SANFORD GUIDE®

熱病®

The Sanford Guide To Antimicrobial Therapy 2016

46th Edition

David N. Gilbert, M.D.
Henry F. Chambers, M.D.
George M. Eliopoulos, M.D.
Michael S. Saag, M.D.
Andrew T. Pavia, M.D.

Douglas Black, Pharm.D.
David O. Freedman, M.D.
Kami Kim, M.D.
Brian S. Schwartz, M.D.

Editorial Note

To our readers,

We have made significant improvements in this 46th edition of The Sanford Guide to Antimicrobial Therapy. First, we thank you for your comments, questions and reviews of our content. You are an integral part of the collaborative process that results in each updated edition of The Sanford Guide.

We strive to provide you with the current range of evidence-based options for treatment, management and prevention of infectious diseases. The Sanford Guide reaches a global audience, which means you should consider our recommendations in light of local resistance and susceptibility patterns, availability of and variations in formulation of antimicrobial agents and other local conditions that guide care for your patients.

New material and areas of significant change in this 46th edition include:

- *Table 1:* major updates include genital tract infections based on new CDC STD Guidelines, kidney & bladder infections, enterococcal endocarditis (also Table 5A), empiric therapy for pneumonia, as well as updated regimens and references.
- *Tables 4A, 4B and 4C: Activity spectra (antibacterial, antifungal and antiviral).* These tables have been completely reworked, updated and are now color-coded. The color coding and associated symbols are intended to provide more descriptive categorization of the table data.
- *Table 7: Drug Desensitization.* Desensitization methods for additional drugs are added.
- *Table 8: Pregnancy Risk and of Antimicrobial During Lactation.* This new table adds data on safety of antimicrobials in lactating mothers.
- *Table 10A (and elsewhere):* New antibacterials added: ceftazidime-avibactam and ceftolozane-tazobactam.
- *Table 11:* New antifungal drug: Isavuconazole added.
- *Table 14 (HCV):* New direct-acting agents and combination agents and updated HCV treatment regimens
- *Table 16: Pediatric Dosing.* Reinstated in this edition is a new table summarizing dosing of antimicrobials in children age 28 days and older.
- *Table 17A: Dosing in Renal Impairment.* This table has also been thoroughly reworked and reviewed for improved clarity in our recommendations.

As always, all content has been updated with new references from the published literature, including new practice and treatment guidelines, updated prescribing information and drug safety information.

Some recommendations suggest the use of agents for indications or in doses other than found in product labeling. Such recommendations are based on published reports in peer-reviewed literature; they are not based on input from any pharmaceutical manufacturer. They are made with due consideration of the concerns of the U.S. Food and Drug Administration (FDA) regarding "off-label" uses. We provide reference(s) for and, in some cases, annotate such recommendations with the notation "NAI" meaning not an FDA-approved indication or dose.

The Editors
January 2016

SANFORD GUIDE®

熱病®

The Sanford Guide To Antimicrobial Therapy 2016

46th Edition

FREE SANFORD GUIDE WEB EDITION TRIAL

Visit **store.sanfordguide.com**, click the Redeem Coupon button and enter **WEB16** to receive a complimentary 60-day trial subscription to the Sanford Guide Web Edition

*Limit one per customer • Offer expires April 30,2017

The Sanford Guide to Antimicrobial Therapy 2016
46th Edition

Editors

David N. Gilbert, M.D.
Chief of Infectious Diseases
Providence Portland Medical Center, Oregon
Professor of Medicine, Oregon Health Sciences University

Henry F. Chambers, M.D.
Professor of Medicine
Director, Clinical Research Services
UCSF Clinical and Translational Sciences Institute
University of California at San Francisco

George M. Eliopoulos, M.D.
Chief, James L. Tullis Firm,
Beth Israel Deaconess Hospital,
Professor of Medicine,
Harvard Medical School,
Boston, Massachusetts

Michael S. Saag, M.D.
Director, UAB Center for AIDS Research,
Professor of Medicine and Director,
Division of Infectious Diseases,
University of Alabama, Birmingham

Andrew T. Pavia, M.D.
George & Esther Gross Presidential Professor
Chief, Division of Pediatric Infectious Diseases
University of Utah, Salt Lake City

Contributing Editors

Douglas Black, Pharm. D.
Associate Professor of Pharmacy,
University of Washington, Seattle

Brian S. Schwartz, M.D.
Associate Professor of Medicine
University of California at San Francisco

David O. Freedman, M.D.
Director, Travelers Health Clinic,
Professor of Medicine,
University of Alabama, Birmingham

Kami Kim, M.D.
Professor of Medicine, Microbiology & Immunology, Pathology
Albert Einstein College of Medicine
New York, NY

Managing Editor

Jeb C. Sanford

Memoriam

Jay P. Sanford, M.D.
1928-1996

Merle A. Sande, M.D.
1935-2007

Robert C. Moellering, Jr., M.D.
1936-2014

Publisher

Antimicrobial Therapy, Inc.

The SANFORD GUIDES are updated annually and published by:

ANTIMICROBIAL THERAPY, INC.
P.O. Box 276, 11771 Lee Highway
Sperryville, VA 22740-0276 USA
Tel 540-987-9480 Fax 540-987-9486
Email: info@sanfordguide.com www.sanfordguide.com

Copyright © 1969-2016 by Antimicrobial Therapy, Inc.

All rights reserved. No part of this publication may be may be reproduced, stored in a retrieval system or transmitted in any form or by any means--digital, electronic, mechanical, optical, photocopying, recording or otherwise--without prior written permission from Antimicrobial Therapy, Inc., 11771 Lee Hwy, P.O. Box 276, Sperryville, VA 22740-0276 USA

"SANFORD GUIDE" and "Hot Disease" logo are ® registered trademarks of Antimicrobial Therapy, Inc.

Acknowledgements

Thanks to Ushuaia Solutions, SA, Argentina; Alcom Printing, Harleysville, PA and Fox Bindery, Quakertown. PA for design and production of this edition of the SANFORD GUIDE.

Note to Readers

Since 1969, the SANFORD GUIDE has been independently prepared and published. Decisions regarding the content of the SANFORD GUIDE are solely those of the editors and the publisher. We welcome questions, comments and feedback concerning the SANFORD GUIDE. All of your feedback is reviewed and taken into account in updating the content of the SANFORD GUIDE.

Every effort is made to ensure accuracy of the content of this guide. However, current full prescribing information available in the package insert for each drug should be consulted before prescribing any product. The editors and publisher are not responsible for errors or omissions or for any consequences from application of the information in this book and make no warranty, express or implied, with respect to the currency, accuracy, or completeness of the contents of this publication. Application of this information in a particular situation remains the professional responsibility of the practitioner.

For the most current information, subscribe to webedition.sanfordguide.com or Sanford Guide mobile device applications

Printed in the United States of America
ISBN 978-1-930808-93-5
Library Edition (English)

QUICK PAGE GUIDE TO THE SANFORD GUIDE

RECOMMENDED TREATMENT—DIFFERENT SITES/MICROBES:			
BY ORGAN SYSTEM:	4 - 68		
CAPD Peritonitis	231		
BY ORGANISM:			
Bacteria	**69 - 71**		
Highly Resistant Bacteria	**81**		
CA-MRSA	**82**		
Fungi	121 - 133		
Mycobacteria	137 - 147		
Parasites	151 - 161		
Non-HIV Viruses	166 - 176		
HIV/AIDS	181 - 191		
Influenza	173		
DURATION OF TREATMENT:	72		
ANTIMICROBIAL PROPHYLAXIS:			
Pregnancy/Delivery	199		
Post-Splenectomy	199		
Sexual Exposure	200		
Sickle Cell Disease	200		
Surgical	200		
Endocarditis	204		
Exposure to HIV/HBV/HCV	205		
Transplants: Opportunistic Infections	209		
IMMUNIZATIONS:			
Anti-tetanus	232		
Rabies Post Exposure	233		
ANTIMICROBIALS:	Spectra	Adverse Effects	Dosage/SE
Antibiotics	73 - 80	115 - 116	102
AG-Once Daily Dosing			**118**
Continuous/Prolonged Infusion			119
Desensitization (Pen, TMP-SMX, ceftriaxone)			83
Inhalation Antibiotics			120
Pregnancy Risk Categories		85	
Antifungals	79		134 - 136
Antimycobacterials			148 - 150
Antiparasitics			162 - 165
Antivirals (Non-HIV)			177 - 180
Antiretrovirals			192 - 195
Pediatric Dosing			211
DOSE ADJUSTMENTS:			
Renal	214 - 228		
Hepatic	230		
Obesity	229		
DRUG INFORMATION:			
Pharmacologic Features	88		
Pharmacodynamics	99		
Drug-Drug Interactions	**235 - 242** (**243** ARV Drugs)		
Generic/Trade Names	244		
MISCELLANEOUS:			
Abbreviations	2		
Parasites Causing Eosinophilia	165		
Parasitic Drugs: Sources	165		
Directory of Resources	234		

—TABLE OF CONTENTS—

ABBREVIATIONS 2

TABLE 1 Clinical Approach to **Initial Choice** of Antimicrobial Therapy 4

TABLE 2 Recommended Antimicrobial Agents Against **Selected Bacteria** 69

TABLE 3 Suggested **Duration** of Antibiotic Therapy in Immunocompetent Patients 72

TABLE 4A **Antibacterial Activity Spectra** 73
4B Antifungal Activity Spectra 79
4C Antiviral Activity Spectra 79

TABLE 5A Treatment Options For Systemic Infection Due To Multi-Drug **Resistant Gram-Positive Bacteria** 81
5B Treatment Options for Systemic Infection Due to Selected **Multi-Drug Resistant Gram-Negative Bacilli** 81

TABLE 6 Suggested Management of Suspected or Culture-Positive **Community-Associated Methicillin-Resistant S. aureus Infections** 82

TABLE 7 **Antibiotic Hypersensitivity Reactions & Drug Desensitization** methods 83

TABLE 8 **Pregnancy Risk** and Safety in Lactation 85

TABLE 9A Selected **Pharmacologic Features** of Antimicrobial Agents 88
9B **Pharmacodynamics of Antibacterials** 99
9C **Enzyme -and Transporter- Mediated Interactions** of Antimicrobials 99

TABLE 10A **Antibiotic Dosage and Side-Effects** 102
10B Selected Antibacterial Agents—**Adverse Reactions**—Overview 115
10C Antimicrobial Agents Associated with **Photosensitivity** 117
10D **Aminoglycoside Once-Daily and Multiple Daily Dosing Regimens** 118
10E **Prolonged or Continuous Infusion Dosing of Selected Beta Lactams** 119
10F **Inhalation Antibiotics** 120

TABLE 11A **Treatment of Fungal Infections**—Antimicrobial Agents of Choice 121
11B **Antifungal Drugs:** Dosage, Adverse Effects, Comments 134

TABLE 12A Treatment of **Mycobacterial Infections** 137
12B **Dosage** and Adverse Effects of Antimycobacterial Drugs 148

TABLE 13A Treatment of **Parasitic Infections** 151
13B **Dosage** and Selected Adverse Effects of Antiparasitic Drugs 162
13C Parasites that Cause **Eosinophilia (Eosinophilia In Travelers)** 165
13D Sources for **Hard-to-Find Antiparasitic Drugs** 165

TABLE 14A **Antiviral Therapy** 166
14B **Antiviral Drugs (Non-HIV)** 177
14C **Antiretroviral Therapy (ART)** in Treatment-Naïve Adults (HIV/AIDS) 181
14D **Antiretroviral Drugs** and Adverse Effects 192
14E **Hepatitis A & HBV Treatment** 196
14F **HCV Treatment** Regimens and Response 197

TABLE 15A **Antimicrobial Prophylaxis** for Selected Bacterial Infections 199
15B **Antibiotic Prophylaxis** to **Prevent Surgical Infections** in **Adults** 200
15C Antimicrobial Prophylaxis for the Prevention of **Bacterial Endocarditis** in Patients with Underlying Cardiac Conditions 204
15D Management of **Exposure to HIV-1 and Hepatitis B and C** 205
15E Prevention of Selected Opportunistic Infections in **Human Hematopoietic Cell Transplantation** (HCT) or **Solid Organ Transplantation** (SOT) in Adults With Normal Renal Function 209

TABLE 16 **Pediatric dosing** (AGE > 28 DAYS) 211

TABLE 17A Dosages of Antimicrobial Drugs in Adult Patients with **Renal Impairment** 214
17B **No Dosage Adjustment** with Renal Insufficiency by Category 229
17C **Antimicrobial Dosing in Obesity** 229

TABLE 18 Antimicrobials and **Hepatic Disease: Dosage Adjustment** 230

TABLE 19 Treatment of **CAPD Peritonitis** in Adults 231

TABLE 20A Anti-**Tetanus** Prophylaxis, Wound Classification, Immunization 232
20B **Rabies Postexposure Prophylaxis** 233

TABLE 21 Selected **Directory of Resources** 234

TABLE 22A Anti-Infective **Drug-Drug Interactions** 235
22B Drug-Drug Interactions Between **Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIS) and Protease Inhibitors** 243

TABLE 23 List of **Generic** and **Common** Trade Names 244

INDEX OF MAJOR ENTITIES 246

ABBREVIATIONS

3TC = lamivudine
AB,% = percent absorbed
ABC = abacavir
ABCD = amphotericin B colloidal dispersion
ABLC = ampho B lipid complex
AD = after dialysis
ADF = adefovir
AG = aminoglycoside
AIDS = Acquired Immune Deficiency Syndrome
AM-CL = amoxicillin-clavulanate
AM-CL-ER = amoxicillin-clavulanate extended release
AMK = amikacin
Amox = amoxicillin
AMP = ampicillin
Ampho B = amphotericin B
AM-SB = ampicillin-sulbactam
AP = atovaquone proguanil
APAG = antipseudomonal aminoglycoside
ARDS = acute respiratory distress syndrome
ARF = acute rheumatic fever
ASA = aspirin
ATS = American Thoracic Society
ATV = atazanavir
AUC = area under the curve
Azithro = azithromycin
bid = 2x per day
BL/BLI = beta-lactam/beta-lactamase inhibitor
BSA = body surface area
BW = body weight
C&S = culture & sensitivity
CARB = carbapenems
CAPD = continuous ambulatory peritoneal dialysis
CDC = Centers for Disease Control
Cefpodox = cefpodoxime proxetil
Ceftaz = ceftazidime
Ceph = cephalosporin
CFB = ceftobiprole
CFP = cefepime
Chloro = chloramphenicol
CIP = ciprofloxacin; **CIP-ER** = CIP extended release
Clarithro = clarithromycin; **ER** = extended release
Clav = clavulanate
Clinda = clindamycin
CLO = clofazimine
Clot = clotrimazole
CMV = cytomegalovirus
CQ = chloroquine phosphate
Cobi = cobicistat
CrCl = creatinine clearance
CrCln = CrCl normalized for BSA
CRRT = continuous renal replacement therapy
C/S = culture & sensitivity
CSD = cat-scratch disease
CSF = cerebrospinal fluid
CXR = chest x-ray
d4T = stavudine
Dapto = daptomycin
DBPCT = double-blind placebo-controlled trial
dc = discontinue
ddC = zalcitabine
ddI = didanosine
DIC = disseminated intravascular coagulation
div = divided
DLV = delavirdine
DORI = doripenem
DOT = directly observed therapy
Doxy = doxycycline
DR = delayed release
DRSP = drug-resistant S. pneumoniae
DS = double strength
EBV = Epstein-Barr virus
EES = erythromycin ethyl succinate
EFZ = efavirenz
ELV = elvitegravir
EMB = ethambutol
ENT = entecavir
ER = extended release
ERTA = ertapenem
Erythro = erythromycin
ESBLs = extended spectrum β-lactamases
ESR = erythrocyte sedimentation rate
ESRD = endstage renal disease
Flu = fluconazole
Flucyt = flucytosine
FOS-APV = fosamprenavir
FQ = fluoroquinolone
FTC = emtricitabine
G = generic
GAS = Group A Strep
Gatl = gatifloxacin
GC = gonorrhea
Gemi = gemifloxacin
Gent = gentamicin
gm = gram
GNB = gram-negative bacilli
Griseo = griseofulvin
HEMO = hemodialysis
HHV = human herpesvirus
HIV = human immunodeficiency virus
HLR = high-level resistance
H/O = history of
HSCT = hematopoietic stem cell transplant
HSV = herpes simplex virus
IA = injectable agent/anti-inflammatory drugs
IDV = indinavir
IFN = interferon
IM = intramuscular
IMP = imipenem-cilastatin
INH = isoniazid
Inv = investigational
IP = intraperitoneal
IT = intrathecal
Itra = itraconazole
IV = intravenous
IVDU = intravenous drug user
IVIG = intravenous immune globulin
Keto = ketoconazole
kg = kilogram
LAB = liposomal ampho B
LCM = lymphocytic choriomeningitis virus
LCR = ligase chain reaction
Levo = levofloxacin
LP/R = lopinavir/ritonavir
mcg (or **μg**) = microgram
MDR = multi-drug resistant
MER = meropenem
Metro = metronidazole
Mino = minocycline
mL = milliliter
Moxi = moxifloxacin
MQ = mefloquine
MSM = men who have sex with men
MSSA/MRSA = methicillin-sensitive/resistant S. aureus
MTB = Mycobacterium tuberculosis
NB = name brand
NF = nitrofurantoin
NAt = not FDA-approved (indication or dose)
NFR = nelfinavir
NNRTI = non-nucleoside reverse transcriptase inhibitor
NRTI = nucleoside reverse transcriptase inhibitor
NSAIDs = non-steroidal
NUS = not available in the U.S.
NVP = nevirapine
O Ceph 1, 2, 3 = oral cephalosporins
Oflox = ofloxacin
P Ceph 1, 2, 3, 4 = parenteral cephalosporins
P Ceph 3 AP = parenteral cephalosporins with antipseudomonal activity
PCR = polymerase chain reaction
PEP = post-exposure prophylaxis
PI = protease inhibitor
PIP-TZ = piperacillin-tazobactam
po = oral dosing
PQ = primaquine
PRCT = Prospective randomized controlled trials
PTLD = post-transplant lymphoproliferative disease
Pts = patients
Pyri = pyrimethamine
PZA = pyrazinamide

ABBREVIATIONS (2)

qid = 4x per day
QS = quinine sulfate
Quinu-dalfo = **Q-D** = quinupristin-dalfopristin
q[x]h = every [x] hours, e.g., q8h = every 8 hrs
q wk = dose weekly
R = resistant
RFB = rifabutin
RFP = rifapentine
Rick = Rickettsia
RIF = rifampin
RSV = respiratory syncytial virus
RTI = respiratory tract infection
RTV = ritonavir
rx = treatment
SA = Staph. aureus **sc** = subcutaneous
SD = serum drug level after single dose
Sens = sensitive (susceptible)
SM = streptomycin
SOV = saquinavir
SS = steady state serum level
STD = sexually transmitted disease
subcut = subcutaneous
Sulb = sulbactam
Sx = symptoms
Tazo = tazobactam
TBc = tuberculosis
TDF = tenofovir
TEE = transesophageal echocardiography
Teico = teicoplanin
Telithro = telithromycin
Tetra = tetracycline
tid = 3x per day
TMP-SMX = trimethoprim-sulfamethoxazole
TNF = tumor necrosis factor
Tobra = tobramycin
TPV = tipranavir
TST = tuberculin skin test
UTI = urinary tract infection
Vanco = vancomycin
VISA = vancomycin intermediately resistant S. aureus
VL = viral load
Vorl = voriconazole
VZV = varicella-zoster virus
ZDV = zidovudine

ABBREVIATIONS OF JOURNAL TITLES

AAC: Antimicrobial Agents & Chemotherapy
Adv PID: Advances in Pediatric Infectious Diseases
AHJ: American Heart Journal
AIDS Res Hum Retrovir: AIDS Research & Human Retroviruses
AJG: American Journal of Gastroenterology
AJM: American Journal of Medicine
AJRCCM: American Journal of Respiratory Critical Care Medicine
AJTMH: American Journal of Tropical Medicine & Hygiene
Aliment Pharmacol Ther: Alimentary Pharmacology & Therapeutics
Am J Hlth Pharm: American Journal of Health-System Pharmacy
Amer J Transpl: American Journal of Transplantation
AnEM: Annals of Emergency Medicine
AnIM: Annals of Internal Medicine
Ann Pharmacother: Annals of Pharmacotherapy
AnSurg: Annals of Surgery
Antivir Ther: Antiviral Therapy
ArDerm: Archives of Dermatology
ArIM: Archives of Internal Medicine
ARRD: American Review of Respiratory Disease
BMJ: British Medical Journal
BMT: Bone Marrow Transplantation
Brit J Derm: British Journal of Dermatology
Can JID: Canadian Journal of Infectious Diseases
Canad Med J: Canadian Medical Journal
CCM: Critical Care Medicine
CCTID: Current Clinical Topics in Infectious Disease
CDBSR: Cochrane Database of Systematic Reviews
CID: Clinical Infectious Diseases
Clin Micro Inf: Clinical Microbiology and Infection
CMN: Clinical Microbiology Newsletter
Clin Micro Rev: Clinical Microbiology Reviews
CMAJ: Canadian Medical Association Journal
COID: Current Opinion in Infectious Disease
Curr Med Res Opin: Current Medical Research and Opinion
Derm Ther: Dermatologic Therapy
Dermatol Clin: Dermatologic Clinics
Dig Dis Sci: Digestive Diseases and Sciences
DMID: Diagnostic Microbiology and Infectious Disease
EID: Emerging Infectious Diseases
EJCMID: European Journal of Clin. Micro. & Infectious Diseases
Eur J Neurol: European Journal of Neurology
Exp Mol Path: Experimental & Molecular Pathology
Exp Rev Antl Infect Ther: Expert Review of Anti-Infective Therapy
Gastro: Gastroenterology
Hpt: Hepatology
ICHE: Infection Control and Hospital Epidemiology
IDC No. Amer: Infectious Disease Clinics of North America
IDCP: Infectious Diseases in Clinical Practice
IJAA: International Journal of Antimicrobial Agents
Inf Med: Infections in Medicine
J AIDS & HR: Journal of AIDS and Human Retrovirology
J All Clin Immun: Journal of Allergy and Clinical Immunology
J Am Ger Soc: Journal of the American Geriatrics Society
J Chemother: Journal of Chemotherapy
J Clin Micro: Journal of Clinical Microbiology
J Clin Virol: Journal of Clinical Virology
J Derm Treat: Journal of Dermatological Treatment
J Hpt: Journal of Hepatology
J Inf: Journal of Infection
J Med Micro: Journal of Medical Microbiology
J Micro Immunol Inf: Journal of Microbiology, Immunology, & Infection
J Ped: Journal of Pediatrics
J Viral Hep: Journal of Viral Hepatitis
JAC: Journal of Antimicrobial Chemotherapy
JACC: Journal of American College of Cardiology
JAIDS: JAIDS Journal of Acquired Immune Deficiency Syndromes
JAMA: Journal of the American Medical Association
JAVMA: Journal of the Veterinary Medicine Association
JCI: Journal of Clinical Investigation
JCM: Journal of Clinical Microbiology
JIC: Journal of Infection and Chemotherapy
JID: Journal of Infectious Diseases
JNS: Journal of Neurosurgery
JTMH: Journal of Tropical Medicine and Hygiene
Ln: Lancet
LnID: Lancet Infectious Disease
Mayo Clin Proc: Mayo Clinic Proceedings
Med Lett: Medical Letter
Med Mycol: Medical Mycology
MMWR: Morbidity & Mortality Weekly Report
NEJM: New England Journal of Medicine
Neph Dial Transpl: Nephrology Dialysis Transplantation
OFID: Open Forum Infectious Diseases
Ped Ann: Pediatric Annals
Peds: Pediatrics
Pharmacother: Pharmacotherapy
PIDJ: Pediatric Infectious Disease Journal
OJM: Quarterly Journal of Medicine
Scand J Inf Dis: Scandinavian Journal of Infectious Diseases
Sem Resp Inf: Seminars in Respiratory Infections
SGO: Surgery Gynecology and Obstetrics
SMJ: Southern Medical Journal
Surg Neurol: Surgical Neurology
Transpl Inf Dis: Transplant Infectious Diseases
Transpl: Transplantation
TRSM: Transactions of the Royal Society of Medicine

TABLE 1 – CLINICAL APPROACH TO INITIAL CHOICE OF ANTIMICROBIAL THERAPY*

Treatment based on presumed site or type of infection. In selected instances, treatment and prophylaxis based on identification of pathogens. Regimens should be reevaluated based on pathogen isolated, antimicrobial susceptibility determination, and individual host characteristics. *(Abbreviations on page 2)*

