERILE BACITRACIN

Dosage: 20,000 units every 8 hours.

Serum concentrations expected:
0.3 unit/ml. (peak)
0.05 unit/ml. (6 hours)

Urinary concentration expected:
15 units/ml. (peak)

ORAL ADMINISTRATION

BACITRACIN TABLETS

Dosage: 100,000 units/day in 4 divided doses.

TOPICAL APPLICATION

STERILE BACITRACIN TOPICAL, BACITRACIN OINTMENT

BACITRACIN

	INHIBITORY CONCENTRATIONS units/ml.		
	LOW	HIGH	MAJORITY
SHIGELLA			
Sh. sp.			
SPIROCHETES			
Borrelia sp.			
Leptospira icterohaemorrhagiae			
Spirillum minus			
Treponema pallidum	0.004	0.025	0.025
T. pertenue			
T. carateum			
STAPHYLOCOCCI			
Staph. aureus	0.05	>500	5.0
Staph. epidermitis	0.005	2.5	1.0
STREPTOCOCCI-PNEUMOCOCCI			
D. pneumoniae	0.002	3.12	3.0
Str. sp. (pyogenic group)	0.0005	5.0	1.0
Str. sp. (viridans group)	0.3	0.5	0.3
Str. sp. (enterococcus group)	0.008	3.0	1.0
VIBRIO			
V. comma	0.01	>100	100
MISCELLANEOUS			
Bacteroides funduliformes	<2.0	>20	>20
YEASTS AND MOLDS			
Asperigillus fumigatus			
Blastomyces dermatiditis			
Candida albicans (monilia)			
Coccidioides immitis			
Crytococcus neoformans			
Epidermophyton inguinale			
Histoplasma capsulatum			
Trichophyton rubrum			
RICKETTSIA			
R. akari			
R. prowazekii			
R. typhi			
R. rickettsii			
R. tsutsugamushi			
R. burneti			
VIRUSES			
Lymphogranuloma			
Psittacosis-lymphogranuloma group			
PROTOZOA			
Endamoeba histolytica			CE*
Trichomonas sp.			

* CE = Clinically effective.

	INHIBITORY CONCENTRATIONS μg./ml.		
	LOW	HIGH	MAJORITY
ACTINOMYCETES			
A. bovis			
A. israelii			
Nocardia asteroides	1.56	500	200
AEROBACTER			
A. aerogenes			
BACILLI			
B. anthracis			
BRUCELLA			
Br. sp.			
CLOSTRIDIA			
Cl. botulinum			
Cl. tetani			
Cl. perfringens			
CORYNEBACTERIA			
C. diphtheriae			
ESCHERICHIA			
E. coli			
HEMOPHILUS			
H. ducreyi			
H. influenzae			
H. parainfluenzae			
H. pertussis			
KLEBSIELLA			
K. pneumoniae			
MYCOBACTERIA			
Myco. tuberculosis			
NEISSERIA			
N. gonorrhoeae			
N. meningitidis			
PASTEURELLA			
Past. pestis			
Past. tularensis			
PROTEUS			
P. sp.			
PSEUDOMONAS			
Ps. sp.			
SALMONELLA			
Sal. typhosa			
Sal. sp.			

CANDICIDIN

GENERAL INDICATIONS

For the topical treatment of superficial monilial infections.

SIDE EFFECTS

There have been no reports of toxicity.

DOSAGE FORMS

TOPICAL APPLICATION

CANDICIDIN VAGINAL TABLETS, CANDICIDIN OINTMENT