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
ABDOMEN: *See Peritoneum, page 46; Gallbladder, page 17; and Pelvic Inflammatory Disease, page 26*				
BONE: Osteomyelitis. Microbiologic diagnosis is essential. If blood culture negative, need culture of bone *(Eur J Clin Microbiol Infect Dis 33:371, 2014)*. Culture of sinus tract drainage not predictive of bone culture. For comprehensive review of antimicrobial penetration into bone, *see Clinical Pharmacokinetics 48:89, 2009.*				
Hematogenous Osteomyelitis *(see IDSA guidelines for vertebral osteo: CID July 29, 2015)*				
Empiric therapy—Collect bone and blood cultures before empiric therapy				
Newborn (<4 mos.)	S. aureus, Gm-neg. bacilli, Group B strep, Kingella kingae in children	**MRSA possible: Vanco + (Ceftaz or CFP)**	**MRSA unlikely:** (**Nafcillin** or **oxacillin**) + (**Ceftaz or CFP**)	Severe allergy or toxicity: (**Linezolid**[NAI] 10 mg/kg IV/po q8h + **aztreonam**).
Children (>4 mos.) — Adult: Osteo of extremity *(NEJM 370:352, 2014)*	S. aureus, Group A strep, Gm-neg. bacilli rare, Kingella kingae in children	**MRSA possible: Vanco** 40 mg/kg/day div q6h	**MRSA unlikely: (Nafcillin or oxacillin)** 150 mg/kg/day div q6h (max 12 gm)	Severe allergy or toxicity: **Clinda** or **TMP-SMX** or **linezolid**[NAI]. Adults: **ceftaz** 2 gm IV q8h, **CFP** 2 gm IV q12h. *See Table 10B for adverse reactions to drugs.*
		Add **Ceftaz or CFP** if Gm-neg. bacilli on Gram stain **Adult doses below.**		
Adult (>21 yrs) **Vertebral osteo ± epidural abscess** *(see IDSA guidelines for vertebral osteo: CID 61:859, 2015)* **Blood & bone cultures essential.**	S. aureus most common but variety other organisms. In Turkey: Brucella & M.TBc common	**MRSA possible: Vanco** 15-20 mg/kg IV q 8-12h for trough of 15-20 µg/mL + (**Ceftriaxone** 2 gm q24h OR **CFP** 2 gm q8h OR **Levo** 750 mg q24h)	**MRSA unlikely: Nafcillin** OR **oxacillin** 2 gm IV q4h + (**Ceftriaxone** 2 gm q24h OR **CFP** 2 gm q8h OR **Levo** 750 mg q24h)	**Dx: MRI diagnostic test of choice, indicated to rule out epidural abscess.** For comprehensive review of vertebral osteomyelitis *see NEJM 362:11, 2010.* Whenever possible empirical therapy should be administered after cultures are obtained.
Specific therapy—Culture and in vitro susceptibility results known. *See CID Jul 29, 2015 for IDSA Guidelines*				
	MSSA	**Nafcillin** or **oxacillin** 2 gm IV q4h or **cefazolin** 2 gm IV q8h	**Vanco** 15-30 mg/kg IV q 8-12h for trough of 15-20 µg/mL OR **Dapto** 6-8 mg/kg IV q24h OR **Linezolid** 600 mg IV/po q12h	**Other options if susceptible In vitro and allergy/toxicity issues *(see NEJM 362:11, 2010):*** 1) **TMP-SMX** 8-10 mg/kg/d po/IV div q8h + **RIF** 300-450 mg bid: limited data, particularly for MRSA *(see AAC 53:2672, 2009)*; 2) **Levo** 750 mg po q24h) + **RIF** 600 mg po q24h; 3) **Fusidic acid**[NUS] 500 mg IV q8h + **RIF** 300 mg po bid. *(CID 42:394, 2006)*; 4) **Ceftriaxone** 2 gm IV q24h *(CID 54:585, 2012)(MSSA only):* Duration of therapy: 6 weeks, provided that epidural or paravertebral abscesses can be drained; consider longer course in those with extensive infection or abscess particularly if not amenable to drainage because of increased risk of treatment failure *(OFID Dec 5:1, 2014)* (although data are lacking that this approach improves efficacy versus a 6 wk course) and >8 weeks in patients undergoing device implantation *(CID 60:1330, 2015)*.
	MRSA – *See Table 6, page 82; IDSA Guidelines CID 52:e18-55, 2011; CID 52:285-92, 2011*	**Vanco** 15-20 mg/kg IV q 8-12h for trough of 15-20 µg/mL + **RIF** 300-450 mg bid.	**Linezolid** 600 mg q12h IV/po ± **RIF** 300 mg po/IV bid OR **Dapto** 6 mg/kg q24h IV + **RIF** 300-450 mg po/IV bid	

* **DOSAGES SUGGESTED are for adults (unless otherwise indicated) with clinically severe (often life-threatening) infections. Dosages also assume normal renal function, and not severe hepatic dysfunction.**

§ **ALTERNATIVE THERAPY INCLUDES these considerations: allergy, pharmacology/pharmacokinetics, compliance, costs, local resistance profiles.**

TABLE 1 (2)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
BONE *(continued)*				
Hemoglobinopathy: Sickle cell/thalassemia	Salmonella; other Gm-neg. bacilli	**CIP** 400 mg IV q12h OR **CIP** 750 mg PO bid	**Levo** 750 mg IV/PO q24h	Thalassemia: transfusion and iron chelation risk factors. Because of decreasing levels of susceptibility to fluoroquinolones among Salmonella spp. and growing resistance among other gram-negative bacilli, would add a second agent (e.g., third-generation cephalosporin) until susceptibility test results available. Alternative for salmonella is Ceftriaxone 2 gm IV q24h if nalidixic acid resistant.
Contiguous Osteomyelitis Without Vascular Insufficiency				
Empiric therapy: Get cultures!				
Foot bone osteo due to nail through tennis shoe	P. aeruginosa	**CIP** 750 mg po bid or **Levo** 750 mg po q24h	**Ceftaz** 2 gm IV q8h or **CFP** 2 gm IV q8h	See *Skin—Nail puncture, page 56*. Need debridement to remove foreign body.
Long bone, post-internal fixation of fracture	S. aureus, Gm-neg. bacilli, P. aeruginosa	**Vanco** 15-20 mg/kg q8-12h IV q 8-12h for trough of 15-20 µg/mL + [**ceftaz** or **CFP**]. See *Comment*	**Linezolid** 600 mg IV/po bid[NAI] + (**ceftaz** or **CFP**). See *Comment*	Often necessary to remove hardware after union to achieve eradication. May need revascularization. **Regimens listed are empiric.** Adjust after culture data available. If susceptible Gm-neg. bacillus, **CIP** 750 mg po bid or **Levo** 750 mg po q24h. For other *S. aureus* options: See *Hem. Osteo. Specific Therapy, page 4*.
Osteonecrosis of the jaw	Probably rare adverse reaction to bisphosphonates	Infection may be secondary to bone necrosis and loss of overlying mucosa. Treatment: minimal surgical debridement, chlorhexidine rinses, antibiotics (e.g. PIP-TZ). Evaluate for concomitant actinomycosis, for which specific long-term antibiotic treatment would be warranted *(CID 49:1729, 2009)*.		
Prosthetic joint	*See prosthetic joint, page 33*			
Spinal implant infection	S. aureus, coag-neg staphylococci, gram-neg bacilli	Onset within 30 days: culture, treat for 3 mos *(CID 55:1481, 2012)*.	Onset after 30 days remove implant, culture & treat	*See CID 55:1481, 2012*
Sternum, post-op	S. aureus, S. epidermidis, occasionally, gram-negative bacilli	**Vanco** 15-20 mg/kg q8-12h IV for trough of 15-20 µg/mL recommended for serious infections.	**Linezolid** 600 mg po/IV[NAI] bid	Sternal debridement for cultures & removal of necrotic bone. For *S. aureus* options: *Hem. Osteo. Specific Therapy, page 4*. If setting or gram stain suggests possibility of gram-negative bacilli, add appropriate coverage based on local antimicrobial susceptibility profiles *(e.g., cefepime, PIP-TZ)*.
Contiguous Osteomyelitis With Vascular Insufficiency.				
Most pts are **diabetics** with peripheral neuropathy & infected skin ulcers *(see Diabetic foot, page 16)*	Polymicrobic [Gm+ cocci (to include MRSA) (aerobic & anaerobic) and Gm-neg. bacilli (aerobic & anaerobic)]	Debride overlying ulcer & submit bone for histology & culture. Select antibiotic based on culture results & treat for 6 weeks. **No empiric therapy unless acutely ill.** If acutely ill, *see suggestions, Diabetic foot, page 16*. Revascularize if possible.		**Diagnosis of osteo:** Culture bone biopsy (gold standard). Poor concordance of culture results between swab of ulcer and bone – need bone. *(CID 42:57, 63, 2006)*. Sampling by needle puncture inferior to biopsy *(CID 48:888, 2009)*. Osteo more likely if ulcer >2 cm^2, positive probe to bone, ESR >70 & abnormal plain x-ray *(JAMA 299:806, 2008)*. **Treatment:** (1) **Revascularize if possible;** (2) Culture bone; (3) Specific antimicrobial(s). Reviews: *BMJ 339:b4905, 2006; Plast Reconstr Surg 117: (7 Suppl) 2125, 2006*.
Chronic Osteomyelitis: Specific therapy By definition, implies presence of dead bone. **Need valid cultures**	S. aureus, Enterobacteriaceae, P. aeruginosa	**Empiric rx not indicated.** Base systemic rx on results of culture, sensitivity testing. If acute exacerbation of chronic osteo, rx as acute hematogenous osteo. Surgical debridement important.		**Important adjuncts:** removal of orthopedic hardware, surgical debridement; vascularized muscle flaps, distraction osteogenesis (Ilizarov) techniques. Antibiotic-impregnated cement & hyperbaric oxygen adjunctive. **NOTE: RIF + (vanco or β-lactam)** effective in animal model and in a clinical trial of S. aureus chronic osteo. The contribution of rifampin-containing regimens in this setting is not clear, however *(AAC 53:2672, 2009)*.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (3)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
BREAST: Mastitis—Obtain culture; need to know if MRSA present. Review with definitions: Review of breast infections: *BMJ 342:d396, 2011.*				
Postpartum mastitis *(Recent Cochrane Review: Cochrane Database Syst Rev 2013 Feb 28;2:CD005458; see also CID 54:71, 2012)*				
Mastitis without abscess	S. aureus; less often S. pyogenes (Gp A or B), E. coli, bacteroides species, maybe Corynebacterium sp., & selected coagulase-neg. staphylococci (e.g., S. lugdunensis)	**NO MRSA: Outpatient: Dicloxacillin** 500 mg po qid or **cephalexin** 500 mg po qid. **Inpatient: Nafcillin/oxacillin** 2 gm IV q4-6h	**MRSA Possible: Outpatient: TMP-SMX-DS** tabs 1-2 po bid or, if susceptible, **clinda** 300 mg po tid **Inpatient: Vanco** 1 gm IV q12h; if over 100 kg, 1.5 gm IV q12h.	If no abscess & controllable pain, ↑ freq of nursing may hasten response.
Mastitis with abscess				For painful abscess I&D is standard; needle aspiration reported successful. Resume breast feeding from affected breast as soon as pain allows. *(Breastfeed Med 9:239, 2014)*
Non-puerperal mastitis with abscess	S. aureus; less often Bacteroides sp., peptostreptococcus, & selected coagulase-neg. staphylococci	*See regimens for Postpartum mastitis, page 6.*		Smoking and diabetes may be risk factors *(BMJ 342:d396, 2011)*. **If subareolar & odoriferous**, most likely anaerobes; need to **add metro** 500 mg IV/po tid. If not subareolar, staph. Need pretreatment aerobic/anaerobic cultures. Surgical drainage for abscess. **I&D standard.** Corynebacterium sp. assoc. with chronic granulomatous mastitis *(JCM 53:2895, 2015)*. **Consider TB in chronic infections.**
Breast implant infection	Acute: *S. aureus, S. pyogenes*. TSS reported. Chronic: Look for rapidly growing Mycobacteria	Acute: **Vanco** 15-20 mg/kg IV q8-12h.	Chronic: Await culture results. *See Table 12A* for mycobacteria treatment.	*Lancet Infect Dis 5:94, 462, 2005.* Coag-negative staph also common *(Aesthetic Plastic Surg 31:325, 2007).*
CENTRAL NERVOUS SYSTEM				
Brain abscess				
Primary or contiguous source In 51 pts, 30 positive by standard culture; using molecular diagnostics, 80 bacterial taxa & many polymicrobics *(CID 54:202, 2012)*. Review: *NEJM 371:447, 2014*. Mild infection: *NEJM 371:150, 2014.*	Streptococci (60–70%), bacteroides (20–40%), Enterobacteriaceae (25–33%), S. aureus (10–15%), S. anginosus grp. Rare: Nocardia *(below)* Listeria. *See S. aureus Comment*	**P Ceph 3** [(**cefotaxime** 2 gm IV q4h or **ceftriaxone** 2 gm IV q12h) + (**metro** 7.5 mg/kg q6h or 15 mg/kg IV q12h)]	**Pen G** 3-4 million units IV q4h + **metro** 7.5 mg/kg q6h or 15 mg/kg IV q12h	If CT scan suggests cerebritis or abscesses <2.5 cm and pt neurologically stable and conscious, start antibiotics and observe. Otherwise, surgical drainage necessary. If blood cultures or other clinical data do not yield a likely etiologic agent, aspirate even small abscesses for diagnosis if this can be done safely.
		Duration of rx unclear; usually 4-6 wks or until resolution by neuroimaging (CT/MRI)		Experience with Pen G (HD) + metro without ceftriaxone or nafcillin/oxacillin has been good. We use ceftriaxone because of frequency of isolation of Enterobacteriaceae. **S. aureus rare without positive blood culture; if S. aureus, use vanco until susceptibility known.** Strep. anginosus group esp. prone to produce abscess. Ceph/metro does not cover listeria.
Post-surgical, post-traumatic. Review: *NEJM 371:447, 2014.*	S. aureus, Enterobacteriaceae	**For MSSA:** (**Nafcillin** or **oxacillin**) 2 gm IV q4h + (**ceftriaxone** or **cefotaxime**)	**For MRSA: Vanco** 15-20 mg/kg IV q 8-12h for trough of 15-20 mcg/mL + (**ceftriaxone** or **cefotaxime**)	Empirical coverage, de-escalated based on culture results. **Aspiration of abscess usually necessary for dx & rx. If P. aeruginosa suspected, substitute (Cefepime or Ceftazidime) for (Ceftriaxone or Cefotaxime).**
HIV-1 infected (AIDS)	Toxoplasma gondii	*See Table 13A, page 156*		

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (4)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
CENTRAL NERVOUS SYSTEM/Brain abscess *(continued)*				
Nocardia: Haematogenous abscess	N. farcinica, N. asteroides & N. brasiliensis See *AAC 58:795, 2014* for other species.	**TMP-SMX:** 15 mg/kg/day of TMP & 75 mg/kg/day of SMX, IV/po div in 2-4 doses + **Imipenem** 500 mg q6h IV. If multiorgan involvement some add **amikacin** 7.5 mg/kg q12h.	**Linezolid** 600 mg IV or po q12h + meropenem 2 gm q8h	**Linezolid** 600 mg po bid reported effective. For in vitro susceptibility testing: Wallace (+1) 903-877-7680 or U.S. CDC (+1) 404-639-3158. In vitro resistance to TMP-SMX may be increasing *(Clin Infect Dis 51:1445, 2010)*, but whether this is associated with worse outcomes is not known; TMP-SMX remains a drug of choice for CNS nocardia infection. If sulfonamide resistant or sulfa-allergic, **amikacin** plus one of: **IMP**, **MER**, **ceftriaxone** or **cefotaxime**. *N. farcinica* is resistant to third-generation cephalosporins, which should not be used for treatment of infection caused by this organism. If TMP-SMX resistance reported, see *JCM 50:670, 2012* (before stopping TMP-SMX).
		After 3-6 wks of IV therapy, switch to po therapy. Immunocompetent pts: **TMP-SMX**, **minocycline** or **AM-CL** x 3+ months. Immunocompromised pts: Treat with 2 drugs x 1 yr.		
Subdural empyema: In adult 60–90% is extension of sinusitis or otitis media. Rx same as primary brain abscess. Surgical emergency: must drain. Review in *LnID 7:62, 2007.*				
Encephalitis/encephalopathy *IDSA Guideline: CID 47:303, 2008; Intl diagnosis consensus: CID 57:1114, 2013.* *(For Herpes see Table 14A, page 169 and for rabies, Table 20B, page 233)*	H. simplex (42%), VZV (15%), M. TB (15%), Listeria (10%) *(CID 49:1838, 2009)*. Other: arbovirus, West Nile, rabies, Lyme, Parvo B19, Cat-scratch, Mycoplasma, EBV and others.	Start IV **acyclovir** while awaiting results of CSF PCR for H. simplex. For amebic encephalitis *see Table 13A*. Start **Doxy** if setting suggests R. rickettsii, Anaplasma, Ehrlichia or Mycoplasma.		Review of all etiologies: *LnID 10:835, 2010*. **Anti-NMDAR** (N-Methyl-D-Aspartate Receptor) encephalitis: an autoimmune encephalitis, more common than individual viral etiologies as a cause of encephalitis in the California Encephalitis Project cohort *(CID 54:899, 2012)*. Refs: *Chest 145:1143, 2014; J Clin Neuroscience 21:722 & 1169, 2014.*
Meningitis, "Aseptic": Pleocytosis of up to 100s of cells, CSF glucose normal, neg. culture for bacteria *(see Table 14A, page 166)* Ref: *CID 47:783, 2008*	Enteroviruses, HSV-2, LCM, HIV, other viruses, drugs [NSAIDs, metronidazole, carbamazepine, lamotrigine TMP-SMX, IVIG, (e.g., detuximab, infliximab)], rarely leptospirosis	For all but leptospirosis, IV fluids and analgesics. D/C drugs that may be etiologic. For lepto (**doxy** 100 mg IV/po q12h) or (**Pen G** 5 million units IV q6h) or (**AMP** 0.5–1 gm IV q6h). Repeat LP if suspect partially-treated bacterial meningitis. **Acyclovir** 5-10 mg/kg IV q8h sometimes given for HSV-2 meningitis (Note: distinct from HSV encephalitis where early rx is mandatory).		If available, PCR of CSF for enterovirus. HSV-2 unusual without concomitant genital herpes (Mollaret's syndrome). For lepto, positive epidemiologic history and concomitant hepatitis, conjunctivitis, dermatitis, nephritis. For list of implicated drugs: *Inf Med 25:331, 2008.*

**NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (5)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
Meningitis, Bacterial, Acute: Goal is empiric therapy, then CSF exam within 30 min. If focal neurologic deficit, give empiric therapy, then head CT, then LP. *(NEJM 354:44, 2006; Ln ID 10:32, 2010)* **NOTE:** In children, treatment caused CSF cultures to turn neg. in 2 hrs with meningococci & partial response with pneumococci in 4 hrs *(Peds 108:1169, 2001).* For distribution of pathogens by age group, *see NEJM 364:2016, 2011.*				
Empiric Therapy—CSF Gram stain is negative—immunocompetent				
Age: Preterm to <1 mo *LnID 10:32, 2010*	Group B strep 49%, E. coli 18%, listeria 7%, misc. Gm-neg. 10%, misc. Gm-pos. 10%	**AMP** 100 mg/kg IV q6h + **cefotaxime** 50 mg/kg IV q6h	**AMP** 100 mg/kg IV q6h + **gentamicin** 2.5 mg/kg IV q8h Intraventricular treatment not recommended. Repeat CSF exam/culture 24–36 hr after start of therapy	Regimens active vs. Group B strep, most coliforms, & listeria. If premature infant with long nursery stay, S. aureus, enterococci, and resistant coliforms potential pathogens. **Optional empiric regimens (except for listeria): [nafcillin + (ceftazidime or cefotaxime)].** **If high risk of MRSA,** use vanco + cefotaxime. Alter regimen after culture/sensitivity data available.
Age: 1 mo– 50 yrs Hearing loss is most common neurologic sequelae *(LnID 10:32, 2010).*	S. pneumo, meningococci, H. influenzae now uncommon, **listeria unlikely if young adult & immunocompetent** (add **ampicillin** if suspect listeria: 2 gm IV q4h)	Adult dosage: **[(Cefotaxime** 2 gm IV q4–6h OR **ceftriaxone** 2 gm IV q12h)] + (**dexamethasone**) + **vanco**.	**[(MER** 2 gm IV q8h) (Peds: 40 mg/kg IV q8h)] + IV **dexamethasone** + **vanco**[1]	Value of **dexamethasone** shown in children with H. influenzae and adults with S. pneumoniae in some studies *(NEJM 357:2431 & 2441, 2007; LnID 4:139, 2004).* In the Netherlands, adoption of dexamethasone treatment in adult pneumococcal meningitis led to reduced mortality and hearing loss compared with historical control group *(Neurology 75:1533, 2010).* For patients with severe **β-lactam allergy,** *see below (Empiric Therapy—positive gram stain and Specific Therapy)* for alternative therapies.
		Dexamethasone: 0.15 mg/kg IV q6h x 2–4 days. **Give with, or just before, 1st dose of antibiotic to block TNF production** *(see Comment).*		
		See footnote[1] for Vanco Adult dosage and[2] for ped. dosage		
Age: >50 yrs or alcoholism or other **debilitating assoc diseases** or **impaired cellular immunity**	S. pneumo, listeria, Gm-neg. bacilli.	(**AMP** 2 gm IV q4h) + (**ceftriaxone** 2 gm IV q12h or **cefotaxime** 2 gm IV q4-6h) + **vanco** + IV **dexamethasone.**	**MER** 2 gm IV q8h + **vanco** + IV **dexamethasone**. *For severe pen. Allergy, see Comment*	For patients with severe **β-lactam allergy,** *see below (Empiric Therapy—positive gram stain and Specific Therapy)* for alternative agents that can be substituted to cover likely pathogens. LP without CT for patients with altered level of consciousness and non-focal neurological exam associated with earlier treatment and improved outcome *(CID 60:1162, 2015)*
		For vanco dose, *see footnote[1].* **Dexamethasone dose:** 0.15 mg/kg IV q6h x 2–4 days; 1st dose before, or concomitant with, 1st dose of antibiotic.		
Post-neurosurgery Ventriculostomy/lumbar catheter; ventriculoperitoneal (atrial) shunt) or Penetrating trauma w/o basilar skull fracture Ref: intraventricular therapy *(J Micro Immunol & Infect 47:204, 2014)*	S. epidermidis, S. aureus, P. acnes. Facultative and aerobic gram-neg bacilli, including: P. aeruginosa & A. baumannii (may be multi-drug resistant)	**Vanco** (to achieve trough level of 15-20 µg/mL) + (**Cefepime** or **Ceftaz** 2 gm IV q8h)	**Vanco** (to achieve trough level of 15-20 µg/mL) + (**MER** 2 gm IV q8h)	• Remove infected shunt and place external ventricular catheter for drainage or pressure control. • Intraventricular therapy used if the shunt cannot be removed or cultures fail to clear with systemic therapy. Logic for intraventricular therapy: achieve a 10-20 ratio of CSF concentration to MIC of infecting bacteria. Use only preservative-free drug. Clamp/close catheter for 1 hr after dose. For potential toxicities see *CMR 23:858, 2010.* • **Systemically ill patient:** systemic therapy + pathogen-directed intraventricular therapy once culture results are available • **Not systemically ill,** indolent Gram-positive: can D/C systemic vancomycin and treat with daily intraventricular therapy • **Shunt reimplantation:** 1) If coagulase-negative staphylococci, diphtheroids, or P. acnes may internalize shunt after 3 serial CSF cultures are negative, no further systemic therapy needed. 2) For Staph. aureus and Gram-negative bacilli, may internalize shunt after 3 serial CSF cultures are negative and then treat with systemic therapy for an additional week. Ref: *N Engl J Med 362:146, 2010.*
		• **If severe Pen/Ceph allergy,** for possible gram-neg. substitute either: **Aztreonam** 2 gm IV q6-8h or **CIP** 400 mg IV q12h.		
		Intraventricular Rx if IV therapy inadequate or device not removed. Intraventricular daily drug doses: **Adult: Vanco** 10-20 mg; **Amikacin** 30 mg; **Tobra** 5-20 mg; **Gent** 4-8 mg; **Colistin** base activity 3.375 mg once daily. **Polymyxin B** 5 mg; **Peds: Gent** 1-2 mg; **Polymyxin B** 2 mg. *See Comment*		
Trauma with basilar skull fracture	S. pneumoniae, H. influenzae, S. pyogenes	**Vanco** (to achieve trough level of 15-20 µg/mL) + (**Ceftriaxone** 2 gm IV q12h or **Cefotax** 2 gm IV q6h) + [**Dexamethasone** 0.15 mg/kg IV q6h x 2-4 d (1st dose with or before 1st antibiotic dose)]. *See Clin Micro Rev 21:519, 2008.*		

[1] **Vanco adult dose:** 15-20 mg/kg IV q8 -12h to achieve trough level of 15-20 µg/mL

[2] **Dosage of drugs used to treat children ≥1 mo of age: Cefotaxime** 50 mg/kg per day IV q6h; **ceftriaxone** 50 mg/kg IV q12h; **vanco** 15 mg/kg IV q6h to achieve trough level of 15-20 µg/mL.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (6)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
CENTRAL NERVOUS SYSTEM/Meningitis, Bacterial, Acute *(continued)*				
Empiric Therapy—Positive CSF Gram stain				
Gram-positive diplococci	S. pneumoniae	(**ceftriaxone** 2 gm IV q12h or **cefotaxime** 2 gm IV q4–6h) + **vanco** 15-20 mg/kg IV q8-12h (to achieve 15-20 µg/mL trough) + timed **dexamethasone** 0.15 mg/kg q6h IV x 2–4 days.		**Alternatives: MER** 2 gm IV q8h or **Moxi** 400 mg IV q24h. **Dexamethasone** does not block penetration of vanco into CSF *(CID 44:250, 2007).*
Gram-negative diplococci	N. meningitidis	(**Cefotaxime** 2 gm IV q4–6h or **ceftriaxone** 2 gm IV q12h)		**Alternatives: Pen G** 4 mill. units IV q4h or **AMP** 2 gm q4h or **Moxi** 400 mg IV q24h or **chloro** 1 gm IV q6h (Chloro less effective than other alternatives: see *JAC 70:979, 2015*)
Gram-positive bacilli or coccobacilli	Listeria monocytogenes	**AMP** 2 gm IV q4h ± **gentamicin** 2 mg/kg IV loading dose then 1.7 mg/kg IV q8h		**If pen-allergic, use TMP-SMX 5 mg/kg q6–8h or MER 2 gm IV q8h**
Gram-negative bacilli	H. influenzae, coliforms, P. aeruginosa	(**Ceftazidime** or **cefepime** 2 gm IV q8h) + **gentamicin** 2 mg/kg IV 1st dose then 1.7 mg/kg IV q8h *(See Comment)*		**Alternatives: CIP** 400 mg IV q8–12h; **MER** 2 gm IV q8h; **Aztreonam** 2 gm IV q6-8h. Consider adding intravenous **Gentamicin** to the **β-lactam** or **CIP** if gram-stain and clinical setting suggest P. aeruginosa or resistant coliforms.
Specific Therapy—Positive culture of CSF with in vitro susceptibility results available.				
H. influenzae	β-lactamase positive	**Ceftriaxone** 2 gm IV q12h (adult), 50 mg/kg IV q12h (peds)		**Pen. allergic: Chloro** 12.5 mg/kg IV q6h (max. 4 gm/day.) (Chloro less effective than other alternatives: see *JAC 70:979, 2015*); **CIP** 400 mg IV q8-12h; **Aztreonam** 2 gm q6-8h.
Listeria monocytogenes *(CID 43:1233, 2006)*		**AMP** 2 gm IV q4h ± **gentamicin** 2 mg/kg IV loading dose, then 1.7 mg/kg IV q8h		**Pen. allergic: TMP-SMX** 20 mg/kg per day div. q6–12h. **Alternative: MER** 2 gm IV q8h. Success reported with **linezolid** + **RIF** *(CID 40:907, 2005)* after AMP rx for brain abscess with meningitis.
N. meningitidis	Pen MIC 0.1–1 mcg per mL	**Ceftriaxone** 2 gm IV q12h x 7 days *(see Comment)*; if β-lactam allergic, **chloro** 12.5 mg/kg (up to 1 gm) IV q6h (Chloro less effective than other alternatives: *see JAC 70:979, 2015*)		Rare isolates chloro-resistant. FQ-resistant isolates encountered. **Alternatives: MER** 2 gm IV q8h or **Moxi** 400 mg q24h.
S. pneumoniae **NOTES:** 1. Assumes dexamethasone just prior to 1st dose & x 4 days. 2. If MIC ≥1, repeat CSF exam after 24–48h. 3. Treat for 10–14 days	Pen G MIC <0.1 mcg/mL	**Pen G** 4 million units IV q4h or **AMP** 2 gm IV q4h		**Alternatives: Ceftriaxone** 2 gm IV q12h, **chloro** 1 gm IV q6h (Chloro less effective than other alternatives: *see JAC 70:979, 2015*)
	0.1–1 mcg/mL	**Ceftriaxone** 2 gm IV q12h or **cefotaxime** 2 gm IV q4–6h		**Alternatives: Cefepime** 2 gm IV q8h or **MER** 2 gm IV q8h
	≥2 mcg/mL	**Vanco** 15-20 mg/kg IV q8-12h (15-20 µg/mL trough target) + (**ceftriaxone** or **cefotaxime** as above)		**Alternatives: Moxi** 400 mg IV q24h
	Ceftriaxone MIC ≥1 mcg/mL	**Vanco** 15-20 mg/kg IV q8-12h (15-20 µg/mL trough target) + (**ceftriaxone** or **cefotaxime** as above)		**Alternatives: Moxi** 400 mg IV q24h If MIC to ceftriaxone >2 mcg/mL, add **RIF** 600 mg po/IV 1x/day to **vanco** + (**ceftriaxone** or **cefotaxime**).
E. coli, other coliforms, or P. aeruginosa	**Consultation advised**—need susceptibility results	(**Ceftazidime** or **cefepime** 2 gm IV q8h) + **gentamicin** 2 mg/kg IV x 1 dose, then 1.7 mg/kg IV q8h x 21 days. Repeat CSF cultures in 2-4 days.		**Alternatives: CIP** 400 mg IV q8–12h; **MER** 2 gm IV q8h. If pos. CSF culture after 2-4 days, start intraventricular therapy; *see Meningitis, Post-neurosurgery, page 8.*
Prophylaxis for H. influenzae and N. meningitidis				
Haemophilus influenzae type B Household and/or day care contact: residing with index case for ≥4 hrs in a day. Day care contact or same day care facility as index case for 5-7 days before onset		**Children: RIF** 20 mg/kg po (not to exceed 600 mg) q24h x 4 doses. **Adults (non-pregnant): RIF** 600 mg q24h x 4 days		**Household:** If there is one unvaccinated contact age ≤4 yrs in the household, give RIF to all household contacts except pregnant women. **Child Care Facilities:** With 1 case, if attended by unvaccinated children ≤ 2 yrs, consider prophylaxis + vaccinate susceptible. If all contacts >2 yrs: no prophylaxis. If ≥ 2 cases in 60 days & unvaccinated children attend, prophylaxis recommended for children & personnel *(Am Acad Ped Red Book 2006, page 313).*

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (7)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
CENTRAL NERVOUS SYSTEM/Meningitis, Bacterial, Acute/Prophylaxis for H. influenzae and N. meningitides *(continued)*				
Prophylaxis for Neisseria meningitidis exposure (close contact) **NOTE:** CDC reports **CIP-resistant group B meningococcus** from selected counties in N. Dakota & Minnesota. **Avoid CIP**. Use **ceftriaxone**, **RIF**, or single 500 mg dose of **azithro** *(MMWR 57:173, 2008)*.		[**Ceftriaxone** 250 mg IM x 1 dose (child <15 yrs 125 mg IM x 1)] **OR** [**RIF** 600 mg po q12h x 4 doses. (Children ≥1 mo 10 mg/kg po q12h x 4 doses, <1 mo 5 mg/kg q12h x 4 doses)] **OR** If not CIP-resistant, **CIP** 500 mg po x 1 dose (adult)		**Spread by respiratory droplets**, not aerosols, hence close contact req. ↑ risk if close contact for at least 4 hrs during wk before illness onset (e.g., housemates, day care contacts, cellmates) or exposure to pt's nasopharyngeal secretions (e.g., kissing, mouth-to-mouth resuscitation, intubation, nasotracheal suctioning).
Meningitis, chronic Defined as symptoms + CSF pleocytosis for ≥4 wks	MTB cryptococcosis, other fungal, neoplastic, Lyme, syphilis, Whipple's disease	Treatment depends on etiology. No urgent need for empiric therapy, but when TB suspected treatment should be expeditious.		Long list of possibilities: bacteria, parasites, fungi, viruses, neoplasms, vasculitis, and other miscellaneous etiologies—*see Neurol Clin 28:1061, 2010. See NEJM 370:2408, 2014* for diagnosis of neuroleptospirosis by next generation sequencing technologies.
Meningitis, eosinophilic *LnID 8:621, 2008*	Angiostrongyliasis, gnathostomiasis, baylisascaris	Corticosteroids	Not sure anthelmintic therapy works	1/3 lack peripheral eosinophilia. Need serology to confirm diagnosis. Steroid ref.: *LnID 8:621, 2008*. Automated CSF count may not correctly identify eosinophils *(CID 48: 322, 2009)*.
Meningitis, HIV-1 infected (AIDS) *See Table 11, SANFORD GUIDE TO HIV/AIDS THERAPY*	As in adults, >50 yrs: also consider cryptococci, M. tuberculosis, syphilis, HIV aseptic meningitis, Listeria monocytogenes	If etiology not identified: treat as adult >50 yrs + obtain CSF/serum cryptococcal antigen *(see Comments)*	For crypto rx, *see Table 11A, page 127*	C. neoformans most common etiology in AIDS patients. H. influenzae, pneumococci, listeria, TBc, syphilis, viral, histoplasma & coccidioides also need to be considered. Obtain blood cultures.
EAR				
External otitis				
Chronic	Usually 2° to seborrhea	Eardrops: [(**polymyxin B** + **neomycin** + **hydrocortisone** qid) + **selenium sulfide shampoo**]		Control seborrhea with dandruff shampoo containing selenium sulfide (Selsun) or [(ketoconazole shampoo) + (medium potency steroid solution, triamcinolone 0.1%)].
Fungal	Candida species	**Fluconazole** 200 mg po x 1 dose & then 100 mg po x 3-5 days.		
"Necrotizing (malignant) otitis externa" Risk groups: Diabetes mellitus, AIDS, chemotherapy.	Pseudomonas aeruginosa in >95% *(Otol & Neurotology 34:620, 2013)*	**CIP** 400 mg IV q8h; 750 mg po q8-12h only for early disease	**PIP-TZ** 3.375 gm q4h or extended infusion (3.375 gm over 4 hrs q8h) + **Tobra**	Very high ESRs are typical. Debridement usually required. R/O osteomyelitis: CT or MRI scan. If bone involved, treat for 6–8 wks. Other alternatives if P. aeruginosa is susceptible: **IMP** 0.5 gm q6h or **MER** 1 gm IV q8h or **CFP** 2 gm IV q12h or **Ceftaz** 2 gm IV q8h.
"Swimmer's ear"; occlusive devices (earphones); contact dermatitis; psoriasis *Otolaryngol Head Neck Surg 150:51, 2014*	Acute infection usually 2° S. aureus (11%); other: Pseudomonas (11%), Anaerobes (2%), S. epidermidis (46%), candida (8%)	Mild: eardrops: **acetic acid** + **propylene glycol** + **HC** (**Vosol HC**) 5 gtts 3-4x/day until resolved. Moderate-severe: Eardrops **CIP** + **HC** (**Cipro HC Otic**) 3 gtts bod x 7 days. Alternative: **Finafloxacin** 0.3% otic suspension 4 gtts q12h x 7d (for P. aeruginosa and S. aureus)		Rx includes gentle cleaning. Recurrences prevented (or decreased) by drying with alcohol drops (1/3 white vinegar, 2/3 rubbing alcohol) after swimming, then antibiotic drops or 2% acetic acid solution. Ointments should not be used in ear. Do not use neomycin or other aminoglycoside drops if tympanic membrane punctured.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (8)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE[§]	
EAR *(continued)*				
Otitis media—infants, children, adults ***(Cochrane review: Cochrane Database Syst Rev. Jan 31;1:CD000219, 2013); American Academy of Pediatrics Guidelines: Pediatrics 131:e964, 2013)***				
Acute Two PRDB trials indicate efficacy of antibiotic rx if age < 36 mos & definite AOM *(NEJM 364:105, 116 & 168, 2011)*				
Initial empiric therapy of acute otitis media (AOM) NOTE: Treat children <2 yrs old. If >2 yrs old, afebrile, no ear pain, neg./questionable exam— consider analgesic treatment without antimicrobials. Favorable results in mostly afebrile pts with waiting 48hrs before deciding on antibiotic use *(JAMA 296:1235, 1290, 2006)*	Overall detection in middle ear fluid: No pathogen 4% Virus 70% Bact. + virus 66% Bacteria 92% Bacterial pathogens from middle ear: S. pneumo 49%, H. influenzae 29%, M. catarrhalis 28%. Ref.: *CID 43:1417 & 1423, 2006.* Children 6 mos-3 yrs, 2 episodes AOM/yrs & 63% are virus positive *(CID 46:815 & 824, 2008).*	**If NO antibiotics in prior month:** **Amox** po HD[3] For dosage, *see footnote*[4]. **All doses are pediatric** **Duration of rx:** <2 yrs old x 10 days; ≥2 yrs x 5–7 days. Appropriate duration unclear. 5 days may be inadequate for severe disease *(NEJM 347:1169, 2002)* **For adult dosages, see *Sinusitis, page 50, and Table 10A***	**Received antibiotics in prior month:** **Amox** HD[3] or **AM-CL** extra-strength[3] or **cefdinir** or **cefpodoxime** or **cefprozil** or **cefuroxime axetil**	**If allergic to β-lactam drugs?** If history unclear or rash, effective oral ceph OK; avoid ceph if IgE-mediated allergy, e.g., anaphylaxis. High failure rate with **TMP-SMX** if etiology is DRSP or H. influenzae; macrolides have limited efficacy against S. pneumo and H. influenza. **Up to 50% S. pneumo resistant to macrolides.** **Spontaneous resolution occurred in:** 90% pts infected with M. catarrhalis, 50% with H. influenzae, 10% with S. pneumoniae; overall 80% resolve within 2–14 days *(Ln 363:465, 2004).* Risk of DRSP ↑ if age <2 yrs, antibiotics last 3 mos, &/or daycare attendance. Selection of drug based on (1) effectiveness against β-lactamase producing H. influenzae & M. catarrhalis & (2) effectiveness against S. pneumo, inc. DRSP. **Cefaclor, loracarbef, & ceftibuten less active vs. resistant S. pneumo.** than other agents listed. No benefit of antibiotics in treatment of otitis media with effusion *(Cochrane Database Syst Rev. Sep 12:9:CD009163, 2012).* For persistent otorrhea with PE tubes, hydrocortisone/bacitracin/colistin eardrops[NUS] 5 drops tid x 7 d more effective than po AM-CL *(NEJM:370:723, 2014).*
Treatment for clinical failure after 3 days	Drug-resistant S. pneumoniae main concern	**NO antibiotics in month prior to last 3 days:** **AM-CL** high dose or **cefdinir** or **cefpodoxime** or **cefprozil** or **cefuroxime axetil** or IM **ceftriaxone** x 3 days. *For dosage, see footnote*[4] **All doses are pediatric** Duration of rx as above	**Antibiotics in month prior to last 3 days:** [(IM **ceftriaxone**) or (**clindamycin**) and/or tympanocentesis] *See clindamycin Comments*	**Clindamycin** not active vs. H. influenzae or M. catarrhalis. S. pneumo resistant to macrolides are usually also resistant to clindamycin. Definition of failure: no change in ear pain, fever, bulging TM or otorrhea after 3 days of therapy. Tympanocentesis will allow culture. **Newer FQs active vs. drug-resistant S. pneumo (DRSP), but not approved for use in children *(PIDJ 23:390, 2004).* Vanco is active vs. DRSP.**
After >48hrs of nasotracheal intubation	Pseudomonas sp., klebsiella, enterobacter	**Ceftazidime** or **CFP** or **IMP** or **MER** or (**PIP-TZ**) or **CIP**. *(For dosages, see Ear, Necrotizing (malignant) otitis externa, page 10)*		With nasotracheal intubation >48 hrs, about ½ pts will have otitis media with effusion.

[3] **Amoxicillin UD or HD** = amoxicillin usual dose or high dose; **AM-CL HD** = amoxicillin-clavulanate high dose. **Dosages in footnote[4].** Data supporting amoxicillin HD; *PIDJ 22:405, 2003.*

[4] **Drugs & peds dosage (all po unless specified) for acute otitis media: Amoxicillin UD** = 40 mg/kg per day div q12h or q8h. **Amoxicillin HD** = 90 mg/kg per day div q12h or q8h. **AM-CL HD** = 90 mg/kg per day of amox component. **Extra-strength AM-CL oral suspension** (Augmentin ES-600) available with 600 mg AM & 42.9 mg CL / 5 mL—dose: 90/6.4 mg/kg per day div bid. **Cefuroxime axetil** 30 mg/kg per day div q12h. **Ceftriaxone** 50 mg/kg IM x 3 days. **Clindamycin** 20–30 mg/kg per day div qid (may be effective vs. DRSP but no activity vs. H. influenzae).
Other drugs suitable for drug (e.g., penicillin) - sensitive S. pneumo: TMP-SMX 4 mg/kg of TMP q12h. **Erythro-sulfisoxazole** 50 mg/kg per day of erythro div q6–8h. **Clarithro** 15 mg/kg per day div q12h; **azithro** 10 mg/kg per day x 1 & then 5 mg/kg q24h on days 2–5. Other FDA-approved regimens: 10 mg/kg q24h x 3 days & 30 mg/kg x 1. **Cefprozil** 15 mg/kg q12h; **cefpodoxime proxetil** 10 mg/kg per day as single dose; **cefaclor** 40 mg/kg per day div q8h; **loracarbef** 15 mg/kg q12h. **Cefdinir** 7 mg/kg q12h or 14 mg/kg q24h.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (9)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
EAR, Otitis Media *(continued)*				
Prophylaxis: acute otitis media *J Laryngol Otol 126:874, 2012*	Pneumococci, H. influenzae, M. catarrhalis, Staph. aureus, Group A strep *(see Comments)*	**Sulfisoxazole** 50 mg/kg po at bedtime or **amoxicillin** 20 mg/kg po q24h	**Use of antibiotics to prevent otitis media is a major contributor to emergence of antibiotic-resistant S. pneumo!** Pneumococcal protein conjugate vaccine decreases freq AOM due to vaccine serotypes. Adenoidectomy at time of tympanostomy tubes ↓ need for future hospitalization for AOM *(NEJM 344:1188, 2001).*	
Mastoiditis: Complication of acute or chronic otitis media. If chronic, look for cholesteatoma (Keratoma)				
Acute				
Generally too ill for outpatient therapy. Complication ref: *Otolaryng Clin No Amer 39:1237, 2006*	*1st episode:* S. pneumoniae H. influenzae M. catarrhalis *If secondary to chronic otitis media:* S. aureus P. aeruginosa S. pneumoniae	Obtain cultures, then empiric therapy. 1st episode: **Ceftriaxone** 2 gm IV once daily OR **Levofloxacin** 750 mg IV once daily	Acute exacerbation of chronic otitis media: Surgical debridement of auditory canal, then [**Vancomycin** (dose to achieve tough of 15-20 mcg/mL) + **PIP-TZ** 3.375 gm IV q6h] OR [**Vancomycin** (dose as above) + **Ciprofloxacin** 400 mg IV q8h]	• Diagnosis: CT or MRI • Look for complication: osteomyelitis, supperative lateral sinus thrombophlebitis, purulent meningitis, brain abscess • ENT consultation for possible mastoidectomy • S. aureus *(J Otolaryng Head Neck Surg 38:483, 2009).*
Chronic				
Generally not ill enough for parenteral antibiotics	As per 1st episode and: S. aureus P. aeruginosa Anaerobes Fungi	Culture ear drainage. May need surgical debridement. Topical Fluoroquinolone ear drops. ENT consult.		• Diagnosis: CT or MRI
EYE				
Eyelid: Little reported experience with CA-MRSA *(See Cochrane Database Syst Rev 5:CD005556, 2012)*				
Blepharitis	Etiol. unclear. Factors include Staph. aureus & Staph. epidermidis, seborrhea, rosacea, & dry eye	Lid margin care with baby shampoo & warm compresses q24h. Artificial tears if assoc. dry eye *(see Comment).*	Usually topical ointments of no benefit. If associated rosacea, add doxy 100 mg po bid for 2 wks and then q24h.	
Hordeolum (Stye)				
External (eyelash follicle)	Staph. aureus	Hot packs only. Will drain spontaneously	Infection of superficial sebaceous gland.	
Internal (Meibomian glands): Can be acute, subacute or chronic.	Staph. aureus, MSSA	Oral **dicloxacillin** + hot packs	Also called acute meibomianitis. Rarely drain spontaneously; may need I&D and culture. Role of fluoroquinolone eye drops is unclear: MRSA often resistant to lower conc.; may be susceptible to higher concentration of FQ in ophthalmologic solutions of gati, levo or moxi.	
	Staph. aureus, MRSA-CA	**TMP-SMX-DS**, tabs ii po bid		
	Staph. aureus, MRSA-HA	**Linezolid** 600 mg po bid possible therapy if multi-drug resistant.		
Conjunctiva: *Review: JAMA 310:1721, 2013.*				
Conjunctivitis of the newborn (**ophthalmia neonatorum**): by day of onset post-delivery—all dose pediatric				
Onset 1st day	Chemical due to silver nitrate prophylaxis	None	Usual prophylaxis is erythro ointment; hence, silver nitrate irritation rare.	
Onset 2–4 days	N. gonorrhoeae	**Ceftriaxone** 25–50 mg/kg IV x 1 dose *(see Comment)*, not to exceed 125 mg	Treat mother and her sexual partners. Hyperpurulent. Topical rx inadequate. **Treat neonate for concomitant Chlamydia trachomatis.**	
Onset 3–10 days	Chlamydia trachomatis	**Erythro base or ethylsuccinate syrup** 12.5 mg/kg q6h x 14 days. No topical rx needed.	Diagnosis by NAAT. Alternative: **Azithro suspension** 20 mg/kg po q24h x 3 days. Treat mother & sexual partner.	

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (10)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
EYE/Conjunctiva *(continued)*				
Onset 2–16 days	Herpes simplex types 1, 2	Topical anti-viral rx under direction of ophthalmologist.		Also give Acyclovir 60 mg/kg/day IV div 3 doses *(Red Book online, accessed Jan 2011).*
Ophthalmia neonatorum prophylaxis: **erythro** 0.5% ointment x 1 or **tetra** 1% ointment[NUS] x 1 application; effective vs. gonococcus but not C. trachomatis				
Pink eye (viral conjunctivitis) Usually unilateral	Adenovirus (types 3 & 7 in children, 8, 11 & 19 in adults)	No treatment. If symptomatic, artificial tears may help. (some studies show 2 day reduction of symptoms with steroids; not recommended)		Highly contagious. Onset of ocular pain and photophobia in an adult suggests associated keratitis—rare.
Inclusion conjunctivitis **(adult)** Usually unilateral & concomitant genital infection	Chlamydia trachomatis	**Azithro** 1 g once	**Doxy** 100 mg po bid x 7 days	Oculogenital disease. Diagnosis NAAT. Urine NAAT for both GC & chlamydia. Treat sexual partner. May need to repeat dose of azithro.
Trachoma —a chronic bacterial keratoconjunctivitis linked to poverty	Chlamydia trachomatis	**Azithro** 20 mg/kg po single dose—78% effective in children; Adults: 1 gm po.	**Doxy** 100 mg po bid x minimum of 21 days or **tetracycline** 250 mg po qid x 14 days.	Starts in childhood and can persist for years with subsequent damage to cornea. Topical therapy of marginal benefit. Avoid doxy/tetracycline in young children. Mass treatment works *(NEJM 358:1777 & 1870, 2008; JAMA 299:778, 2008).*
Suppurative conjunctivitis, bacterial: Children and Adults (Eyedrops speed resolution of symptoms: *Cochrane Database Syst Rev. Sep 12;9:CD001211, 2012*)				
JAMA 310:1721, 2013	Staph. aureus, S. pneumoniae, H. influenzae, Viridans Strep., Moraxella sp.	FO ophthalmic solns: **CIP** (generic); others expensive (**Besi, Levo, Moxi**) All 1–2 gtts q2h while awake 1st 2 days, then q4–8h up to 7 days.	**Polymyxin B + trimethoprim** solution 1–2 gtts q3–6h x 7–10 days.	**FQs** best spectrum for empiric therapy. High concentrations ↑ likelihood of activity vs. S. aureus—even MRSA. **TMP** spectrum may include MRSA. Polymyxin B spectrum only Gm-neg. bacilli but no ophthal. prep of only **TMP**. Most S. pneumo resistant to **gent** & tobra.
Gonococcal (peds/adults)	N. gonorrhoeae	**Ceftriaxone** 25-50 mg/kg IV/IM (not to exceed 125 mg) as one dose in children; 1 gm IM/IV as one dose in adults		
Cornea (keratitis): Usually serious and often sight-threatening. Prompt ophthalmologic consultation essential for diagnosis, antimicrobial and adjunctive therapy! Herpes simplex most common etiology in developed countries; bacterial and fungal infections more common in underdeveloped countries.				
Viral				
H. simplex	H. simplex, types 1 & 2	**Trifluridine** ophthalmic sol'n, one drop q2h up to 9 drops/day until re-epithelialized, then one drop q4h up to 5x/day, for total not to exceed 21 days. See *Comment*	**Ganciclovir** 0.15% ophthalmic gel: Indicated for acute herpetic keratitis. One drop 5 times per day while awake until corneal ulcer heals; then, one drop three times per day for 7 days. **Vidarabine** ointment— useful in children. Use 5x/day for up to 21 days (currently listed as discontinued in U.S.).	Approx 30% recurrence rate within one year; consider prophylaxis with acyclovir 400 mg bid for 12 months to prevent recurrences *(Arch Ophthal 130:108, 2012).* Severe infection or immunocompromised host, consider adding **acyclovir** 400 mg po tid.
Varicella-zoster ophthalmicus	Varicella-zoster virus	**Famciclovir** 500 mg po tid or **valacyclovir** 1 gm po tid x 10 days	**Acyclovir** 800 mg po 5x/day x 10 days	Clinical diagnosis most common: dendritic figures with fluorescein staining in patient with varicella-zoster of ophthalmic branch of trigeminal nerve.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (11)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
EYE/Cornea (keratitis) *(continued)*				
Bacterial		**All treatment listed for bacterial, fungal, protozoan is topical unless otherwise indicated**		
Acute: No comorbidity	*S. aureus, S. pneumo., S. pyogenes, Haemophilus sp.*	**Moxi:** ophthalmic 0.5%: 1 drop q1h for the first 48h then taper according to response	**CIP** 0.3% ophthat or **Levo** 0.5% ophthal. 1-2 gtts/hr x 24-72 hrs, then taper	Regimens vary: some start rx by appling drops q5 min for 5 doses; some apply drops q15-30 min for several hours; some extend interval to q2h during sleep. In a clinical trial, drops were applied q1h for 48-72h, then q2h through day 6; then q2h during waking hours on days 7-9; then q6h until healing *(Cornea 29:751, 2010)*. **Note:** despite high concentrations, may fail vs. MRSA. Prior use of fluoroquinolones associated with increased MICs (*JAMA Ophthalmol. 131:310, 2013)*; high MICs associated with poorer outcome *(Clin Infect Dis 54:1381, 2012)*.
Contact lens users	P. aeruginosa	**CIP** 0.3% ophthalmic solution or **Levo** 0.5% ophthalmic solution 1-2 gtts hourly x24-72h, taper based on response.	**Gent** or **Tobra** 0.3% ophthalmic solution 1-2 gtts hourly x24h then taper based on clinical response.	Recommend alginate swab culture and susceptibility testing; refer to ophthalmologist. **Cornea abrasions:** treated with Tobra, Gent, or CIP gtts qid for 3-5 days; referral to ophthalmologist recommended cornea infiltrate or ulcer, visual loss, lack of improvement or worsening symptoms *(Am Fam Physician. 87:114, 2013)*.
Dry cornea, diabetes, immunosuppression	Staph. aureus, S. epidermidis, S. pneumoniae, S. pyogenes, Enterobacteriaceae, listeria	**CIP** 0.3% ophthalmic solution 1-2 gtts hourly x24–72 hrs, then taper based on clinical response.	**Vanco** (50 mg/mL) + **Ceftaz** (50 mg/mL) hourly for 24-72h, taper depending upon response. *See Comment.*	Specific therapy guided by results of alginate swab culture.
Fungal	Aspergillus, fusarium, candida and others.	**Natamycin** (5%): 1 drop every 1-2 h for several days; then q3-4h for several days; can reduce frequency depending upon response.	**Amphotericin B** (0.15%): 1 drop every 1-2 hours for several days; can reduce frequency depending upon response.	Obtain specimens for fungal wet mount and cultures. Numerous other treatment options (1% topical Itra for 6 wks, oral Itra 100 mg bid for 3 wks, topical voriconazole 1% hourly for 2 wks, topical miconazole 1% 5x a day, topical silver sulphadiazine 0.5-1.0% 5x a day) appear to have similar efficacy *(Cochrane Database Syst Rev 2:004241, 2012)*
Mycobacteria: Post-refractive eye surgery	*M. chelonae; M. abscessus*	**Moxi** eye drops: 1 gtt qid, probably in conjunction with other active antimicrobials		Alternative: systemic rx: Doxy 100 mg po bid + Clarithro 500 mg po bid *(PLoS One 10:doi16236, 2015)*.
Protozoan Soft contact lens users. Ref: *CID 35:434, 2002.*	Acanthamoeba, sp.	Optimal regimen uncertain. Suggested regimen: [(**Chlorhexidine** 0.02% or Polyhexamethylene biguanide 0.02%) + (Propamidine isethionate 0.1% or Hexamidine 0.1%)] drops. Apply one drop every hour for 48h, then one drop every hour only while awake for 72h, then one drop every two hours while awake for 3-4 weeks, then reducing frequency based on response *(Ref: Am J Ophthalmol 148:487, 2009; Curr Op Infect Dis 23:590, 2010)*.		Uncommon. Trauma and soft contact lenses are risk factors. To obtain suggested drops: Leiter's Park Ave Pharmacy (800-292-6773; *www.leiterrx.com)*. Cleaning solution outbreak: *MMWR 56: 532, 2007.*

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (12)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
EYE/Cornea (keratitis) *(continued)*				
Lacrimal apparatus				
Canaliculitis	Actinomyces Staph., Strept. Rarely, Arachnia, fusobacterium, nocardia, candida	Remove granules & irrigate with **pen G** (100,000 mcg/mL)	If fungi, irrigate with **nystatin** approx. 5 mcg/mL: **1** gtt **lid**	Digital pressure produces exudate at punctum; Gram stain confirms diagnosis. Hot packs to punctal area qid. M. chelonae reported after use of intracanalic plugs *(Ophth Plast Reconstr Surg 24: 241, 2008).*
		Child: AM-CL or **cefprozil or cefuroxime.**		
Dacryocystitis (lacrimal sac)	S. pneumo, S. aureus, H. influenzae, S. pyogenes, P. aeruginosa	Often consequence of obstruction of lacrimal duct. Empiric systemic antimicrobial therapy based on Gram stain of aspirate—*see Comment.*		Need ophthalmologic consultation. Surgery may be required. Can be acute or chronic. Culture to detect MRSA.
Endophthalmitis: Endogenous (secondary to bacteremia or fungemia) and exogenous (post-injection, post-operative) types				
Bacterial; Haziness of vitreous key to diagnosis. Needle aspirate of both vitreous and aqueous humor for culture prior to therapy. Intravitreal administration of antimicrobials essential.				
Postocular surgery (cataracts)				
Early, acute onset (incidence 0.05%)	S. epidermidis 60%, Staph. aureus, streptococci, & enterococci each 5–10%, Gm-neg. bacilli 6%	**Immediate ophthal. consult.** If only light perception or worse, immediate vitrectomy + intravitreal vanco 1 mg & intravitreal ceftazidime 2.25 mg. No clear data on intravitreal steroid. May need to repeat intravitreal antibiotics in 2–3 days. Can usually leave lens in. Adjunctive systemic antibiotics (e.g., Vancomycin, Ceftazidime, Moxifloxacin or Gatifloxacin[NUS]) not of proven value, but recommended in endogenous infection.		
Low grade, chronic	Propionibacterium acnes, S. epidermidis, S. aureus (rare)	Intraocular **vanco**. Usually requires vitrectomy, lens removal.		
Post filtering blebs for glaucoma	Strep. species (viridans & others), H. influenzae	Intravitreal agent (e.g., **Vanco** 1 mg + **Ceftaz** 2.25 mg) and a topical agent. Consider a systemic agent such as **Amp-Sulb** or **Cefuroxime** or **Ceftaz** (add **Vanco** if MRSA is suspected)		
Post-penetrating trauma	Bacillus sp., S. epiderm.	Intravitreal agent as above + systemic **clinda** or **vanco**. Use topical antibiotics post-surgery (tobra & cefazolin drops).		
None, suspect hematogenous	S. pneumoniae, N. meningilidis, Staph. aureus, Grp B Strep, K. pneumo	(**cefotaxime** 2 gm IV q4h or **ceftriaxone** 2 gm IV q24h) + **vanco** 30-60 mg/kg/day in 2-3 div doses to achieve target trough serum concentration of 15-20 mcg/mL pending cultures. Intravitreal antibiotics as with early post-operative.		
IV heroin abuse	Bacillus cereus, Candida sp.	Intravitreal agent + systemic agent based on etiology and antimicrobial susceptibility.		
Mycotic (fungal): Broad-spectrum antibiotics, often corticosteroids, indwelling venous catheters	Candida sp., Aspergillus sp.	Intravitreal **ampho B** 0.005–0.01 mg in 0.1 mL. *Also see Table 11A, page 125 for concomitant systemic therapy. See Comment.*		Patients with *Candida* spp. chorioretinitis usually respond to systemically administered antifungals *(Clin Infect Dis 53:262, 2011).* Intravitreal amphotericin and/or vitrectomy may be necessary for those with vitritis or endophthalmitis *(Br J Ophthalmol 92:466, 2008; Pharmacotherapy 27:1711, 2007).*
Retinitis				
Acute retinal necrosis	Varicella zoster, Herpes simplex	IV **acyclovir** 10–12 mg/kg IV q8h x 5–7 days, then 800 mg po 5x/day x 6 wks		Strong association of VZ virus with atypical necrotizing herpetic retinopathy.
HIV+ (AIDS) CD4 usually <100/mm^3	Cytomegalovirus	*See Table 14A, page 168*		Occurs in 5–10% of AIDS patients

**NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (13)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE[5]	
EYE/Retinitis *(continued)*				
Progressive outer retinal necrosis	VZV, H. simplex, CMV (rare)	**Acyclovir** 10-12 mg/kg IV q8h for 1-2 weeks, then (**valacyclovir** 1000 mg po tid, or **famciclovir** 500 mg po tid, or **acyclovir** 800 mg po tid). Ophthalmology consultation imperative: approaches have also included intra-vitreal injection of anti-virals (foscarnet, ganciclovir implant). In rare cases due to CMV use **ganciclovir/valganciclovir** *(see CMV retinitis, Table 14A).*		Most patients are highly immunocompromised (HIV with low CD4 or transplantation). In contrast to Acute Retinal Necrosis, lack of intraocular inflammation or arteritis. May be able to stop oral antivirals when CD4 recovers with ART *(Ocul Immunol Inflammation 15:425, 2007).*
Orbital cellulitis *(see page 54 for erysipelas, facial)*	S. pneumoniae, H. influenzae, M. catarrhalis, S. aureus, anaerobes, group A strep, occ. Gm-neg. bacilli post-trauma	**Vancomycin** 15-20 mg/kg IV q8-12h (target **vancomycin** trough serum concentrations of 15-20 µg/mL) + ([**Ceftriaxone** 2 gm IV q24h + **Metronidazole** 1 gm IV q12h] OR **PIP-TZ** 3.375 gm IV q6h		**If penicillin/ceph allergy: Vanco** + **levo** 750 mg IV once daily + **metro** IV. Problem is frequent inability to make microbiologic diagnosis. Image orbit (CT or MRI). Risk of cavernous sinus thrombosis. If vanco intolerant, another option for s. aureus is dapto 6 mg/kg IV q24h.
FOOT				
"Diabetic foot"—Two thirds of patients have triad of neuropathy, deformity and pressure-induced trauma. IDSA Guidelines *CID 54:e132, 2012.*				
Ulcer without inflammation	Colonizing skin flora	No antibacterial therapy. Moderate strength evidence for improved healing with biologic skin equivalent or negative pressure wound therapy. Low strength evidence for platelet derived growth factor and silver cream *(AnIM 159:532, 2013).*		**General:** 1. Glucose control, eliminate pressure on ulcer 2. **Assess for peripheral vascular disease** 3. Caution in use of TMP-SMX in patients with diabetes, as many have risk factors for hyperkalemia (e.g., advanced age, reduced renal function, concomitant medications) *(Arch Intern Med 170:1045, 2010).* **Principles of empiric antibacterial therapy:** 1. Obtain culture; cover for MRSA in moderate, more severe infections pending culture data, local epidemiology. 2. Severe limb and/or life-threatening infections require initial parenteral therapy with predictable activity vs. Gm-positive cocci including MRSA, coliforms & other aerobic Gm-neg. rods, & anaerobic Gm-neg. bacilli. 3. **NOTE:** The regimens listed are suggestions consistent with above principles. Other alternatives exist & may be appropriate for individual patients. 4. Is there an associated osteomyelitis? Risk increased if ulcer area >2 cm^2, positive probe to bone, ESR >70 and abnormal plain x-ray. Negative MRI reduces likelihood of osteomyelitis *(JAMA 299:806, 2008).* MRI is best imaging modality *(CID 47:519 & 528, 2008).*
Mild infection	*S. aureus (assume MRSA), S. agalactiae (Gp B), S. pyogenes predominate*	**Oral therapy:** Diclox or cephalexin or AM-CL (not MRSA) Doxy or TMP-SMX-DS (MRSA) CLINDA (covers MSSA, MRSA, strep) *Dosages in footnote[5]*		
Moderate infection. **Osteomyelitis** *See Comment.*	As above, plus coliforms possible	**Oral:** As above **Parenteral therapy:** [based on prevailing susceptibilities: (**AM-SB** or **PIP-TZ** or **ERTA** or other carbapenem)] plus [**vanco** (or alternative anti-MRSA drug as below) until MRSA excluded]. *Dosages in footnotes[6, 7]*		
Extensive local inflammation plus systemic toxicity.	As above, plus anaerobic bacteria. Role of enterococci unclear.	**Parenteral therapy:** (**Vanco** plus **β-lactam/β-lactamase inhibitor**) or (**vanco** plus [**DORI** or **IMP** or **MER**]). Other alternatives: 1. **Dapto** or **linezolid** for vanco 2. (**CIP** or **Levo** or **Moxi** or **aztreonam**) plus **metronidazole** for β-lactam/β-lactamase inhibitor *Dosages in footnote[7]* **Assess for arterial insufficiency!**		

[5] **TMP-SMX-DS** 1-2 tabs po bid, **minocycline** 100 mg po bid, **Pen VK** 500 mg po qid, (O Ceph 2, 3: **cefprozil** 500 mg po q12h, **cefuroxime axetil** 500 mg po q12h, **cefdinir** 300 mg po q12h or 600 mg po q24h, **cefpodoxime** 200 mg po q12h), **CIP** 750 mg po bid. **Levo** 750 mg po q24h. **Diclox** 500 mg qid. **Cephalexin** 500 mg qid. **AM-CL** 875/125 bid. **Doxy** 100 mg bid. **CLINDA** 300-450 mg tid

[6] **AM-CL-ER** 2000/125 mg po bid, **TMP-SMX-DS** 1-2 tabs po bid, **CIP** 750 mg po bid, **Levo** 750 mg po q24h, **Moxi** 400 mg po q24h, **linezolid** 600 mg po bid.

[7] **Vanco** 1 gm IV q12h, (**parenteral β-lactam/β-lactamase inhibitors**; **AM-SB** 3 gm IV q6h, **PIP-TZ** 3.375 gm IV q6h or 4.5 gm IV q8h or 4 hr infusion of 3.375 gm q8h; **carbapenems: Doripenem** 500 mg (1-hr infusion) q8h, **ERTA** 1 gm IV q24h, **IMP** 0.5 gm IV q6h, **MER** 1 gm IV q8h, **daptomycin** 6 mg per kg IV q24h, **linezolid** 600 mg IV q12h, **aztreonam** 2 gm IV q8h. **CIP** 400 mg IV q12h, **Levo** 750 mg IV q24h, **Moxi** 400 mg IV q24h, **metro** 1 gm IV loading dose & then 0.5 gm IV q6h or 1 gm IV q12h.

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (14)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
FOOT *(continued)*				
Onychomycosis: *See Table 11, page 129, fungal infections*				
Puncture wound: Nail/Toothpick	P. aeruginosa (Nail), S. aureus, Strept (Toothpick)	Cleanse. Tetanus booster. Observe.		*See page 4. 1–2% evolve to osteomyelitis.*
GALLBLADDER				
Cholecystitis, cholangitis, biliary sepsis, or common duct obstruction (partial: 2nd to tumor, stones, stricture). Cholecystitis Ref: *NEJM 358:2804, 2008.*	Enterobacteriaceae 68%, enterococci 14%, bacteroides 10%, Clostridium sp. 7%, rarely candida	(**PIP-TZ** or **AM-SB**) If life-threatening: **IMP** or **MER** or **DORI**	(**P Ceph 3*** + **metro**) or (**Aztreonam*** + **metro**) or (**CIP*** + **metro**) or **Moxi** *Dosages in footnote' on page 16.* * Add vanco for empiric activity vs. enterococci	In severely ill pts, antibiotic therapy complements adequate biliary drainage. 15-30% pts will require decompression: surgical, percutaneous or ERCP-placed stent. Gallbladder bile is culture pos. in 40-60% *(J Infect 51:128, 2005)*. No benefit to continuation of antibiotics after surgery in pts with acute calculous cholecystitis *(JAMA 3312:145, 2014)*.
GASTROINTESTINAL				
Gastroenteritis—Empiric Therapy (laboratory studies not performed or culture, microscopy, toxin results NOT AVAILABLE)				
Premature infant with necrotizing enterocolitis	Associated with intestinal flora	Treatment should cover broad range of intestinal bacteria using drugs appropriate to age and local susceptibility patterns, rationale as in diverticulitis/peritonitis, *page 22.*		Pneumatosis intestinalis, if present on x-ray confirms diagnosis. Bacteremia-peritonitis in 30–50%. If Staph. epidermidis isolated, add vanco (IV). For review and general management, see *NEJM 364:255, 2011.*
Mild diarrhea (≤3 unformed stools/day, minimal associated symptomatology)	Bacterial *(see Severe, below)*, viral (norovirus), parasitic. Viral usually causes mild to moderate disease. For traveler's diarrhea, *see page 20*	Fluids only + lactose-free diet, avoid caffeine		**Rehydration: For po fluid replacement,** *see Cholera, page 19.* **Antimotility** (Do not use if fever, bloody stools, or suspicion of HUS): Loperamide (Imodium) 4 mg po, then 2 mg after each loose stool to max. of 16 mg per day. Bismuth subsalicylate (Pepto-Bismol) 2 tablets (262 mg) po qid. **Hemolytic uremic syndrome (HUS):** Risk in **children** infected with E. coli 0157:H7 is 8–10%. Early treatment with TMP-SMX or FQs ↑ risk of HUS. **Norovirus**: Etiology of over 90% of non-bacterial diarrhea (± nausea/vomiting). Lasts 12-60 hrs. Hydrate. No effective antiviral. **Other potential etiologies:** Cryptosporidia—no treatment in immunocompetent host. Cyclospora—usually chronic diarrhea, responds to TMP-SMX *(see Table 13A)*. Klebsiella oxytoca identified as cause of antibiotic-associated hemorrhagic colitis (cytotoxin positive): *NEJM 355:2418, 2006.*
Moderate diarrhea (≥4 unformed stools/day &/or systemic symptoms)		Antimotility agents *(see Comments)* + fluids		
Severe diarrhea (≥6 unformed stools/day, &/or temp ≥101°F, tenesmus, blood, or fecal leukocytes) **NOTE: Severe afebrile bloody diarrhea should ↑ suspicion of Shiga-toxin E. coli 0157:H7 & others** *(MMWR 58 (RR-12):1, 2009).*	Shigella, salmonella, C. jejuni, Shiga toxin + E. coli, toxin-positive C. difficile, Klebsiella oxytoca, E. histolytica. *For typhoid fever,* see *page 62*	**FQ** (**CIP** 500 mg po q12h or **Levo** 500 mg q24h) times 3–5 days	**TMP-SMX-DS** po bid times 3–5 days. Campylobacter resistance to TMP-SMX common in tropics.	
		If recent antibiotic therapy (C. difficile toxin colitis possible) **add:**		
		Metro 500 mg po tid times 10–14 days	**Vanco** 125 mg po qid times 10–14 days	

TABLE 1 (15)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
GASTROINTESTINAL *(continued)*				
Gastroenteritis—Specific Therapy (results of culture, microscopy, toxin assay AVAILABLE) (Ref.: *NEJM 370:1532, 2014*)				
If culture negative, probably **Norovirus (Norwalk)** other virus *(EID 17:1381, 2011)* — *see Norovirus, page 174* **NOTE:** WBC > 15,000 suggestive of *C. difficile* in hospitalized patient.	**Aeromonas/Plesiomonas**	**CIP** 750 mg po bid x3 days.	**TMP-SMX DS** tab 1 po bid x 3 days	Although no absolute proof, increasing evidence for Plesiomonas as cause of diarrheal illness *(NEJM 361:1560, 2009)*.
	Amebiasis (Entamoeba histolytica, Cyclospora, Cryptosporidia and **Giardia),** *see Table 13A*			
	Campylobacter jejuni Hislory of fever in 53-83%. Self-limited diarrhea in normal host.	**Azithro** 500 mg po q24h x 3 days.	**Erythro stearate** 500 mg po qid x 5 days or **CIP** 500 mg po bid (CIP resistance increasing).	**Post-Campylobacter Guillain-Barré;** assoc. 15% of cases *(Ln 366:1653, 2005)*. Assoc. with small bowel lymphoproliferative disease; may respond to antimicrobials *(NEJM 350:239, 2004)*. **Reactive arthritis** another potential sequelae. *See Traveler's diarrhea, page 20.*
	Campylobacter fetus Diarrhea uncommon. More systemic disease in debilitated hosts	**Gentamicin** *(see Table 10D)*	**AMP** 100 mg/kg/day IV div q6h or **IMP** 500 mg IV q6h	Draw blood cultures. In bacteremic pts, 32% of *C. fetus* resistant to FQs *(CID 47:790, 2008)*. Meropenem inhibits *C. fetus* at low concentrations in vitro. Clinical review: *CID 58:1579, 2014*.
Differential diagnosis of toxin-producing diarrhea: • *C. difficile* • Klebsiella oxytoca • S. aureus • Shiga toxin producing E. coli (STEC) • Enterotoxigenic B. fragilis *(CID 47:797, 2008)* More on C. difficile: *Treatment review: CID 51:1306, 2010. SHEA/IDSA treatment guidelines: ICHE 31:431, 2010; ESCMID guidelines: Clin Microbiol Infect 15:1067, 2009; AnIM 155:839, 2011*	**C. difficile** toxin positive antibiotic-associated colitis. **Probiotics:** (lactobacillus or saccharomyces) inconsistent results *(AnIM 157:878, 2012; Lancet 382:1249, 2013)*.			
	po meds okay; WBC <15,000; no increase in serum creatinine.	**Metro** 500 mg po tid or 250 mg qid x 10-14 days	**Vanco** 125 mg po qid x 10-14 days **Teicoplanin**[NUS] 400 mg po bid x 10 days	**D/C antibiotic if possible; avoid antimotility agents, hydration, enteric isolation.** Recent review suggests antimotility agents can be used cautiously in certain pts with mild disease who are receiving rx *(CID 48: 598, 2009)*. **Relapse in 10-20%.**
	po meds okay; Sicker; WBC >15,000; ≥ 50% increase in baseline creatinine	**Vanco** 125 mg po qid x 10-14 days. To use IV **vanco po**, *see* Table 10A, *page 107.*	**Fidaxomicin** 200 mg po bid x 10 days	Vanco superior to metro in sicker pts. Relapse in 10-20%. Fidaxomicin had lower rate of recurrence than Vanco for diarrhea with non-NAP1 strains *(N Engl J Med 364:422, 2011)*.
	Post-treatment relapse	**1st relapse** **Metro** 500 mg po tid x 10 days	**2nd relapse** **Vanco** 125 mg po qid x 10-14 days, then immediately start taper *(See Comments)*	**Vanco** taper (all doses 125 mg po): week 1– bid, week 2 – q24h; week 3 – qod; then every 3rd day for 5 doses *(NEJM 359, 1932, 2008)*. Another option: After initial vanco, **rifaximin**[NAI] 400-800 mg po daily divided bid or tid x 2 wks. **Fecal transplant** more efficacious than vancomycin (15/16 [93%] versus 7/26 [27%]) in curing recurrent C. difficile infection *(New Engl J Med 368:407, 2013)*
	Post-op ileus; severe disease with toxic megacolon *(NEJM 359:1932, 2008; CID 61:934, 2015)*.	**Metro** 500 mg IV q6h + **vanco** 500 mg q6h via nasogastric tube (or naso-small bowel tube) ± retrograde via catheter in cecum. *See comment* for dosage. No data on efficacy of **Fidaxomicin** in severe life-threatening disease.		For vanco instillation into bowel, add 500 mg vanco to 1 liter of saline and perfuse at 1-3 mL/min to maximum of 2 gm in 24 hrs *(CID 690, 2002)*. **Note: IV vanco not effective.** Indications for colectomy, see *ICHE 31:431, 2010*. Reported successful use of tigecycline[NAI] IV to treat severe *C. diff* refractory to standard rx *(CID 48:1732, 2009)*.
	Enterohemorrhagic E. coli (EHEC). Some produce **Shiga toxin E. coli (STEC)** and cause **hemolytic uremic syndrome (HUS).** Strains: 0157:H7, 0104:H4 and others. Classically bloody diarrhea and afebrile	**Hydration:** avoid antiperistaltic drugs. 25% increased risk of precipitating HUS in children < age 10 yrs given TMP-SMX, beta lactam, metronidazole or azithromycin for diarrhea *(CID 55:33, 2012)*. In uncontrolled study, antibiotic treatment of STEC outbreak, shorter excretion of E. coli, fewer seizures, lower mortality *(BMJ 345:e4565, 2012)*. If on empiric antibiotics, then Dx of STEC, reasonable to discontinue antibiotics. Avoid all antibiotics in children age < 10 yrs with bloody diarrhea. If antibiotics used, azithromycin may be the safest choice *(JAMA 307:1046, 2012)*.		• HUS more common in children, 15% in age < 10 yrs; 6-9% overall. • Diagnosis: EIA for Shiga toxins 1 & 2 in stool *(MMWR 58(RR-12), 2009)*. • Treatment: In vitro and in vivo data, that exposure of STEC to TMP-SMX and CIP causes burst of HUS toxin production as bacteria die *(JID 181:664, 2000)*. • HUS bad disease: 10% mortality; 50%-some degree of permanent renal damage *(CID 38:1298, 2004)*.

(Continued on next page)

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (16)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
GASTROINTESTINAL/Gastroenteritis—Specific Therapy *(continued)*				
(Continued from previous page)	**Klebsiella oxytoca—antibiotic-associated diarrhea**	Responds to stopping antibiotic		Suggested that stopping NSAIDs helps. Ref.: *NEJM 355:2418, 2006.*
	Listeria monocytogenes	Usually self-limited. Value of oral antibiotics (e.g., ampicillin or TMP-SMX) unknown, but their use might be reasonable in populations at risk for serious listeria infections. Those with bacteremia/meningitis require parenteral therapy: *see pages 9 & 61.*		Recognized as a cause of food-associated febrile gastroenteritis. Not detected in standard stool cultures. Populations at ↑ risk of severe systemic disease: pregnant women, neonates, the elderly, and immunocompromised hosts *(MMWR 57:1097, 2008).*
	Salmonella, non-typhi—For typhoid (enteric) fever, *see page 62* Fever in 71–91%, history of bloody stools in 34%	If pt asymptomatic or illness mild, antimicrobial therapy not indicated. **Treat if** age <1 yr or >50 yrs, if immunocompromised, if vascular grafts or prosthetic joints, bacteremic, hemoglobinopathy, or hospitalized with fever and severe diarrhea *(see typhoid fever, page 62).*		
		(**CIP** 500 mg bid) or (**Levo** 500 mg q24h) x 7-10 days (14 days if immunocompromised).	**Azithro** 500 mg po once daily x 7 days (14 days if immunocompromised).	↑ resistance to TMP-SMX and chloro. Ceftriaxone, cefotaxime usually active if IV therapy required *(see footnote 11, page 25, for dosage).* CLSI has established new interpretive breakpoints for susceptibility to CIP: susceptible strains, MIC < 0.06 µg/mL *(Clin Infect Dis 55:1107, 2012).* **Primary treatment of enteritis is fluid and electrolyte replacement.**
	Shigella Fever in 58%, history of bloody stools 51%	**CIP** 750 mg po bid x 3 days **Pockets of resistance *(see Comment)*** **Peds doses: Azithro** 10 mg/kg/day once daily x 3 days. For severe disease, ceftriaxone 50–75 mg/kg per day x 2–5 days. CIP suspension 10 mg/kg bid x 5 days.	**Azithro** 500 mg po once daily x 3 days	Recommended adult CIP dose of 750 mg once daily for 3 days *(NEJM 361:1560, 2009).* **Immunocompromised children & adults: Treat for 7–10 days. Pockets of resistance: *S. flexneri* resist to CIP & ceftriaxone *(MMWR 59:1619, 2010)*; S. *sonnei* resist to CIP in travelers *(MMWR 64:318, 2015)*; S. *sonnei* suscept to CIP but resist to azithro in MSM *(MMWR 64:597, 2015).***
	Spirochetosis (Brachyspira pilosicoli)	Benefit of treatment unclear. Susceptible to **metro**, **ceftriaxone**, and **Moxi**.		Anaerobic intestinal spirochete that colonizes colon of domestic & wild animals plus humans. Called enigmatic disease due to uncertain status *(Digest Dis & Sci 58:202, 2013).*
	Vibrio cholerae (toxigenic - *01* & *039*) Treatment decreases duration of disease, volume losses, & duration of excretion	**Primary therapy is rehydration.** Select antibiotics based on susceptibility of locally prevailing isolates. Options include: **Doxycycline** 300 mg po single dose **OR Azithromycin** 1 gm po single dose **OR Tetracycline** 500 mg po qid x 3 days **OR Erythromycin** 500 mg po qid x 3 days.	**For pregnant women: Azithromycin** 1 gm po single dose **OR Erythromycin** 500 mg po qid x 3 days **For children: Azithromycin** 20 mg/kg po as single dose; for other age-specific alternatives, *see CDC website http://www.cdc.gov/haitiCholera/hcp_goingtohaiti.htm*	**Antimicrobial therapy shortens duration of illness, but rehydration is paramount.** When IV hydration is needed, use Ringer's lactate. Switch to PO repletion with Oral Rehydration Salts (ORS) as soon as able to take oral fluids. ORS are commercially available for reconstitution in potable water. If not available, WHO suggests a substitute can be made by dissolving ½ teaspoon salt and 6 level teaspoons of sugar per liter of potable water *(http://www.who.int/cholera/technical/en/).* CDC recommendations for other aspects of management developed for Haiti outbreak can be found at *http://www.cdc.gov/haitiCholera/hcp_goingtohaiti.htm* Isolates from this outbreak demonstrate reduced susceptibility to ciprofloxacin and resistance to sulfisoxazole, nalidixic acid and furazolidone.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (17)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
GASTROINTESTINAL/Gastroenteritis—Specific Therapy *(continued)*				
	Vibrio parahaemolyticus, V. mimicus, V. fluvialis	Antimicrobial rx does not shorten course. Hydration.		Shellfish exposure common. Treat severe disease: **FQ, doxy, P Ceph 3**
	Vibrio vulnificus	Usual presentation is skin lesions & bacteremia; life-threatening; treat early: **ceftaz** + **doxy**—see page 54; *Levo or CIP + ceftaz or ceftriaxone. Ref: Epidemiol Infect. 142:878, 2014.*		
	Yersinia enterocolitica Fever in 68%, bloody stools in 26%	No treatment unless severe. If severe, combine **doxy** 100 mg IV bid + (**tobra** or **gent** 5 mg/kg per day once q24h). **TMP-SMX** or **FQs** are alternatives.		Mesenteric adenitis pain can mimic acute appendicitis. Lab diagnosis difficult: requires "cold enrichment" and/or yersinia selective agar. Desferrioxamine therapy increases severity, discontinue if pt on it. Iron overload states predispose to yersinia.
Gastroenteritis—Specific Risk Groups–Empiric Therapy				
Anoreceptive Intercourse				
Proctitis (distal 15 cm only)	Herpes viruses, gonococci, chlamydia, syphilis *See Genital Tract, page 22*			
Colitis	Shigella, salmonella, campylobacter, E. histolytica *(see Table 13A)*			*See specific GI pathogens, Gastroenteritis, above.*
HIV-1 infected (AIDS): >10 days diarrhea	G. lamblia Acid fast: Cryptosporidium parvum, Cyclospora cayetanensis Other: Isospora belli, microsporidia (Enterocytozoon bieneusi, Septata intestinalis)			*See Table 13A*
Neutropenic enterocolitis or "typhlitis" *(CID 56:711, 2013)*	Mucosal invasion by **Clostridium septicum**. Occasionally caused by C. sordellii or P. aeruginosa	Appropriate agents include PIP-TZ, IMP, MER, DORI plus bowel rest.		Tender right lower quadrant may be clue, but may be diffuse or absent in immunocompromised. Need surgical consult. Surgical resection controversial but may be necessary. **NOTE:** Resistance of clostridia to clindamycin reported. PIP-TZ, IMP, MER, DORI should cover most pathogens.
Traveler's diarrhea, self-medication. Patient often afebrile	**Acute**: 60% due to diarrheagenic E. coli; shigella, salmonella, or campylobacter. C. difficile, amebiasis *(see Table 13A)*. **If chronic**: cyclospora, cryptosporidia, giardia, isospora	**CIP** 750 mg po bid for 1-3 days **OR** **Levo** 500 mg po q24h for 1-3 days **OR** **Oflox** 300 mg po bid for 3 days **OR** **Rifaximin** 200 mg po tid for 3 days **OR** **Azithro** 1000 mg po once or 500 mg po q24h for 3 days **For pediatrics:** Azithro 10 mg/kg/day as a single dose for 3 days or Ceftriaxone 50 mg/kg/day as single dose for 3 days. Avoid FQs. **For pregnancy:** Use Azithro. Avoid FQs.		**Antimotility agent:** For non-pregnant adults with no fever or blood in stool, add loperamide 4 mg po x 1, then 2 mg po after each loose stool to a maximum of 16 mg per day. **Comments:** Rifaximin approved only for ages 12 and older. Works only for diarrhea due to non-invasive E. coli; do not use if fever or bloody stool. **Ref:** *NEJM 361:1560, 2009;* Note: Self treatment with FQs associated with acquisition of resistant Gm-neg bacilli *(CID 60:837, 847, 872, 2015).*
Prevention of Traveler's diarrhea	Not routinely indicated. Current recommendation is to take **FQ** + **Imodium** with 1st loose stool.			

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (18)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
GASTROINTESTINAL *(continued)*				
Gastrointestinal Infections by Anatomic Site: Esophagus to Rectum				
Esophagitis	Candida albicans, HSV, CMV	*See SANFORD GUIDE TO HIV/AIDS THERAPY and Table 11A.*		
Duodenal/Gastric ulcer; gastric cancer, MALT lymphomas (not 2°NSAIDs) Comparative effectiveness & tolerance of treatment *(BMJ 351:4052, 2015)*	**Helicobacter pylori** *See Comment* Prevalence of pre-treatment resistance increasing	**Sequential therapy:** (**Rabeprazole** 20 mg + **amox** 1 gm) bid x 5 days, then (**rabeprazole** 20 mg + **clarithro** 500 mg + **tinidazole** 500 mg) bid for another 5 days. *See footnote[8].* Can modify by substituting Levo for Clarithro *(JAMA 309:578, 2013; Ln 381:205, 2013).*	**Quadruple therapy (10-14 days): Bismuth** *(see footnote[9])*, bismuth subsalicylate 2 tabs qid + **tetracycline** 500 mg qid + **metro** 500 mg tid + **omeprazole** 20 mg bid.	**Comment:** In many locations, 20% failure rates with previously recommended *triple* regimens **(PPI + Amox + Clarithro)** are not acceptable. With 10 days of quadruple therapy [(**omeprazole** 20 mg po twice daily) + (3 capsules po four times per day, each containing **Bismuth subcitrate potassium** 140 mg + **Metro** 125 mg + **Tetracycline** 125 mg)], eradication rates were 93% in a per protocol population and 80% in an intention-to-treat population, both significantly better than with 7-day triple therapy regimen (PPI + Amox + Clarithro) *(Lancet 377:905, 2011).* Exercise caution regarding potential interactions with other drugs, contraindications in pregnancy and warnings for other special populations. **Dx: Stool antigen**—Monoclonal EIA >90% sens. & 92% specific. Other tests: if endoscoped, rapid urease &/or histology &/or culture; urea breath test, but some office-based tests underperform. Testing ref: *BMJ 344:44, 2012.* **Test of cure:** Repeat stool antigen and/or urea breath test >8 wks post-treatment. **Treatment outcome:** Failure rate of triple therapy 20% due to clarithro resistance. Cure rate with sequential therapy 90%.
		100% compliance/94% eradication rate reported: (**Pantoprazole** 40 mg + **Clarithro** 500 mg + **Amox** 1000 mg + **Metro** 500 mg) po bid x 7 d *(AAC 58:5936, 2014).* High cure rates reported in Taiwan with (**Rabeprazole** 20 mg + **Amox** 750 mg) po 4x/day x 14 days		
Small intestine: Whipple's disease *(NEJM 356:55, 2007; LnID 8:179, 2008)* Treatment: *JAC 69:219, 2014.* *See Infective endocarditis, culture-negative, page 30.*	Tropheryma whipplei	(**Doxycycline** 100 mg po bid + **Hydroxychloroquine** 200 mg pot id) x 1 year, then **Doxycycline** 100 mg po bid for life Immune reconstitution inflammatory response (IRIS) reactions occur: Thalidomide therapy may be better than steroids for IRIS reaction *(J Infect 60:79, 2010)*		In vitro susceptibility testing and collected clinical experience *(JAC 69:219, 2014).* In vitro resistance to TMP-SMX plus frequent clinical failures & relapses. Frequent in vitro resistance to carbapenems. Complete in vitro resistance to Ceftriaxone.

[8] Can substitute other proton pump inhibitors for omeprazole or rabeprazole--all bid: **esomeprazole** 20 mg (FDA-approved), **lanzoprazole** 30 mg (FDA-approved), **pantoprazole** 40 mg (not FDA-approved for this indication).

[9] **Bismuth preparations:** (1) In U.S., **bismuth subsalicylate (Pepto-Bismol)** 262 mg tabs; adult dose for helicobacter is 2 tabs (524 mg) qid. (2) Outside U.S., colloidal bismuth subcitrate (De-Nol) 120 mg chewable tablets; dose is 1 tablet qid. In the U.S., bismuth subcitrate is available in combination cap only (Pylera: each cap contains bismuth subcitrate 140 mg + Metro 125 mg + Tetracycline 125 mg), given as 3 caps po 4x daily for 10 days **together with** a twice daily PPI.

TABLE 1 (19)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
GASTROINTESTINAL/Gastrointestinal Infections by Anatomic Site: Esophagus to Rectum *(continued)*				
Diverticulitis, perirectal abscess, peritonitis *Also see Peritonitis, page 46*	Enterobacteriaceae, occasionally P. aeruginosa, Bacteroides sp., enterococci	**Outpatient rx—mild diverticulitis, drained perirectal abscess:** [(**TMP-SMX-DS** bid) or (**CIP** 750 mg bid or **Levo** 750 mg q24h)] + **metro** 500 mg q6h. All po x 7–10 days.	**AM-CL-ER** 1000/62.5 mg 2 tabs po bid x 7–10 days **OR Moxi** 400 mg po q24h x 7-10 days	Must "cover" both Gm-neg. aerobic & Gm-neg. anaerobic bacteria. **Drugs active only vs. anaerobic Gm-neg. bacilli:** clinda, metro. **Drugs active only vs. aerobic Gm-neg. bacilli:** APAG[10], P Ceph 2/3/4 *(see Table 10A, page 102)*, aztreonam, PIP-TZ, CIP, Levo. **Drugs active vs. both aerobic/anaerobic Gm-neg. bacteria:** cefoxitin, cefotetan, TC-CL, PIP-TZ, AM-SB, ERTA, DORI, IMP, MER, Moxi, & tigecycline. **Increasing resistance of B. fragilis group**
		Mild-moderate disease—Inpatient—Parenteral Rx: (e.g., focal periappendiceal peritonitis, peridiverticular abscess, endomyometritis)		
		PIP-TZ 3.375 gm IV q6h **or** 4.5 gm IV q8h **or ERTA** 1 gm IV q24h **or MOXI** 400 mg IV q24h	[(**CIP** 400 mg IV q12h) or (**Levo** 750 mg IV q24h)] + (**metro** 500 mg IV q6h or 1 gm IV q12h) **OR Moxi** 400 mg IV q24h	
		Severe life-threatening disease, ICU patient: **IMP** 500 mg IV q6h **or MER** 1 gm IV q8h **or DORI** 500 mg q8h (1-hr infusion).	**AMP** + **metro** + (**CIP** 400 mg IV q12h or **Levo** 750 mg IV q24h) **OR** [**AMP** 2 gm IV q6h + **metro** 500 mg IV q6h + **aminoglycoside**[10] *(see Table 10D, page 118)*]	
		Severe penicillin/cephalosporin allergy: (aztreonam 2 gm IV q6h to q8h) + [**metro** (500 mg IV q6h) or (1 gm IV q12h)] **OR** [(**CIP** 400 mg IV q12h) or (**Levo** 750 mg IV q24h) + **metro**].		

	Clinda	Moxi	Cefoxitin	Cefotetan
% Resistant:	42-80	34-45	48-60	19-35

Ref: Anaerobe 17:147, 2011; AAC 56:1247, 2012, Surg Infect 10:111, 2009.

Resistance (B. fragilis): Metro, PIP-TZ rare. Resistance to FQ increased in enteric bacteria, particularly if any FQ used recently.

Ertapenem poorly active vs. P. aeruginosa/Acinetobacter sp.

Concomitant surgical management important, esp. with moderate-severe disease. **Role of enterococci remains debatable.** Probably pathogenic in intections of biliary tract. Probably need drugs active vs. enterococci in pts with valvular heart disease.

Tigecycline: Black Box Warning: All cause mortality higher in pts treated with tigecycline (2.5%) than comparators (1.8%) in meta-analysis of clinical trials. Cause of mortality risk ditference of 0.6% (95% CI 0.1, 1.2) not established. Tigecycline should be reserved for use in situations when alternative treatments are not suitable *(FDA MedWatch Sep 27, 2013)*

GENITAL TRACT: Mixture of empiric & specific treatment. Divided by sex of the patient. For sexual assault (rape), *see Table 15A, page 200.* **See CDC Guidelines for Sexually Transmitted Diseases,** *MMWR 64(RR-3):1, 2015.*				
Both Women & Men:				
Chancroid	H. ducreyi	**Ceftriaxone** 250 mg IM single dose OR **azithro** 1 gm po single dose	**CIP** 500 mg bid po x 3 days OR **erythro base** 500 mg po tid x 7 days.	In HIV+ pts, failures reported with single dose azithro *(CID 21:409, 1995)*. Evaluate after 7 days, ulcer should objectively improve. All patients treated for chancroid should be tested for HIV and syphilis. All sex partners of pts with chancroid should be examined and treated if they have evidence of disease or have had sex with index pt within the last 10 days.

[10] **Aminoglycoside = antipseudomonal aminoglycosidic aminoglycoside, e.g., amikacin, gentamicin, tobramycin**

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (20)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
GENITAL TRACT/Both Women & Men *(continued) CDC Guidelines: MMWR 64(RR-3):1, 2015*				
Non-gonococcal or post-gonococcal urethritis, cervicitis **NOTE: Assume concomitant N. gonorrhoeae** (Chlamydia conjunctivitis, *see page 12)*	Chlamydia 50%, Mycoplasma genitalium (30%). Other known etiologies (10–15%): trichomonas, herpes simplex virus, *see JID 206:357, 2012.* Ref: *CID 61:S774, 2015*	(**Doxy** 100 mg bid po x 7 days) or (**azithro** 1 gm po as single dose). Evaluate & treat sex partner **In pregnancy: Azithromycin** 1 gm po single dose OR **amox** 500 mg po tid x 7 days.	(**Erythro base** 500 mg qid po x 7 days) or (**Oflox** 300 mg q12h po x 7 days) or (**Levo** 500 mg q24h x 7 days) **In pregnancy: Erythro** base 500 mg po qid for 7 days **Doxy & FQs contraindicated**	**Diagnosis:** NAAT for C. trachomatis & N. gonorrhoeae on urine or cervix or urethra specimens *(AnIM 142:914, 2005)*. Test all urethritis/cervicitis pts for HIV & syphilis. **For proctitis**: prefer **doxy** x 7d (Sex Trans Dis 41:79, 2014). **Evaluate & treat sex partners.** Re-test for cure in pregnancy. Azithromycin 1 gm was superior to doxycycline for M. genitalium male urethritis *(CID 48:1649, 2009)*, but may select resistance leading to ↑ failure of multi-dose azithromycin retreatment regimens *(CID 48:1655, 2009)*.
Non-gonococcal urethritis: **Mycoplasma genitalium**	Mycoplasma genitalium. Ref: *CID 61:S802, 2015.*	**Azithro** 500 mg po x1 then 250 mg po once daily x 4 days	**Moxl** 400 mg once daily x 10-14 days	Diagnosis by NAAT, if available. Doxy ineffective. No cell wall so beta-lactams ineffective. Cure with single dose Azithro only 67% *(CID 61:1389, 2015)*.
Recurrent/persistent urethritis	**C. trachomatis** (43%), **M. genitalium** (30%), **T. vaginalis** (13%) *(CID 52:163, 2011)*.	**Metro** 2 gm po x 1 dose + **Azithro** 1 gm po x 1 dose	**Tinidazole** 2 gm po X 1 + **Azithromycin** 1 gm po X 1	High failure rate of Azithro if M. genitalium *(CID 56:934, 2013)*. Can try Moxi 400 mg po once daily x 10 days if Azithro failure *(PLoS One 3:e3618, 2008)*. New FQ resistance in Japan *(JAC 69:2376, 2014)*.
Gonorrhea. FQs no longer recommended for treatment of gonococcal infections *(See CDC Guidelines MMWR 64(RR-3):1, 2015; CID 61:S785, 2015).* **Cephalosporin resistance:** *JAMA 309:163 & 185, 2013.*				
Conjunctivitis (adult)	N. gonorrhoeae	**Ceftriaxone** 1 gm IM or IV single dose + **Azithro**		Consider one-time saline lavage of eye.
Disseminated gonococcal infection (DGI, dermatitis-arthritis syndrome)	N. gonorrhoeae	**Ceftriaxone** 1 gm IV q24h + **Azithro** 1 gm po x 1	(**Cefotaxime** 1 gm q8h IV or **Ceftizoxime** 1 gm q8h IV) + **Azithro** 1 gm po x 1	Treat for a minimum of 7 days. Owing to high-level resistance to oral cephalosporins and fluoroquinolones in the community, "Step-down" therapy should be avoided unless susceptibilities are known and demonstrate full activity of cephalosporin or fluoroquinolone R/O meningitis/ endocarditis. **Treat presumptively for concomitant C. trachomatis.** Azithro now recommended to cover resistant GC (usually tetra resistant, too) and C. trachomatis
Endocarditis	N. gonorrhoeae	**Ceftriaxone** 1-2 gm IV q12-24 hours x 4 weeks + **Azithro** 1 gm po x 1		GC endocarditis may occur in the absence of concomitant urogenital symptoms *(Infection 42: 425, 2014)*. Severe valve destruction may occur. Ceftriaxone resistance in *N. gonorrhoeae* has been reported *(AAC 55: 3538, 2011)*; determine susceptibility of any isolate recovered.
Pharyngitis Dx: NAAT	N. gonorrhoeae	**Ceftriaxone** 250 mg IM x 1 + (**Azithro** 1 gm po x 1).	Due to resistance concerns, **do not use FQs**.	Pharyngeal GC more difficult to eradicate. **Repeat NAAT 14 days post-rx. Spectinomycin[NUS], cefixime, cefpodoxime & cefuroxime not effective**
Urethritis, cervicitis, proctitis (uncomplicated) For prostatitis, *see page 27.* **Diagnosis:** Nucleic acid amplification test (NAAT) on vaginal swab, urine or urethral swab *MMWR 64(RR-3):1, 2015*	N. gonorrhoeae (50% of pts with urethritis, cervicitis have concomitant C. trachomatis — **treat for both even if NAAT indicates single pathogen**).	**Ceftriaxone** 250 mg IM x 1 + **Azithro** 1 gm po x 1 **Alternative: Azithro** 2 gm po x 1 **Rx failure: Ceftriaxone** 500 mg IM x 1 + **Azithro** 2 gm po x 1; treat partner; NAAT for test of cure one week post-treatment **Severe Pen/Ceph allergy**: (**Gent** 240 mg IM + **Azithro** 2 gm po x 1 dose) OR (**Gemi** 320 mg + **Azithro** 2 gm po x 1 dose) *(CID 59:1083, 2014)* (nausea in >20%)		Screen for syphilis. **Other alternatives for GC (Test of Cure recommended one week after Rx for ALL of these approaches listed below):** • **Oral** cephalosporin use is no longer recommended as primary therapy owing to emergence of resistance, *MMWR 61:590, 2012.* • Other single-dose cephalosporins: ceftizoxime 500 mg IM, cefotaxime 500 mg IM, cefoxitin 2 gm IM + probenecid 1 gm po.
Pregnancy		**Ceftriaxone** 250 mg IM x 1 + **Azithro** 1 gm po x 1		

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (21)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
GENITAL TRACT/Both Women & Men *(continued)*				
Granuloma inguinale (Donovanosis)	Klebsiella (formerly Calymmatobacterium) granulomatis	**Azithro** 1 gm po q wk x 3 wks	**TMP-SMX** one DS tablet bid x 3 wks **OR Erythro** 500 mg po qid x 3 wks OR **CIP** 750 mg po bid x 3 wks OR **Doxy** 100 mg po bid x 3 wks	Clinical response usually seen in 1 wk. **Rx until all lesions healed,** may take 4 wks. Treatment failures & recurrence seen with doxy & TMP-SMX. Relapse can occur 6-18 months after apparently effective Rx. If improvement not evidence in first few days, some experts add gentamicin 1 mg/kg IV q8h.
Herpes simplex virus	See *Table 14A, page 169*			
Human papilloma virus (HPV)	See *Table 14A, page 174*			
Lymphogranuloma venereum Ref: *CID 61:S865, 2015*	Chlamydia trachomatis, serovars. L1, L2, L3	**Doxy** 100 mg po bid x 21 days	**Erythro** 0.5 gm po qid x 21 days or **Azithro** 1 gm po qwk X 3 weeks (clinical data lacking)	Dx based on serology; biopsy contraindicated because sinus tracts develop. Nucleic acid ampli tests for *C. trachomatis* will be positive. In MSM, presents as fever, rectal ulcer, anal discharge *(CID 39:996, 2004; Dis Colon Rectum 52:507, 2009).*
Phthirus pubis (**pubic lice, "crabs"**) & scabies	Phthirus pubis & Sarcoptes scabiei		*See Table 13A, page 161*	
Syphilis Diagnosis: *JAMA 312:1922, 2014*; treatment: *JAMA 312:1905, 2014;* management: *CID 61:S818, 2015.*				
Early: primary, secondary, or latent <1 yr. Screen with treponema-specific antibody or RPR/VDRL, see *JCM 50:2 & 148, 2012; CID 58:1116, 2014.*	T. pallidum NOTE: Test all pts with syphilis for HIV; test all HIV patients for latent syphilis.	**Benzathine pen G (Bicillin L-A)** 2.4 million units IM x 1 or **Azithro** 2 gm po x 1 dose *(See Comment)*	(**Doxy** 100 mg po bid x 14 days) or (**tetracycline** 500 mg po qid x 14 days) or (**ceftriaxone** 1 gm IM/IV q24h x 10–14 days). Follow-up mandatory.	If early or congenital syphilis, **quantitative VDRL at 0**, 3, 6, 12 & 24 mos after rx. If 1° or 2° syphilis, VDRL should ↓ 2 tubes at 6 mos, 3 tubes 12 mos, & 4 tubes 24 mos. Update on congenital syphilis *(MMWR 59:413, 2010).* Early latent: 2 tubes ↓ at 12 mos. With 1°, 50% will be RPR seronegative at 12 mos, 24% neg. FTA/ABS at 2–3 yrs *(AnIM 114:1005, 1991).* If titers fail to fall, examine CSF; if CSF (+), treat as neurosyphilis; if CSF is negative, retreat with benzathine Pen G 2.4 mu IM weekly x 3 wks. If no other options: **Azithro** 2 gm po x 1 dose (equivalent to **benzathine Pen** 2.4 M x 1 dose in early syphilis *(J Infect Dis 201:1729, 2010).* **Azithro-resistant syphilis** documented in California, Ireland, & elsewhere *(CID 44:S130, 2007; AAC 54:583, 2010).* NOTE: Use of **benzathine procaine penicillin** is inappropriate!!
More than 1 yr's duration (latent of indeterminate duration, cardiovascular, late benign gumma)	For penicillin desensitization method, see *Table 7, page 83* and *MMWR 64 (RR-3):1, 2015*	**Benzathine pen G (Bicillin L-A)** 2.4 million units IM q week x 3 = 7.2 million units total	**Doxy** 100 mg po bid x 28 days or **tetracycline** 500 mg po qid x 28 days; **Ceftriazone** 1 gm IV or IM daily for 10-14 days MAY be an alternative (No clinical data; consult an ID specialist)	No published data on efficacy of alternatives. **Indications for LP (CDC): neurologic symptoms, treatment failure, any eye or ear involvement, other evidence of active syphilis (aortitis, gumma, iritis).**
Neurosyphilis—Very difficult to treat. Includes ocular (retrobulbar neuritis) syphilis **All need CSF exam.**		**Pen G** 18-24 million units per day either as continuous infusion or as 3-4 million units IV q4h x 10–14 days.	(**Procaine pen G** 2.4 million units IM q24h + **probenecid** 0.5 gm po qid) both x 10–14 days—*See Comment*	**Ceftriaxone** 2 gm (IV or IM) q24h x 14 days. 23% failure rate reported *(AJM 93:481, 1992).* For penicillin allergy: either desensitize to penicillin or obtain infectious diseases consultation. **Serologic criteria for response to rx: 4-fold or greater ↓ in VDRL titer over 6–12 mos.** *[CID 28(Suppl. 1):S21, 1999].*
HIV infection (AIDS) *CID 44:S130, 2007.*		Treatment same as HIV uninfected with closer follow-up. Treat early neurosyphilis for 10-14 days regardless of CD4 count: *MMWR 56:625, 2007.*		*See Syphilis discussion in CDC Guidelines MMWR 64(RR-3):1, 2015.* Treat for neurosyphilis if CSF VDRL negative but >20 CSF WBCs *(STD 39:291, 2012).*
Pregnancy and syphilis		Same as for non-pregnant, some recommend 2nd dose (2.4 million units) **benzathine pen G** 1 wk after initial dose esp. in 3rd trimester or with 2° syphilis	Skin test for penicillin allergy. Desensitize if necessary, as parenteral pen G is only therapy with documented efficacy!	Monthly quantitative VDRL or equivalent. If 4-fold ↑, re-treat. Doxy, tetracycline contraindicated. Erythro not recommended because of high risk of failure to cure fetus.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (22)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
GENITAL TRACT/Both Women & Men *(continued)*				
Congenital syphilis *(Update on Congenital Syphilis: MMWR 64(RR-3):1, 2015)*	T. pallidum	**Aqueous crystalline pen G** 50,000 units/kg per dose IV q12h x 7 days, then q8h for 10 day total	**Procaine pen G** 50,000 units/kg IM q24h for 10 days	Another alternative: Ceftriaxone ≤30 days old, 75 mg/kg IV/IM q24h (use with caution in infants with jaundice) or >30 days old 100 mg/kg IV/IM q24h. Treat 10–14 days. If symptomatic, ophthalmologic exam indicated. If more than 1 day of rx missed, restart entire course. **Need serologic follow-up!**
Warts, anogenital	*See Table 14A, page 174*			
Women:				
Amnionitis, septic abortion	Bacteroides, esp. Prevotella bivius; Group B, A strepto-cocci; Enterobacteriaceae; C. trachomatis. Rarely U. urealyticum.	[(**Cefoxitin** or **DORI**[NAI] or **IMP** or **MER** or **AM-SB** or **ERTA** or **PIP-TZ**) + **doxy**] **OR** [**Clinda** + (**aminoglycoside** or **ceftriaxone**)] *Dosage: see footnote*[11] **Note:** in US and Europe, 1/3 of Grp B Strep resistant to clindamycin.		D&C of uterus. **In septic abortion,** Clostridium perfringens may cause fulminant intravascular hemolysis. **In postpartum patients** with enigmatic fever and/or pulmonary emboli, **consider septic pelvic vein thrombophlebitis** *(see Vascular septic pelvic vein thrombophlebitis, page 68)*. After discharge: doxy or clinda for C. trachomatis.
Cervicitis, mucopurulent Treatment based on results of nucleic acid amplification test	N. gonorrhoeae	Treat for Gonorrhea, *page 23*		Criteria for diagnosis: 1) (muco) purulent endocervical exudate and/or 2) sustained endocervical bleeding after passage of cotton swab. >10 WBC/hpf of vaginal fluid is suggestive. Intracellular gram-neg diplococci are specific but insensitive. If in doubt, send swab or urine for culture, EIA or nucleic acid amplification test and treat for both.
	Chlamydia trachomatis	Treat for non-gonococcal urethritis, *page 23* . If due to *Mycoplasma genitalium*, less likely to respond to doxy than azithro.		
Endomyometritis/septic pelvic phlebitis Early postpartum (1st 48 hrs) (usually after C-section)	Bacteroides, esp. Prevotella bivius; Group B, A strepto-cocci; Enterobacteriaceae; C. trachomatis	[(**Cefoxitin** or **ERTA** or **IMP** or **MER** or **AM-SB** or **PIP-TZ**) + **doxy**] or [**Clinda** + (**aminoglycoside** or **ceftriaxone**)] *Dosage: see footnote*[11]		*See Comments under Amnionitis, septic abortion, above*
Late postpartum (48 hrs to 6 wks) (usually after vaginal delivery)	Chlamydia trachomatis, M. hominis	**Doxy** 100 mg IV or po q12h times 14 days		Tetracyclines not recommended in nursing mothers; discontinue nursing. M. hominis sensitive to tetra, clinda, not erythro.
Fitzhugh-Curtis syndrome	C. trachomatis, N. gonorrhoeae	Treat as for pelvic inflammatory disease immediately below.		Perihepatitis (violin-string adhesions). Sudden onset of RUQ pain. Associated with salpingitis. Transaminases elevated in < 30% of cases.
Pelvic actinomycosis; usually tubo-ovarian abscess	A. Israelii most common	**AMP** 50 mg/kg/day IV div 3-4 doses x 4-6 wks, then **Pen VK** 2-4 gm/day po x 3-6 mos.	**Doxy** or **ceftriaxone** or **clinda**.	Complication of intrauterine device (IUD). Remove IUD. Can use **Pen G** 10-20 million units/day IV instead of **AMP** x 4-6 wks.

[11] **P Ceph 2** (**cefoxitin** 2 gm IV q6–8h, **cefotetan** 2 gm IV q12h, **cefuroxime** 750 mg IV q8h); **AM-SB** 3 gm IV q6h; **PIP-TZ** 3.375 gm q6h or for nosocomial pneumonia: 4.5 gm IV q6h or 4-hr infusion of 3.375 gm q8h; **doxy** 100 mg IV/po q12h; **clinda** 450–900 mg IV q8h; **aminoglycoside** (**gentamicin**, *see Table 10D, page 118)*; **P Ceph 3** (**cefotaxime** 2 gm IV q8h, **ceftriaxone** 2 gm IV q24h); **doripenem** 500 mg IV q8h (1-hr infusion); **ertapenem** 1 gm IV q24h; **IMP** 0.5 gm IV q6h; **MER** 1 gm IV q8h; **azithro** 500 mg IV q24h; **linezolid** 600 mg IV/po q12h; **vanco** 1 gm IV q12h

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (23)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
GENITAL TRACT/Women *(continued)*				
Pelvic Inflammatory Disease (PID), salpingitis, tubo-ovarian abscess				
Outpatient rx: limit to pts with temp <38°C, WBC <11,000 per mm³, minimal evidence of peritonitis, active bowel sounds & able to tolerate oral nourishment *NEJM 372:2039, 2015; CDC Guidelines MMWR 64(RR-3):1, 2015*	N. gonorrhoeae, chlamydia, bacteroides, Enterobacteriaceae, streptococci, especially S. agalactiae Less commonly: G. vaginalis, Haemophilus influenzae, cytomegalovirus (CMV), M. genitalium, U. urealyticum	**Outpatient rx:** [(**ceftriaxone** 250 mg IM or IV x 1) (± **metro** 500 mg po bid x 14 days) + (**doxy** 100 mg po bid x 14 days)]. **OR** (**cefoxitin** 2 gm IM with **probenecid** 1 gm po both as single dose) plus (**doxy** 100 mg po bid with **metro** 500 mg bid—both times 14 days)	**Inpatient regimens:** [(**Cefotetan** 2 gm IV q12h or **cefoxitin** 2 gm IV q6h) + (**doxy** 100 mg IV/po q12h)] (**Clinda** 900 mg IV q8h) + (**gentamicin** 2 mg/kg loading dose, then 1.5 mg/kg q8h or 4.5 mg/kg once per day), then **doxy** 100 mg po bid x 14 days	Another alternative parenteral regimen: **AM-SB** 3 gm IV q6h + **doxy** 100 mg IV/po q12h. Recommended treatments don't cover M. genitalium so if no response after 7-10 d consider M. genitalium NAAT and treat with Moxi 400 mg/day 14 days. Remember: Evaluate and treat sex partner. FQs not recommended due to increasing resistance *MMWR 64(RR-3):1, 2015 & www.cdc.gov/std/treatment).* Suggest initial inpatient evaluation/therapy for pts with tubo-ovarian abscess. For inpatient regimens, continue treatment until satisfactory response for ≥ 24-hr before switching to outpatient regimen. Improved routine testing for chlamydia and N. gonorrhoeae among outpatients resulted in reduced hospitalization and ectopic pregnancy rates *(J Adolescent Health 51:80, 2012).*
Vaginitis— *MMWR 64(RR-3):1, 2015*				
Candidiasis Pruritus, thick cheesy discharge, pH <4.5 *See Table 11A, page 125*	Candida albicans 80–90%. C. glabrata, C. tropicalis may be increasing—they are less susceptible to azoles	**Oral azoles: Fluconazole** 150 mg po x 1; **itraconazole** 200 mg po bid x 1 day. For milder cases, Topical Therapy with one of the over the counter preparations usually is successful (e.g., clotrimazole, butoconazole, miconazole, or tioconazole) as creams or vaginal suppositories.	**Intravaginal azoles**: variety of strengths—from 1 dose to 7–14 days. Drugs available (all end in -azole): butocon, clotrim, micon, tiocon, tercon *(doses: Table 11A)*	Nystatin vag. tabs times 14 days less effective. Other rx for azole-resistant strains: gentian violet, boric acid. If recurrent candidiasis (4 or more episodes per yr): 6 mos. suppression with: fluconazole 150 mg po q week or itraconazole 100 mg po q24h or clotrimazole vag. suppositories 500 mg q week.
Trichomoniasis *(CID 61:S837, 2015)* Copious foamy discharge, pH >4.5 Treat sexual partners—see *Comment*	Trichomonas vaginalis **Dx:** NAAT & PCR available & most sensitive; wet mount not sensitive. Ref: *JCM 54:7, 2016.*	**Metro** 2 gm as single dose or 500 mg po bid x 7 days OR **Tinidazole** 2 gm po single dose **Pregnancy:** See *Comment*	**For rx failure:** Re-treat with metro 500 mg po bid x 7 days; if 2nd failure: metro 2 gm po q24h x 3–5 days. If still failure, **Tinidazole** 2 gm po q24h x 5 days	**Treat male sexual partners (2 gm metronidazole as single dose).** Nearly 20% men with NGU are infected with trichomonas *(JID 188:465, 2003).* For alternative option in refractory cases, see *CID 33:1341, 2001.* **Pregnancy:** No data indicating metro teratogenic or mutagenic. For discussion of treating trichomonas, including issues in pregnancy, *see MMWR 64(RR 3):1, 2015.*
Bacterial vaginosis (BV) Malodorous vaginal discharge, pH >4.5	Etiology unclear; associated with Gardnerella vaginalis, mobiluncus, Mycoplasma hominis, Prevotella sp., & Atopobium vaginae et al.	**Metro** 0.5 gm po bid x 7 days or **metro vaginal gel**[12] (1 applicator intravaginally) 1x/day x 5 days OR 2% **clinda vaginal cream** 5 gm intravaginally at bedtime x 7 days	**Clinda** 0.3 gm bid po x 7 days or **clinda ovules** 100 mg intravaginally at bedtime x 3 days.	Reported 50% ↑ in cure rate if abstain from sex or use condoms: *CID 44:213 & 220, 2007.* Treatment of male sex partner **not** indicated unless balanitis present. Metro extended release tabs 750 mg po q24h x 7 days available; no published data. **Pregnancy:** Oral **metro** or oral **clinda** 7-day regimens *(see CDC STD Guidelines: MMWR 64(RR-3):1, 2015).* If recurrent BV, can try adding **boric acid** to suppressive regimen: Metro 0.5 gm po bid x 7 days, then vaginal boric acid gelatin capsule 600 mg hs x 21 days, followed by Metro vaginal gel 2x/week x 16 weeks *(Sex Trans Dis 36:732, 2009).*

[12] 1 applicator contains 5 gm of gel with 37.5 mg metronidazole

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (24)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
GENITAL TRACT *(continued)*				
Men:				
Balanitis	Candida 40%, Group B strep, gardnerella	**Metro** 2 gm po as a single dose OR **Fluc** 150 mg po x 1 OR **Itra** 200 mg po bid x 1 day.		Occurs in 1/4 of male sex partners of women infected with candida. Exclude circinate balanitis (Reiter's syndrome); (non-infectious) responds to hydrocortisone cream.
Epididymo-orchitis *(CID 61:S770, 2015)*				
Age <35 years	N. gonorrhoeae, Chlamydia trachomatis	(**Ceftriaxone** 250 mg IM x 1 + **doxy** 100 mg po bid x 10 days) + bed rest, scrotal elevation, analgesics		Enterobacteriaceae occasionally encountered. Test all pts age < 35 yrs for HIV and syphilis.
Age >35 years or MSM (insertive partners in anal intercourse)	Enterobacteriaceae (coliforms)	[**Levo** 500-750 mg IV/po once daily] OR [(**Oflox** 300 mg po bid) or (400 mg IV twice daily)] for 10–14 days. **AM-SB**, **P Ceph 3**, **PIP-TZ** *(Dosage: see footnote page 29)* for MSM can be mixed GC/chlamydia with enterics so treat with FQ AND Ceftriaxone 250 mg IM x 1 Also: bed rest, scrotal elevation, analgesics		Midstream pyuria and scrotal pain and edema. NOTE: Do urine NAAT (nucleic acid amplification test) to ensure absence of N. gonorrhoeae with concomitant risk of FQ-resistant gonorrhoeae or of chlamydia if using agents without reliable activity. Other causes include: mumps, brucella, TB, intravesicular BCG, B. pseudomallei, coccidioides, Behcet's.
Non-gonococcal urethritis	*See page 23 (CID 61:S763, 2015)*			
Prostatitis—Review: *CID 50:1641, 2010. See Guidelines 2015 http://onlinelibrary.wiley.com/doi/10.1111/bju.13101/epdf*				
Acute Uncomplicated (with risk of STD; age < 35 yrs)	N. gonorrhoeae, C. trachomatis	**ceftriaxone** 250 mg IM x 1 then **doxy** 100 mg bid x 10 days.		FQs no longer recommended for gonococcal infections. Test for HIV. In AIDS pts, prostate may be focus of Cryptococcus neoformans.
Uncomplicated with low risk of STD	Enterobacteriaceae (coliforms)	**FQ** *(dosage: see Epididymo-orchitis, >35 yrs, above)* or **TMP-SMX** 1 DS tablet (160 mg TMP) po bid x 10–14 days (minimum). Some authorities recommend 4 weeks of therapy.		Treat as acute urinary infection, 14 days (not single dose regimen). Some recommend 3–4 wks therapy. If uncertain, do NAAT for C. trachomatis and N. gonorrhoeae. If resistant enterobacteriaceae, use ERTA 1 gm IV qd. If resistant pseudomonas, use IMP or MER (500 mg IV q6 or q8 respectively)
Chronic bacterial	Enterobacteriaceae 80%, enterococci 15%, P. aeruginosa	**CIP** 500 mg po bid x 4-6 wks OR **Levo** 750 mg po q24h x 4 wks.	**TMP-SMX-DS** 1 tab po bid x 1–3 mos (Fosfomycin: *see Comment*)	**With treatment failures** consider infected prostatic calculi. FDA approved dose of levo is 500 mg; editors prefer higher dose. Fosfomycin penetrates prostate; case report of success with 3 gm po q24h x 12-16 wks *(CID 61:1141, 2015)*.
Chronic prostatitis/chronic pain syndrome	The most common prostatitis syndrome. Etiology is unknown.	**α-adrenergic blocking agents are controversial** *(AnIM 133:367, 2000)*.		Pt has sx of prostatitis but negative cultures and no cells in prostatic secretions. Rev. *JAC 46:157, 2000*. In randomized double-blind study, CIP and an alpha blocker of no benefit *(AnIM 141:581 & 639, 2004)*.
HAND *(Bites: See Skin)*				
Paronychia				
Nail biting, manicuring	Staph. aureus (maybe MRSA)	Incision & drainage; culture	**TMP-SMX-DS** 1-2 tabs po bid while waiting for culture result.	*See Table 6 for alternatives*. Occasionally--candida, gram-negative rods.
Contact with saliva— dentists, anesthesiologists, wrestlers	Herpes simplex (Whitlow)	**Acyclovir** 400 mg tid po x 10 days	**Famciclovir** or **valacyclovir**, *see Comment*	Gram stain and routine culture negative. Famciclovir/valacyclovir for primary genital herpes; *see Table 14A, page 169*
Dishwasher (prolonged water immersion)	Candida sp.	**Clotrimazole** (topical)		Avoid immersion of hands in water as much as possible.

**NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (25)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
HEART				
Infective endocarditis—Native valve—empirical rx awaiting cultures—No IV illicit drugs	**NOTE: Diagnostic criteria** include evidence of continuous bacteremia (multiple positive blood cultures), new murmur (worsening of old murmur) of valvular insufficiency, definite emboli, and echocardiographic (transthoracic or transesophageal) evidence of valvular vegetations. Refs.: *Circulation 132:1435, 2015.* For antimicrobial prophylaxis, see *Table 15C, page 204.*			
Valvular or congenital heart disease but no modifying circumstances *See Table 15C, page 204 for prophylaxis*	Viridans strep 30–40%, "other" strep 15–25%, enterococci 5–18%, staphylococci 20-35% (including coag-neg staphylococci-*CID 46:232, 2008).*	**Vanco** 15-20 mg/kg q8-12h (target trough conc of 15-20 µg/mL) + **Ceftriaxone** 2g 24h OR **Vanco** 15-20 mg/kg q8-12h (target trough conc of 15-20 µg/mL) + **Gent** 1 mg/kg q8h IV/IM	Substitute **Dapto** 6 mg/kg IV q24h (or q48h for CrCl < 30 mL/min) for **Vanco**	If patient not acutely ill and not in heart failure, wait for blood culture results. If initial 3 blood cultures neg. after 24–48 hrs, obtain 2–3 more blood cultures before empiric therapy started. Gent dose is for CrCl of 80 mL/min or greater; even low-dose Gentamicin for only a few days carries risk of nephrotoxicity *(CID 48:713, 2009).* Gent is used for synergy; peak levels need not exceed 4 µg/mL and troughs should be < 1 µg/mL. Coagulase-negative staphylococci can occasionally cause native valve endocarditis *(CID 46:232, 2008).* Modify therapy based on identification of specific pathogen as soon as possible to obtain best coverage and to avoid toxicities.
Infective endocarditis—Native valve—IV illicit drug use ± evidence rt-sided endocarditis — empiric therapy	S. aureus*(MSSA & MRSA).* All others rare	**Vanco** 15-20 mg/kg q8-12h to achieve target trough concentrations of 15-20 mcg/mL recommended for serious infections.	**Dapto** 6 mg/kg IV q24h Approved for right-sided endocarditis.	**Surgery indications:** *See NEJM 368:1425, 2013.* Role of surgery in pts with left-sided endocarditis & large vegetation *(NEJM 366:2466, 2012).* No difference in 15 yr survival between bioprosthetic and mechanical valve *(JAMA 312:1323, 2014).*
Infective endocarditis—Native valve—culture positive *Ref:* Circulation 132:1435, 2015.				
Viridans strep, S. bovis *(S. gallolyticus)* with **penicillin G MIC ≤0.12 mcg/mL**	**Viridans strep, S. bovis (S. gallolyticus subsp. gallolyticus)**	[(**Pen G** 12–18 million units/day IV, divided q4h **x 2 wks**) PLUS (**gentamicin** IV 1 mg/kg q8h IV **x 2 wks**)] **OR** (**Pen G** 12–18 million units/day IV, divided - q4h **x 4 wks**) **OR** (**ceftriaxone** 2 gm IV q24h **x 4 wks**)	(**Ceftriaxone** 2 gm IV q24h + **gentamicin** 1 mg per kg IV q8h both **x 2 wks**). If allergy pen G or ceftriax, use **vanco** 15 mg/kg IV q12h to 2 gm/day max unless serum levels measured **x 4 wks**	Target **gent levels:** peak 3 mcg/mL, trough <1 mcg/mL. If very obese pt, recommend consultation for dosage adjustment. Infuse vanco over ≥1 hr to avoid "red man" syndrome. **S. bovis suggests occult bowel pathology (new name: S. gallolyticus).** Since relapse rate may be greater in pts ill for >3 mos. prior to start of rx, the penicillin-gentamicin synergism theoretically may be advantageous in this group.
Viridans strep, S. bovis (S. gallolyticus) with **penicillin G MIC >0.12 to ≤0.5 mcg/mL**	**Viridans strep, S. bovis, nutritionally variant streptococci, (e.g. S. abiotrophia) tolerant strep[17]**	**Pen G** 18 million units/day IV (divided q4h) **x 4 wks** **PLUS Gent** 1 mg/kg IV q8h **x 2 wks** **NOTE: Low dose of Gent**	**Vanco** 15 mg/kg IV q12h to max. 2 gm/day unless serum levels documented **x 4 wks**	Can use cefazolin for pen G in pt with allergy that is not IgE-mediated (e.g., anaphylaxis). Alternatively, can use vanco. *(See Comment above on gent and vanco).* **NOTE: If necessary to remove infected valve & valve culture neg., 2 weeks antibiotic treatment post-op sufficient** *(CID 41:187, 2005).*
For viridans strep or S. bovis with **pen G MIC >0.5** and enterococci susceptible to AMP/pen G, vanco, gentamicin (synergy positive) **NOTE:** Inf. Dis. consultation suggested	**"Susceptible" anterococci, viridans strep, S. bovis, nutritionally variant streptococci** (new names are: Abiotrophia sp. & Granulicatella sp.)	[(**Pen G** 18–30 million units per 24h IV, divided q4h **x 4–6 wks**) **PLUS** (**gentamicin** 1 mg/kg q8h IV **x 4–6 wks**)] **OR** (**AMP** 12 gm/day IV, divided q4h + **gent** as above **x 4–6 wks**)	**Vanco** 15 mg/kg IV q12h to max of 2 gm/day unless serum levels measured **PLUS gentamicin** 1 mg/kg q8h IV **x 4–6 wks** **NOTE: Low dose of gent**	**4 wks of rx if symptoms <3 mos.; 6 wks of rx if symptoms >3 mos.** Vanco for pen-allergic pts; do not use cephalosporins. Do **not** give gent once-q24h for enterococcal endocarditis. Target gent levels: peak 3 mcg/mL, trough <1 mcg/mL. Vanco target serum levels: peak 20–50 mcg/mL, trough 5–12 mcg/mL. **NOTE:** Because of ↑ frequency of resistance *(see below)*, all enterococci causing endocarditis should be tested in vitro for susceptibility to penicillin, gentamicin and vancomycin plus β lactamase production.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (26)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
HEART/Infective endocarditis—Native valve—culture positive *(continued)* Ref: *Circulation 132:1435, 2015*				
Enterococci: MIC streptomycin >2000 mcg/mL; MIC gentamicin >500-2000 mcg/mL; no resistance to penicillin	**Enterococci, high-level aminoglycoside resistance.** Esp with E. faecium; often concomitant resistance to Vanco	**E. faecium** (assumes Vanco-resistance): **Dapto** 8-12 mg/kg IV q24h + (**AMP** 2 gm IV q4h OR **Ceftaroline** 600 mg IV q8h) *(Curr Infect Dis Rep 16:431, 2014)*	**E. faecalis**: (**Ceftriaxone** 2 gm IV q12h + **AMP** 2 gm IV q4h) x 6 wks *(CID 56:1261, 2013 & AHA Guidelines)*	10–25% E. faecalis and 45–50% E. faecium resistant to high gent levels. May have to consider surgical removal of infected valve. Theory of efficacy of combination of Amp + Ceftriaxone: sequential blocking of PBPs 4&5 (Amp) and 2&3 (ceftriaxone).
Enterococci: pen G MIC >16 mcg/mL; no gentamicin resistance	**Enterococci, intrinsic pen G/AMP resistance** (E. faecium or E. faecalis)	**E. faecium: Dapto** 8-12 mg/kg IV q24h + (**AMP** 2 gm IV q4h OR **Ceftarotine** 600 mg IV q8h) *(Curr Infect Dis Rep 16:431, 2014)* OR **Dapto** 8-12 mg/kg IV q24h + **Gent** 1 mg/kg q8h	**E. faecalis: Vanco** 15 mg/kg IV q12h + **Gent** 1 mg/kg IV q8h OR, if beta-lactamase positive, **AM-SB** 3 gm IV q6h + **Gent** 1 mg/kg IV q8h	Target Vanco trough levels at 10-20 mcg/mL **Gentamicin** used for synergy; peak levels need not exceed 4 mcg/mL and trough should be <1.
Enterococci: Pen/AMP resistant + high-level gent/strep resistant + vanco resistant; usually VRE **Consultation suggested**	**Enterococci, vanco-resistant, resistant to beta-lactams & aminoglycosides. Common VRE pattern of susceptibilities**	**E. faecium: Dapto** 8-12 mg/kg IV q24h + (**AMP** 2 gm IV q4h OR **Ceftaroline** 600 mg IV q8h) *(Curr Infect Dis Rep 16:431, 2014)*	**E. faecalis** (susceptible): **Dapto** 8-12 mg/kg IV q24h + (**AMP** 2 gm IV q4h OR **Ceftaroline** 600 mg IV q8h)*(Curr Infect Dis Rep 16:431, 2014)*	AMP or Ceftaroline lessens risk of developing Dapto resistance & reverses resistance if present. Quinu-dalfo 7.5 mg/kg IV (central line) q8h is alternative for E. faecium (E. faecalis is resistant). Quinu-dalfo + AMP: see *Circulation 127:1810, 2013*) (success reported). Linezolid mono- or combo-therapy for both E. faecium / E. faecalis: variable success; bacteriostatic for enterococci *(Curr Infect Dis Rep 16:431, 2014)*.
Staphylococcal endocarditis Aortic &/or mitral valve infection—MSSA Surgery indications: see *Comment page 28.*	**Staph. aureus, methicillin-sensitive**	**Nafcillin (oxacillin)** 2 gm IV q4h **x 4–6 wks**	[(**Cefazolin** 2 gm IV q8h **x 4–6 wks**) **OR** **Vanco** 30-60 mg/kg/d in 2-3 divided doses to achieve trough of 15-20 mcg/ml **x 4–6 wks**	If IgE-mediated penicillin allergy, 10% cross-reactivity to cephalosporins *(AnIM 141:16, 2004)*. **Cefazolin** and **Nafcillin** probably similar in efficacy and Celazolin better tolerated *(AAC 55:5122, 2011)*
Aortic and/or mitral valve—MRSA	**Staph. aureus, methicillin-resistant**	**Vanco** 30-60 mg/kg per day in 2-3 divided doses to achieve target trough concentrations of 15-20 mcg/mL recommended for serious infections.	**Dapto** 8-10 mg/kg q24h IV (NOT FDA approved for this indication or dose)	In clinical trial *(NEJM 355:653, 2006)*, high failure rate with both vanco and daplo in small numbers of pts. For other alternatives, see *Table 6, pg 82.* Daptomycin references: *JAC 68:936 & 2921, 2013.* Case reports of success with Telavancin *(JAC 65:1315, 2010; AAC 54 5376, 2010; JAC (Jun 8), 2011)* and ceftaroline *(JAC 67:1267, 2012; J Infect Chemo online 7/14/12).*
Tricuspid valve infection (usually IVDUs): MSSA	**Staph. aureus, methicitlin-sensitive**	**Nafcillin (oxacillin)** 2 gm IV q4h **PLUS gentamicin** 1 mg/kg IV q8h **x 2 wks. NOTE: low dose of gent**	**If penicillin allergy: Vanco** 30-60 mg/kg/d in 2-3 divided doses to achieve trough of 15-20 mcg/mL x 4 wks **OR** **Dapto** 6 mg/kg IV q24h (avoid if concomitant left-sided endocarditis). 8-12 mg/kg IV q24h used in some cases, but not FDA approved.	**2-week regimen not long** enough if metastatic infection (e.g., osteo) or left-sided endocarditis. If **Dapto** is used treat for at least 4 weeks. **Dapto** resistance can occur de novo, after or during vanco, or after/during dapto therapy. Cefazofin 2 gm q8h also an option. Fewer adverse events and discontinuations vs nafcillin *(Clin Infect Dis 59:369, 2014).*

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (27)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
HEART/Infective endocarditis—Native valve—culture positive *(continued)*				
Tricuspid valve--MRSA	**Staph. aureus, methicillin-resistant**	**Vanco** 15-20 mg/kg q8-12h to achieve target trough concentrations of 15-20 mcg/mL recommended for serious infections **x 4–6 wks**	**Dapto** 6 mg/kg IV q24h x 4-6 wks equiv to **vanco** for rt-sided endocarditis; both vanco & dapto did poorly if lt-sided endocarditis *(NEJM 355: 653, 2006). (See Comments & table 6, page 82)*	**Linezolid:** Limited experience *(see JAC 58:273, 2006)* in patients with few treatment options; 64% cure rate; clear failure in 21%; thrombocytopenia in 31%. **Dapto** dose of 8-12 mg/kg may help in selected cases, but not FDA-approved.
Slow-growing fastidious Gm-neg. bacilli--any valve	**HACEK group** *(see Comments).*	**Ceftriaxone** 2 gm IV q24h **x 4 wks** OR **CIP** 400 mg IV q12h x 4 wks (Bartonella resistant – *see below).*	**AM-SB** 3 gm IV q6h x 4 wks or **CIP** (400 mg IV q12h or 500 mg po bid) x 4 wks	**HACEK (acronym for Haemophilus parainfluenzae, H. (aphrophilus) aggregatibacter, Actinobacillus, Bartonella, Cardiobacterium, Eikenella, Kingella)**. Penicillinase-positive HACEK organisms should be susceptible to AM-SB + gentamicin. *Ref: Circulation 111:e394, 2005.*
Bartonella species--any valve	B. henselae, B. quintana	(**Doxy** 100 mg IV/po bid + **RIF** 300 mg IV/po bid) x 6-8 wks		**Dx:** Immunofluorescent antibody titer ≥1:800; blood cultures only occ. positive, or PCR of tissue from surgery. **Surgery:** Over ½ pts require valve surgery; relation to cure unclear. B. quintana transmitted by body lice among homeless.
Infective endocarditis— "culture negative" Fever, valvular disease, and ECHO vegetations ± emboli and neg. cultures.		Etiology in 348 cases studied by serology, culture, histopath, & molecular detection: C. burnetii 48%, Bartonella sp. 28%, and rarely (Abiotrophia elegans (nutritionally variant strep), Mycoplasma hominis, Legionella pneumophila, Tropheryma whipplei—together 1%), & rest without etiology identified (most on antibiotic). *See CID 51:131, 2010 for approach to work-up.* Chronic Q fever: *JCM 52:1637, 2014.*		
Infective endocarditis—Prosthetic valve—empiric therapy (cultures pending) S. aureus now most common etiology *(JAMA 297:1354, 2007).*				
Early (<2 mos post-op)	S. epidermidis, S. aureus. Rarely, Enterobacteriaceae, diphtheroids, fungi	**Vanco** 15-20 mg/kg q8-12h + **gentamicin** 1 mg/kg IV q8h + **RIF** 600 mg po q24h		Early surgical consultation advised especially if etiology is S. aureus, evidence of heart failure, presence of diabetes and/or renal failure, or concern for valve ring abscess *(JAMA 297:1354, 2007; CID 44:364, 2007).* Early valve surgery not associated with improved 1 year survival in patients with S. aureus prosthetic valve infection *(CID 60:741, 2015).*
Late (>2 mos post-op)	S. epidermidis, viridans strep, enterococci, S. aureus			
Infective endocarditis—Prosthetic valve—positive blood cultures Treat for 6 weeks, even if suspect Viridans Strep. **Surgical consultation advised:** Indications for surgery: severe heart failure, S. aureus infection, prosthetic dehiscence, resistant organism, emboli due to large vegetation *(JACC 48:e1, 2006). See also, Eur J Clin Micro Infect Dis 38:528, 2010.*	Staph. epidermidis	(**Vanco** 15-20 mg/kg IV q8-12h + **RIF** 300 mg po q8h) **x 6 wks** + **gentamicin** 1 mg/kg IV q8h **x 14 days.**		If S. epidermidis is susceptible to nafcillin/oxacillin in vitro (not common), then substitute nafcillin (or oxacillin) for vanco. Target vanco trough concentrations 15-20 µg/mL. Some clinicians prefer to wait 2-3 days after starting vanco/ gent before starting RIF, to decrease bacterial density and thus minimize risk of selecting rifampin-resistant subpopulations.
	Staph. aureus	Methicillin sensitive: (**Nafcillin** 2 gm IV q4h + **RIF** 300 mg po q8h) **times 6 wks** + **gentamicin** 1 mg per kg IV q8h **times 14 days.** Methicillin resistant: (**Vanco** 15-20 mg/kg IV q8-12h (to achieve a target trough of 15-20 mcg/mL) + **RIF** 300 mg po q8h) **times 6 wks** + **gentamicin** 1 mg per kg IV q8h **times 14 days.**		
	Viridans strep, enterococci	*See infective endocarditis, native valve, culture positive, page 28.* Treat for 6 weeks.		
	Enterobacteriaceae or P. aeruginosa	**Aminoglycoside** (**tobra** if P. aeruginosa) + (**PIP-TZ** or **P Ceph 3 AP** or **P Ceph 4** or **an anti-pseudomonal Pen**)		In theory, could substitute CIP for aminoglycoside, but no clinical data and resistance is common. Select definitive regimen based on susceptibility results. Can occur with native valves also.
	Candida, aspergillus	*Table 11, page 122*		High mortality. Valve replacement plus antifungal therapy standard therapy but some success with antifungal therapy alone.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (28)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
HEART *(continued)*				
Infective endocarditis—Q fever *LnID 10:527, 2010; NEJM 356:715, 2007.*	Coxiella burnetii	**Doxy** 100 mg po bid + **hydroxychloroquine** 600 mg/day for at least 18 mos *(Mayo Clin Proc 83:571, 2008)* *Pregnancy: Need long term* **TMP-SMX** *(see CID 45:548, 2007).*		**Dx:** Phase I IgG titer >800 plus clinical evidence of endocarditis. Treatment duration: 18 mos for native valve, 24 mos for prosthetic valve. Monitor serologically for 5 yrs.
Pacemaker/defibrillator infections (British guidelines: *JAC 70:325, 2015*)	S. aureus (40%), S. epidermidis (40%), Gram negative bacilli (5%), fungi (5%).	**Device removal + vanco** 15-20 mg/kg (IV q8-12h+ **RIF** 300 mg po bid	**Device removal + dapto** 6 mg/kg/d IV q24h[NAI] + **RIF** *(pocket)* 300 mg po bid	**Duration of rx after device removal:** For "pocket" or subcutaneous infection, 10–14 days; if lead-assoc. endocarditis, 4–6 wks depending on organism. Device removal and absence of valvular vegetation assoc. with significantly higher survival at 1 yr *(JAMA 307:1727, 2012).*
Pericarditis, purulent— empiric therapy *Ref: Medicine 88: 52, 2009.*	Staph. aureus, Strep. pneumoniae, Group A strep, Enterobacteriaceae	**Vanco + CIP** *(Dosage, see footnote[14])*	**Vanco + CFP** *(see footnote[14])*	Drainage required if signs of tamponade. Forced to use empiric vanco due to high prevalence of MRSA.
Rheumatic fever with carditis Ref.: *Ln 366:155, 2005*	Post-infectious sequelae of Group A strep infection (usually pharyngitis)	ASA, and usually prednisone 2 mg/kg/day po x 2 wks for symptomatic treatment of fever, arthritis, arthralgia. May not influence carditis.		Clinical features: Carditis, polyarthritis, chorea, subcutaneous nodules, erythema marginatum. *Prophylaxis:* see *page 62*
Ventricular assist device-related infection *CID 57:1438, 2013*	S. aureus, S. epidermidis, aerobic gm-neg bacilli, Candida sp	After culture of blood, wounds, drive line, device pocket and maybe pump: **Vanco** 15-20 mg/kg IV q8-12h + (**Cefepime** 2 gm IV q12h) + **fluconazole** 800 mg IV q24h.		Can substitute **daptomycin** 10 mg/kg/d[NAI] for **vanco,** (**CIP** 400 mg IV q12h or **Levo** 750 mg IV q24h) for cefepime, and (**vori, caspo, micafungin or anidulafungin**) for **fluconazole**. Modify regimen based on results of culture and susceptibility tests. Higher than FDA-approved Dapto dose because of potential emergence of resistance.
JOINT—*Also see Lyme Disease, page 58*				
Reactive arthritis				
Reiter's syndrome *(See Comment for definition)*	Occurs wks after infection with C. trachomatis, Campylobacter jejuni, Yersinia enterocolitica, Shigella/Salmonella sp.	Only treatment is non-steroidal anti-inflammatory drugs		Definition: Urethritis, conjunctivitis, arthritis, and sometimes uveitis and rash. Arthritis: asymmetrical oligoarthritis of ankles, knees, feet, sacroiliitis. Rash: palms and soles—keratoderma blennorrhagica; circinate balanitis of glans penis. HLA-B27 positive predisposes to Reiter's.
Poststreptococcal reactive arthritis *(See Rheumatic fever, above)*	Immune reaction after strep pharyngitis: (1) arthritis onset in <10 days, (2) lasts months, (3) unresponsive to ASA	Treat strep pharyngitis and then NSAIDs (prednisone needed in some pts)		Migrative arthritis after a β-hemolytic strep infection in absence of sufficient Jones criteria for acute rheumatic fever. Ref.: *Mayo Clin Proc 75:144, 2000.*

[14] **Aminoglycosides** *(see Table 10D, page 118),* **IMP** 0.5 gm IV q6h, **MER** 1 gm IV q8h, **nafcillin** or **oxacillin** 2 gm IV q4h, **PIP-TZ** 3.375 gm IV q6h or 4.5 gm q8h, **AM-SB** 3 gm IV q6h, **P Ceph** 1 (cephalothin 2 gm IV q4h or cefazolin 2 gm IV q8h), **CIP** 750 mg po bid or 400 mg IV bid, **vanco** 1 gm IV q12h, **RIF** 600 mg po q24h, **aztreonam** 2 gm IV q8h, **CFP** 2 gm IV q12h

TABLE 1 (29)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
JOINT *(continued)*				
Septic arthritis: Treatment requires both adequate drainage of purulent joint fluid and appropriate antimicrobial therapy. **There is no need to inject antimicrobials into joints.** Empiric therapy after collection of blood and joint fluid for culture; review Gram stain of joint fluid.				
Infants <3 mos (neonate)	Staph. aureus, Enterobacteriaceae, Group B strep	**If MRSA not a concern: (Nafcillin** or **oxacillin)** + **P Ceph 3**	**If MRSA a concern: Vanco + P Ceph 3**	Blood cultures frequently positive. Adjacent bone involved in 2/3 pts. Group B strep and gonococci most common community-acquired etiologies.
Children (3 mos–14 yrs)	S. aureus 27%, S. pyogenes & S. pneumo 14%, H. influ 3%, Gm-neg. bacilli 6%, other (GC, N. mening) 14%, unk 36%	**Vanco** + **(Cefotaxime, ceftizoxime or ceftriaxone)** until culture results available Steroids—see *Comment*		Marked ↓ in H. influenzae since use of conjugate vaccine. **NOTE:** Septic arthritis due to salmonella has no association with sickle cell disease, unlike salmonella osteomyelitis. 10 days of therapy as effective as a 30-day treatment course if there is a good clinical response and CRP levels normalize quickly *(CID 48:1201, 2009).*
Adults *(review Gram stain)*: *See page 58 for Lyme Disease and page 58 for gonococcal arthritis*				
Acute monoarticular				
At risk for sexually-transmitted disease	**N. gonorrhoeae** *(see page 23)*, S. aureus, streptococci, rarely aerobic Gm-neg. bacilli	**Gram stain negative: Ceftriaxone** 1 gm IV q24h or **cefotaxime** 1 gm IV q8h or **ceftizoxime** 1 gm IV q8h	If Gram stain shows Gm+ cocci in clusters: **vanco** 15-20 mg/kg IV q8-12h.	For treatment comments, see *Disseminated GC, page 23*
Not at risk for sexually-transmitted disease	S. aureus, streptococci, Gm-neg. bacilli	**All empiric choices guided by Gram stain** **Vanco + P Ceph 3** | **Vanco + (CIP** or **Levo)** *For treatment duration, see Table 3, page 72*		Differential includes gout and chondrocalcinosis (pseudogout). **Look for crystals in joint fluid.** **NOTE:** *See Table 6 for MRSA treatment.*
Chronic monoarticular	Brucella, nocardia, mycobacteria, fungi	*See Table 2 & Table 12*		
Polyarticular, usually acute	**Gonococci,** B. burgdorferi, acute rheumatic fever, viruses, e.g., hepatitis B, rubella vaccine, parvo B19	Gram stain usually negative for GC. If sexually active, culture urethra, cervix, anal canal, throat, blood, joint fluid, and then: **ceftriaxone** 1 gm IV q24h		If GC, usually associated petechiae and/or pustular skin lesions and tenosynovitis. Consider Lyme disease if exposure areas known to harbor infected ticks. *See page 58.* Expanded differential includes gout, pseudogout, reactive arthritis (HLA-B27 pos.).
Septic arthritis, post intra-articular injection	MSSE/MRSE 40%, MSSA/ MRSA 20%, P. aeruginosa, Propionibacteria, AFB	**NO empiric therapy.** Arthroscopy for culture/sensitivity, crystals, washout		Treat based on culture results x 14 days (assumes no foreign body present).

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (30)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
JOINT *(continued)*				
Infected prosthetic joint (PJI) • Suspect infection if sinus tract or wound drainage; acutely painful prosthesis; chronically painful prosthesis; or high ESR/CRP assoc. w/painful prosthesis. • **Empiric therapy is NOT recommended.** Treat based on culture and sensitivity results. • **3 surgical options:** 1) debridement and prosthesis retention (if sx < 3 wks or implantation < 30 days); 2) 1 stage, direct exchange; 3) 2 stage: debridement, removal, reimplantation • **IDSA Guidelines:** *CID 56:e1, 2013.* • Data do not allow assessment of value of adding antibacterial cement to temporary joint spacers *(CID 55:474, 2012).* • Evidence of systemic absorption of Tobra from antibiotic-impregnated cement spacers (CID 58:1783, 2014).	MSSA/MSSE	**Debridement/Retention** [(**Nafcillin** 2 gm IV q4h or **Oxacillin** 2 gm IV q4h IV) + **Rifampin** 300 mg po bid] OR (**Cefazolin** 2 gm IV q8h + **Rifampin** 300 mg po bid) x 2-6 weeks followed by [(**Ciprofloxacin** 750 mg po bid OR **Levofloxacin** 750 mg po q24h) + **Rifampin** 300 mg po bid] for 3-6 months (shorter duration for total hip arthroplasty) **1-stage exchange:** IV/PO regimen as above for 3 mos **2-stage exchange:** regimen as above for 4-6 wks	(**Daptomycin** 6-8 mg/kg IV q24h OR **Linezolid** 600 mg po/IV bid) ± **Rifampin** 300 mg po bid	• **Confirm isolate susceptibility to fluoroquinolone and rifampin:** for fluoroquinolone-resistant isolate consider using other active highly bioavailable agent, e.g., TMP-SMX, Doxy, Minocycline, Amoxicillin-Clavulanate, Clindamycin, or Linezolid • Enterococcal infection: addition of aminoglycoside optional. • *P. aeruginosa* infection: consider adding aminoglycoside if isolate is susceptible, (but if this improves outcome unclear). • Prosthesis retention most important risk factor for treatment failure *(Clin Microbiol Infect 16:1789, 2010).* (Linezolid 600 mg + Rifampin 300 mg) may be effective as salvage therapy if device removal not possible *(Antimicrob Agents Chemother 55:4308, 2011)* • If prosthesis is retained, consider long-term, suppressive therapy, particularly for staphylococcal infections: depending on in vitro susceptibility options include TMP-SMX, Doxycycline, Minocycline, Amoxicillin, Ciprofloxacin, Cephalexin. • Culture yield may be increased by sonication of prosthesis *(N Engl J Med 357:654, 2007).* • Other treatment consideration: Rifampin is bactericidal vs. biofilm-producing bacteria. Never use Rifampin alone due to rapid development of resistance. Rifampin 300 mg po/IV bid + Fusidic acid[NIS] 500 mg po/IV tid is another option *(Clin Micro Inf 12(S3):93, 2006).* • Watch for toxicity if Linezolid is used for more than 2 weeks of therapy.
	MRSA/MRSE	**Debridement/Retention:** (**Vancomycin** 15-20 mg/kg IV q8-12h + **Rifampin** 300 mg po bid) x 2-6 weeks *followed by* [(**Ciprofloxacin** 750 mg po bid OR **Levofloxacin** 750 mg po q24h) + **Rifampin** 300 mg po bid] for 3-6 months (shorter duration for total hip arthroplasty) **1-stage exchange:** IV/PO regimen as above for 3 mos **2-stage exchange:** regimen as above for 4-6 wks	(**Daptomycin** 6-8 mg/kg IV q24h OR **Linezolid** 600 mg po/IV bid) ± **Rifampin** 300 mg po bid	
	Streptococci (Grps A, B, C, D, viridans, other)	**Debridement/Retention: Penicillin** G 20 million units IV continuous infusion q24h or in 6 divided doses OR **Ceftriaxone** 2 gm IV q24h x 4-6 weeks **1 or 2 stage exchange:** regimen as above for 4-6 wks	**Vancomycin** 15 mg/kg IV q12h	
	Enterococci	**Debridement/Retention: Pen-susceptible: Ampicillin** 12 gm IV OR **Penicillin** G 20 million units IV continuous infusion q24h or in 6 divided doses x 4-6 weeks **Pen-resistant: Vancomycin** 15 mg/kg IV q12h x 4-6 weeks **1 or 2 stage exchange:** regimen as above for 4-6 wks	**Daptomycin** 6-8 mg/kg IV q24h OR **Linezolid** 600 mg po/IV bid	
	Propionibacterium acnes	**Debridement/Retention: Penicillin** G 20 million units IV continuous infusion or in 6 divided doses OR **Ceftriaxone** 2 gm IV q24h x 4-6 weeks **1 or 2 stage exchange:** regimen as above for 4-6 wks	**Vancomycin** 15 mg/kg IV q12h OR **Clindamycin** 300-450 mg po qid	
	Gm-neg enteric bacilli	**Debridement/Retention: Ertapenem** 1 gm q24h IV OR other beta-lactam (e.g., **Ceftriaxone** 2 gm IV q24h OR **Cefepime** 2 gm IV q12h, based on susceptibility) x 4-6 weeks **1 or 2 stage exchange:** regimen as above for 4-6 wks	**Ciprofloxacin** 750 mg po bid	
	P. aeruginosa	**Debridement/Retention: Cefepime** 2 gm IV q12h OR **Meropenem** 1 gm IV q8h + **Tobramycin** 5.1 mg/kg once daily IV **1 or 2 stage exchange:** regimen as above for 4-6 wks	**Ciprofloxacin** 750 mg po bid or 400 mg IV q8h	
Rheumatoid arthritis	**TNF inhibitors** (adalimumab, certolizumab, etanercept, golimumab, infliximab) and other anti-inflammatory biologics (tolacitinib, rituximab, tocilizumab, abatacept) ↑ risk of TBc, fungal infection, legionella, listeria, and malignancy. *See Med Lett 55:1, 2013 for full listing.*			
Septic bursitis: Olecranon bursitis; prepatellar bursitis	Staph. aureus >80%, M. tuberculosis (rare), M. marinum (rare)	(**Nafcillin** or **oxacillin** 2 gm IV q4h or **Cefazolin** 2 gm IV q8h if **MSSA**	(**Vanco** 15-20 mg/kg IV q8-12h or **linezolid** 600 mg po bid) if **MRSA**	Empiric MRSA coverage recommended if risk factors are present and in high prevalence areas. Immunosuppression, not duration of therapy, is a risk factor for recurrence; 7 days of therapy may be sufficient for immunocompetent patients undergoing one-stage bursectomy *(JAC 65:1008, 2010).* If MSSA **Dicloxacillin** 500 mg po qid as oral step-down. If MRSA **Daptomycin** 6 mg/kg IV q24h.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (31)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
KIDNEY & BLADDER				
Acute Uncomplicated Cystitis & Pyelonephritis in Women				
Cystitis Diagnosis: dysuria, frequency, urgency, suprapubic pain & no vaginal symptoms	E. coli (75-95%) P. mirabilis K. pneumoniae S. saprophyticus	**TMP-SMX DS** 1 tab po bid x 3 days. Avoid if 20% or more local E. coli are resistant	**Fosfomycin** 3 gm po x 1 dose	• Pyridium (phenazopyridine) may hasten resolution of dysuria • Other beta lactams are less effective • Nitrofurantoin & Fosfomycin active vs. ESBLs; however, if early pyelonephritis avoid these drugs due to low renal concentrations • On occasion vaginitis can mimic symptoms of cystitis
	Presence of enterococci, Grp B streptococcus, other S. epidermidis suggests contamination	**Nitrofurantoin** 100 mg po bid x 5 days	**Pivmecillinam** (NUS) 400 mg po bid x 3-7 days	
	Often no need for culture if uncomplicated	(**CIP** 250 mg po bid OR **CIP-ER** 500 mg po once daily OR **Moxi** 400 g po once daily) x 3 days		
Pyelonephritis Diagnosis: fever, CVA, pain, nausea/vomiting	Same as for Cystitis, above. Need urine culture & sensitivity testing	**Outpatient:** **Ceftriaxone** 1 gm IV, then (**CIP** 500 mg po bid OR **CIP-ER** 1000 mg po once daily OR **Levo** 750 mg po once daily) x 7 days Culture/sens results may allow **TMP-SMX DS** 1 tab po bid	**Inpatient:** Local resistance data important **Ceftriaxone** 1 gm IV q24h OR (**CIP** 400 mg IV q12h OR **Levo** 750 mg IV once daily OR **Moxi** 400 mg IV once daily. If ESBL S & E coli: **MER** 0.5-1 gm IV q8h	• When tolerating po fluids, can transition to oral therapy; drug choice based on culture/sens results • No need for follow-up urine cultures in pts who respond to therapy • If symptoms do not abate quickly, imaging of urinary tract for complications, e.g., silent stone or stricture • Avoid Fosfomycin, Nitrofurantoin, Pivmecillinam due to low renal concentrations
Pregnancy: Asymptomatic bacteriuria & cystitis Drug choice based on culture / sensitivity results; do follow-up culture one week after last dose of antibiotic	E. coli (70%) Klebsiella sp. Enterobacter sp. Proteus sp. Grp B Streptococcus	**Nitrofurantoin** (but not in 1st trimester) 100 mg po q12h x 5-7 days, OR **Amox-Clav** 500 mg po q8h x 3-7 days; OR **Cephalexin** 500 mg po q6h x 3-7 days	**TMP-SMX DS** (but not in 1st trimester or at term) 1 tab po q12h x 3 days OR **Cefpodoxime** 100 mg po q12h x 3-7 days	• Treatment recommended to avoid progression to cystitis or pyelonephritis • Untreated bacteriuria associated with increased risk of low birth wt, preterm birth & increased perinatal mortality • If post-treatment culture positive, re-treat with different drug of longer course of same drug • If documented failure after 2nd course, Nitrofurantoin 50 or 100 g po qhs for duration of pregnancy
Pregnancy: Acute pyelonephritis Diagnosis: CVA pain, fever, nausea/vomiting in 2nd/3rd trimester. *See Comment*	Same as for Cystitis, above. Regimens are empiric therapy *(see Comment)*	**Moderately ill: Ceftriaxone** 1 gm IV q24h OR **Cefepime** 1 gm IV q12h. If Pen-allergic, **Aztreonam** 1 gm IV q8h (no activity vs Gram-pos cocci)	**Severely ill: Pip-Tazo** 3.375 gm IV q6h OR **MER** 500 mg IV q8h OR **ERTA** 1 gm IV q24h	• Differential dx includes: placental abruption & infection of amniotic fluid • Try to avoid FQs and AGs during pregnancy • Switch to po therapy after afebrile x 48 hrs • **Treat for 10-14 days** • If pyelo recurs, re-treat. Once asymptomatic continue suppressive therapy for duration of pregnancy: Nitrofurantoin 50-100 mg po qhs OR Cephalexin 250-500 mg po qhs
Recurrent UTIs in Women (2 or more infections in 6 mos / 3 or more infections in 1 yr) Risk factors: family history, spermicide use, presence of cystocele, elevated post-void residual urine volume	Same as for Cystitis, above. Regimens are options for antimicrobial prophylaxis	Continuous: (**TMP-SMX SS** OR **TMP** 100 mg OR **Cephalexin** 250 mg OR **CIP** 125 mg) po once daily	Post-coital: (**TMP-SMX SS** OR **Cephalexin** 250 mg OR **CIP** 125 mg) 1 tab po	• No strong evidence to support use of cranberry juice • Topical estrogen cream reduces risk of recurrent UTI in postmenopausal women • Probiotics need more study

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (32)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
KIDNEY & BLADDER/Acute Uncomplicated Cystitis & Pyelonephritis in Women *(continued)*				
Asymptomatic Bacteriuria in Women Defined: 2 consecutive clean catch urine cultures with ≥ 105 CFU/mL of same organism	Same as for Cystitis, above	**Treatment indicated:** pregnancy, urologic procedure causing bleeding from mucosa	**No treatment indicated:** non-pregnant premenopausal women, spinal cord injury pts, elderly women in/out of long-term home, pre-elective pelvic surgery	• Asymptomatic bacteriuria & pyuria are discordant. 60% of pts with pyuria have no bacteriuria and pyuria commonly accompanies asymptomatic bacteriuria.
Acute Uncomplicated Cystitis & Pyelonephritis in Men. Risk of uncomplicated UTI increased with history of receptive anal sex & lack of circumcision. See also, Complicated UTIs in Men & Women, below				
Cystitis	E. coli (75-95%) Rarely other enterobacteriaceae	**TMP-SMX DS** 1 tab po bid x 7-14 days	(**CIP** 500 mg po bid OR **CIP-ER** 1000 mg po once daily OR **Levo** 750 mg po once daily) x 7-14 days	• If recurrent, evaluate for prostatitis. • Cystitis plus symptoms of bladder outlet obstruction suggests concomitant acute bacterial prostatitis • Consider presence of STDs. Recommend NAAT for C. trachomatis & N. gonorrhoeae • Avoid Nitrofurantoin due to low renal concentration in prostate • If any hint of obstructive uropathy, image collecting system asap • Case report: Fosfomycin 3 gm daily used for MDR gm-neg bacilli *(CID 61:1141, 2015)*
Pyelonephritis		*Low risk of MDR-GNB:* (**CIP** 400 mg IV q12h OR **Levo** 750 mg IV once daily) x 7-14 days	*High risk of MDR-GNB:* **MER** 0.5-1 gm IV q8h x 7-14 days	
Acute Complicated UTIs in Men & Women				
Defined: UTI plus co-morbid condition that increases infection severity & risk of failure, e.g., diabetes, pregnancy, late diagnosis, chronic foley catheter, suprapubic tube, obstruction secondary to stone, anatomic abnormalities, immunosuppression	E. coli or Other enterobacteriaceae plus: P. aeruginosa Enterococci S. aureus Candida sp.	Prior to empiric therapy: urine culture & sensitivity If hypotensive: blood cultures. If obstructive uropathy suspected, need imaging of urinary tract asap *See Comments* *Low risk of MDR GNB:* **Levo** 750 mg IV once daily OR **Ceftriaxone** 1 gm IV once daily OR **Cefepime** 1 gm IV q12h OR **Pip-Tazo** 3.375 gm IV q6h OR **Gent** 5 mg/kg IV Once daily. If Pen-allergic: **Aztreonam** 2 gm IV q8h	*Risk of MDR GNB:* **MER** 0.5-1 gm IV q8h OR **Ceftolozane-tazobactam** 1.5 gm IV q8h OR **Ceftazidime-avibactam** 2.5 gm IV q8h	• Uncontrolled infection, esp. if obstruction, can result in emphysematous pyelonephritis, renal abscess, carbuncle, papillary necrosis or perinephric abscess • Due to co-morbidities & frequent infections, increased risk of drug-resistance pathogens • Due to high incidence of resistance and infection severity, Nitrofurantoin, Fosfomycin & TMP-SMX should not be used for empiric therapy • If enterococci cultured, need to adjust therapy based on in vitro susceptibility • Duration of treatment varies with status of co-morbid conditions, need for urologic procedures & individualized pt clinical response

Abbreviations on page 2.

**NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (33)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
LIVER *(for spontaneous bacterial peritonitis, see page 46)*				
Chofangitis		*See Gallbladder, page 17*		
Cirrhosis & variceal bleeding	Esophageal flora	(**Norfloxacin** *400* mg po bid or **CIP** *400* mg IV q12h) x max. of 7 days	**Ceftriaxone** 1 gm IV once daily for max. of 7 days	Short term prophylactic antibiotics in cirrhotics with G-I hemorr, with or without ascites, decreases rate of bacterial infection & ↑ survival *(Hepatology 46:922, 2007).*
Hepatic abscess Klebsiella liver abscess ref.: *Ln ID 12:881, 2012*	Enterobacteriaceae (esp. Klebsiella sp.), bacteroides, enterococci, Entamoeba histolytica, Yersinia enterocolitica (rare), Fusobacterium necrophorum *(Lemierre's).* *For echinococcus, see Table 13, page 160. For cat-scratch disease (CSD), see pages 45 & 57*	**Metro** + (**ceftriaxone** or **cefoxitin** or **PIP-TZ** or **AM-SB** or **CIP** or **levo**.	**Metro** (for amoeba) + either **IMP**, **MER** or **DORI**	**Serological tests for amebiasis should be done on all patients;** if neg., surgical drainage or percutaneous aspiration. In pyogenic abscess, ½ have identifiable GI source or underlying biliary tract disease. If amoeba serofogy positive, treat with **metro** alone without surgery. Empiric **metro** included for both E. histolytica & bacteroides. **Hemochromatosis** associated with Yersinia enterocolitica liver abscess; regimens listed are effective for yersinia. Klebsiella pneumonia genotype K1 associated ocular & CNS Klebsiella infections.
Hepatic encephalopathy	Urease-producing gut bacteria	**Rifaximin** 550 mg po bid (take with lactulose)		Refs: *NEJM 362:1071, 2010; Med Lett 52:87, 2010.*
Leptospirosis	Leptospirosis, *see page 61*			
Peliosis hepatis in AIDS pts	Bartonella henselae and B. quintana	*See page 57*		
Post-transplant infected "biloma"	Enterococci (incl. VRE), candida, Gm-neg. bacilli (P. aeruginosa 8%), anaerobes 5%	**Linezolid** 600 mg IV bid + **CIP** 400 mg IV q12h + **fluconazole** 400 mg IV q24h	**Dapto** 6 mg/kg per day + **Levo** 750 mg IV q24h + **fluconazole** 400 mg IV q24h	Suspect if fever & abdominal pain post-transplant. Exclude hepatic artery thrombosis. Presence of candida and/or VRE bad prognosticators.
Viral hepatitis	Hepatitis A, B, C, D, E, G	*See Table 14E and Table 14F*		
LUNG/Bronchi				
Bronchiolitis/wheezy bronchitis (expiratory wheezing)				
Infants/children (≤ age 5) *See RSV, Table 14A page 175* Ref: *Ln 368:312, 2006*	**Respiratory syncytial virus** (RSV) 50%, parainfluenza 25%, human metapneumovirus	Antibiotics not useful, mainstay of therapy is oxygen. Ribavirin for severe disease: 6 gm vial (20 mg/mL) in sterile H_2O by SPAG-2 generator over 18-20 hrs daily times 3-5 days.		RSV most important. Rapid diagnosis with antigen detection methods. For prevention a humanized mouse monoclonal antibody, **palivizumab**. *See Table 14A, page 175.* RSV immune globulin is no longer available. Guidance from the American Academy of Pediatrics recommends use of Palivizumab only in newborn infants born at 29 weeks gestation (or earlier) and in special populations (e.g., those infants with significant heart disease). *(Pediatrics 2014;134:415–420)*
Bronchitis				
Infants/children (≤ age 5)	< Age 2: Adenovirus; age 2-5: Respiratory syncytial virus, parainfluenza 3 virus, human metapneumovirus		Antibiotics indicated only with associated sinusitis or heavy growth on throat culture for S. pneumo., Group A strep, H. influenzae or no improvement in 1 week. Otherwise rx is symptomatic.	
Adolescents and adults with acute tracheobronchitis (Acute bronchitis) Ref.: *JAMA 312:2678, 2014*	Usually viral. M. pneumoniae 5%; C. pneumoniae 5%. *See Persistent cough (Pertussis)*	**Antibiotics not indicated.** Antitussive ± inhaled bronchodilators. Throat swab PCR available for Dx of mycoplasma or chlamydia.		Purulent sputum alone not an indication for antibiotic therapy. Expect cough to last 2 weeks. If fever/rigors, get chest x-ray. **If mycoplasma documented, prefer doxy over macrolides due to increasing macrolide resistance *(JAC 68:506, 2013).***

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (34)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
LUNG/Bronchi/Bronchitis *(continued)*				
Persistent cough (>14 days), afebrile during community outbreak: Pertussis (whooping cough) 10–20% adults with cough >14 days have pertussis (Review: *Chest 146:205, 2014*)	Bordetella pertussis & occ. Bordetella parapertussis. Also consider asthma, gastroesophageal reflux, post-nasal drip, mycoplasma and also chlamydia.	**Peds doses: Azithro/ clarithro** OR **erythro estolate**[15] OR **erythro base**[15] OR **TMP-SMX** *(doses in footnote[15])*	**Adult doses**: **Azithro** po 500 mg day 1, 250 mg q24h days 2–5 OR **erythro estolate** 500 mg po qid times 14 days; OR **TMP-SMX-DS** 1 tab po bid times 14 days OR (**clarithro** 500 mg po bid or 1 gm **ER** q24h times 7 days)	**3 stages of illness:** catarrhal (1–2 wks), paroxysmal coughing (2–4 wks), and convalescence (1–2 wks). Treatment may abort or eliminate pertussis in catarrhal stage, but does not shorten paroxysmal stage. **Diagnosis:** PCR on nasopharyngeal secretions or ↑ pertussis-toxin antibody. **Rx aimed at eradication of NP carriage.** In non-outbreak setting, likelihood of pertussis increased if post-tussive emesis or inspiratory whoop present *(JAMA 304:890, 2010)*.
Pertussis: Prophylaxis of household contacts	Drugs and doses as per treatment immediately above. Vaccination of newborn contacts: *CID 58:830, 2014*.			Recommended by Am. Acad. Ped. Red Book 2006 for all household or close contacts; community-wide prophylaxis not recommended.
Acute bacterial exacerbation of chronic bronchitis (ABECB), adults (almost always smokers with COPD) Ref: *NEJM 359:2355, 2008.*	Viruses 20–50%, C. pneumoniae 5%, M. pneumoniae <1%; role of S. pneumo, H. influenzae & M. catarrhalis controversial. Tobacco use, air pollution contribute.	**Severe ABECB** = ↑ dyspnea, ↑ sputum viscosity/purulence, ↑ sputum volume. For severe ABECB: (1) consider chest x-ray, esp. if febrile &/or low O_2 sat.; (2) inhaled anticholinergic bronchodilator; (3) oral corticosteroid for just 5 days (*JAMA 309:2223, 2013*); (4) D/C tobacco use; (5) non-invasive positive pressure ventilation **Role of antimicrobial therapy is debated even for severe disease, but recent study of >80,000 patients shows value of antimicrobial treatment** or maybe **amox**, **doxy**, **TMP-SMX**, or **O Ceph. For severe disease, AM-CL**, **azithro/clarithro**, or **O Ceph** or FQs with enhanced activity vs. drug-resistant S. pneumo (**Gemi**, **Levo**, **Moxi** or **Pruliflox**). *Drugs & doses in footnote*. **Duration** varies with drug; range 3–10 days. Limit **Gemi** to 5 days to decrease risk of rash. **Azithro** 250 mg daily x 1 yr modestly reduced frequency of acute exacerbations in pts with milder disease *(NEJM 365:689, 2011)*.		
Fever, cough, myalgia during influenza season *(See NEJM 360:2605, 2009 regarding novel H1N1 influenza A)*	Influenza A & B	*See Influenza, Table 14A, page 173.*		**Complications: Influenza pneumonia, secondary bacterial pneumonia** Community MRSA and MSSA, *S. pneumoniae*, *H. influenzae*.
Bronchiectasis. Thorax 65 (Suppl 1): i1, 2010; *Am J Respir Crit Care Med 188:647, 2013.*	H. influ., P. aeruginosa, and rarely S. pneumo.	**Gemi**, **levo**, or **moxi** x 7-10 days. *Dosage in footnote[15].*		Many potential etiologies: obstruction, ↓ immune globulins, cystic fibrosis, dyskinetic cilia, tobacco, prior severe or recurrent necrotizing bronchitis: e.g. pertussis.
Acute exacerbation Prevention of exacerbation	Not applicable	Two randomized trials of **Erythro** 250 mg bid *(JAMA 309:1260, 2013)* or **Azithro** 250 mg qd *(JAMA 309:1251, 2013)* x 1 year showed significant reduction in the rate of acute exacerbations, better preservation of lung function, and better quality of life versus placebo in adults with non-cystic fibrosis bronchiectasis.		**Caveats:** higher rates of macrolide resistance in oropharyngeal flora; potential for increased risk of a) cardiovascular deaths from macrolide-induced QTc prolongation, b) liver toxicity, or c) hearing loss *(see JAMA 309:1295, 2013)*. **Pre-treatment screening:** baseline liver function tests, electrocardiogram; assess hearing; sputum culture to exclude mycobacterial disease.
Specific organisms	Aspergillus *(see Table 11)* MAI *(Table 12)* and P. aeruginosa *(Table 5A)*.			

[15] **ADULT DOSAGE: AM-CL** 875/125 mg po bid or 500/125 mg po q8h or 2000/125 mg po bid; **azithro** 500 mg po x 1 dose, then 250 mg q24h x 4 days or 500 mg po q24h x 3 days; *Oral cephalosporins*: **cefaclor** 500 mg po q8h or 500 mg extended release q12h; **cefdinir** 300 mg po q12h or 600 mg po q24h; **cefditoren** 200 mg tabs—2 tabs bid; **cefixime** 400 mg po q24h; **cefpodoxime proxetil** 200 mg po q12h; **cefprozil** 500 mg po q12h; **ceftibuten** 400 mg po q24h; **cefuroxime axetil** 250 or 500 mg q12h; **loracarbef** 400 mg po q12h; **clarithro** extended release 1000 mg po q24h; **doxy** 100 mg po bid; **erythro base** 40 mg/kg/day po div q6h; **erythro estolate** 40 mg/kg/day po div qid; *FQs*: **CIP** 750 mg po q12h; **gemi** 320 mg po q24h; **levo** 500 mg po q24h; **moxi** 400 mg po q24h; **prulifloxacin** 600 mg po q24h (where available);**TMP-SMX** 1 DS tab po bid.
PEDS DOSAGE: azithro 10 mg/kg/day po on day 1, then 5 mg/kg po q24h x 4 days; **clarithro** 7.5 mg/kg po q12h; **erythro base** 40 mg/kg/day div q6h; **erythro estolate** 40 mg/kg/day div q8-12h; **TMP-SMX** (>6 mos. of age) 8 mg/kg/day (TMP component) div bid.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (3S)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
LUNG/Bronchi *(continued)*				
Pneumonia: CONSIDER TUBERCULOSIS IN ALL PATIENTS; ISOLATE ALL SUSPECT PATIENTS				
Neonatal: Birth to 1 month	**Viruses:** CMV, rubella, H. simplex **Bacteria:** Group B strep, listeria, coliforms, S. aureus, P. aeruginosa **Other:** Chlamydia trachomatis, syphilis	**AMP** + **gentamicin** ± **cefotaxime**. Add **vanco** if MRSA a concern. For chlamydia therapy, **erythro** 12.5 mg per kg po or IV qid times 14 days.		Blood cultures indicated. Consider C. trachomatis if afebrile pneumonia, staccato cough, IgM > 1:8; therapy with erythro or sulfisoxazole. If MRSA documented, **vanco**, **TMP-SMX**, & **linezolid** alternatives. **Linezolid** dosage from birth to age 11 yrs is **10 mg per kg q8h**.
Age 1–3 months				
Pneumonitis syndrome. Usually afebrile	C. trachomatis, RSV, parainfluenza virus 3, human metapneumovirus, Bordetella, S. pneumoniae, S. aureus (rare)	**Outpatient: po erythro** 12.5 mg/kg q6h x 14 days or po **azithro** 10 mg/kg x dose, then 5 mg/kg x 4 days.	**Inpatient: If afebrile erythro** 10 mg/kg IV q6h or **azithro** 2.5 mg/kg IV q12h *(see Comment)*. **If febrile**, add **cefotaxime** 200 mg/kg per day div q8h	Pneumonitis syndrome: Cough, tachypnea, dyspnea, diffuse infiltrates, afebrile. Usually requires hospital care. Reports of hypertrophic pyloric stenosis after erythro under age 6 wks; not sure about azithro; bid azithro dosing theoretically might ↓ risk of hypertrophic pyloric stenosis. If lobar pneumonia, give AMP 200–300 mg per kg per day for S. pneumoniae. No empiric coverage for S. aureus, as it is rare etiology.
		For **RSV**, *see Bronchiolitis, page 36*		
Infants and Children, age > 3 months to 18 yrs (IDSA Treatment Guidelines: *CID 53:617, 2011*).				
Outpatient	RSV, human metapneumovirus, rhinovirus, influenza virus, adenovirus, parainfluenza virus, Mycoplasma, H. influenzae, S. pneumoniae, S. aureus (rare)	**Amox** 90 mg/kg in 2 divided doses x 5 days	**Azithro** 10 mg/kg x 1 dose(max 500 mg), then 5 mg/kg (max 250 mg) x 4 days OR **Amox-Clav** 90 mg/kg (Amox) in 2 divided doses x 5 days	Antimicrobial therapy not routinely required for preschool-aged children with CAP as most infections are viral etiologies.
Inpatient	As above	Fully immunized: **AMP** 50 mg/kg IV q6h Not fully immunized: **Cefotaxime** 150 mg/kg IV divided q8h	Fully immunized: **Cefotaxime** 150 mg/kg IV divided q8h	If atypical infection suspected, add **Azithro** 10 mg/kg x 1 dose (max 500 mg), then 5 mg/kg (max 250 mg) x 4 days. If community MRSA suspected, add **Vanco** 15-20 mg/kg q8-12h OR **Clinda** 40 mg/kg/day divided q6-8h. Duration of therapy: 10-14 days. Depending on clinical response, may switch to oral agents as early as 2-3 days.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (36)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
LUNG/Bronchi/Pneumonia *(continued)*				
Adults (over age 18) — IDSA/ATS Guideline for CAP in adults: *CID 44 (Suppl 2):S27-S72, 2007, NEJM 370:543, 2014, NEJM 371:1619, 2014.*				
Community-acquired, empirical therapy for outpatient Prognosis prediction: CURB-65 (Thorax 58:377, 2003) C: confusion = 1 pt U: BUN > 19 mg/dl = 1 pt R: RR > 30/min = 1 pt B: BP <90/60 = 1 pt Age > 65 yr = 1 pt Total = 1, ok to treat as out-patient, ≥ 2 hospitalization recommended	S. pneumo, atypicals and mycoplasma in particular, Hemophilus, Moraxella, viral pathogens: up to 30% of cases *(BMC Infect Dis 15:89, 2015)* and co-infection, often viral, in ~20% of cases *(BMC Infect Dis 15:64, 2015.)*	**Azithro** 0.5 gm po day 1 then 250 mg daily day 2-5 OR **Clarithro** 500 mg po bid or **Clarithro-ER** 1 gm po q24h x 5-7 days; OR **Doxy** 100 mg po bid x 5-7 days; OR if Doxy unavailable **Minocycline** 200 mg po/IV x 1, then 100 mg po/IV bid	**Levo** 750 mg po q24h x 5 days; OR **Moxi** 400 mg po q24h x 5 days; OR [**Amox-Clav (1000/62.5)** (Augmentin-XR) 2 tabs po bid or **Amox** 1 g po tid] + [**Azithro** or **Clarithro** x 7 days]	**Azithro/clarithro:** active against atypical pneumonia agents, but S. pneumo resistance as high as 20-30%; **alternative regimen** (**Levo** or **Moxi**) recommended if high local prevalence of macrolide resistance or co-morbidities (e.g., COPD, alcoholism, CHF). **Moxi** has anaerobic activity and may be preferred over levo for post-obstructive pneumonia or aspiration. **Amox-Clav or Amox** + **Azithro** or **Clarithro** another alternative for patients with comorbidities, in setting of high prevalence of S. pneumo macrolide resistance, or if prior antibiotic in last 3 mo. Oral cephalosporins (cefdinir 300 mg q12h, cefpodoxime 200 mg q12h or cefprozil 500 mg q12h) can be substituted for Amox-Clav or Amox.
Community-acquired, empirical therapy for patient admitted to hospital, non-ICU *(See NEJM 370:543, 2014)*	As above + legionella, Gram-negative bacilli IVDU: S. aureus Post influenza: S. aureus, S. pneumo. No pathogen detected in majority of patients, viruses more common than bacteria *(NEJM 373:415, 2015)*	**Ceftriaxone** 1 g IV q24h + [**Azithro** 500 mg IV/po q24h or **Doxy** 100 mg IV/po q12h]	**Levo** 750 mg IV/po q24h OR **Moxi** 400 mg IV/po q24h or **Gati** 400 mg IV q24h (not available in US)	Administration of antibiotic within 6h associated with improved survival in pneumonia with severe sepsis *(Eur Respir J 39:156, 2012)* Duration of therapy 5-7 days. Improved outcome with β-lactam/macrolide combo vs β-lactam alone in hospitalized CAP of moderate- or high- but not low-severity *(Thorax 68:493, 2013).* Blood and sputum cultures recommended. Test for influenza during influenza season. Consider urinary pneumococcal antigen and urinary legionella for sicker patients. Add **vanco** 15-20 mg/kg IV q8-12h to cover MRSA for pneumonia with concomitant or precedent influenza or for pneumonia in an IVDU.
Community-acquired, empirical therapy for patient admitted to ICU	As above	As above + [**Vanco** 15-20 mg/kg IV q8-12h OR **Linezolid** 600 mg IV/PO q12h]	As above + [**Vanco** 15-20 mg/kg IV q8-12h OR **Linezolid** 600 mg IV/PO q12h]	**Ertapenem** could substitute for ceftriaxone; need azithro for atypical pathogens; do not use if suspect P. aeruginosa. **Legionella:** Not all legionella species detected by urine antigen; if suspicious do PCR on airway secretions. *(CID 57:1275, 2013).*
		Procalcitonin: Several clinical trials and meta-analyses indicate that normalization of procalcitonin levels can be used to guide duration of antibiotic therapy: Safe to discontinue antibiotics when procalcitonin level has decreased to 0.1-0.2 mcg/mL *(CID 55:651, 2012; JAMA 309:717, 2013).*		

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (37)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
LUNG/Bronchi/Pneumonia/Adults (over age 18) *(continued)*				
Health care or hospital-acquired, or ventilator-associated pneumonia	As above + MDR Gram-negatives	**Cefepime** 2 gm IV q12h or **PIP-TZ** 4.5 mg/kg q8h	**MERO** 1 gm IV q8h	For patients with early onset HAP or VAP, no recent prior hospitalization, low risk for MDR options include **ceftriaxone** 1 gm q24h, **erta** 1 gm q24h, or **levo** 750 mg IV/po q24h For late-onset infections (> 5 days in the hospital, risk factors for MDR organisms) or risk factors for MRSA add **vanco** 15-20 mg/kg IV q8h or **linezolid** 600 mg IV/po q12h. If legionella suspected, add **levo** 750 mg IV/po or **Azithro** 500 mg to the regimen. If pseudomonas suspected add **CIP** [400 mg IV q8h] or levo 750 mg IV/po or **Tobra** 5 mg/kg q24h to increase likelihood that at **least** one drug will be active.
Pneumonia —Selected specific therapy after culture results (sputum, blood, pleural fluid, etc.) available. *Also see Table 2, page 69*				
Acinetobacter baumannii *(See also Table 5A); Crit Care Med 43:1194 & 1332, 2015*	Patients with VAP	Use **IMP**, or **MER** if susceptible *(See Comment)*	If **IMP** resistant: **Polymyxin B** (preferred) OR **colistin** + **MER**. Colistin Dose: *Table 10A, page 112.*	Sulbactam portion of AM-SB often active; dose: 3 gm IV q6h. Polymyxin resistance may evolve. Treatment options: *CID 60:1295 & 1304, 2015.* Some add nebulized Colistin 75 mg q12h
Actinomycosis	A. Israelii and rarely others	**AMP** 50 mg/kg/day IV div in 3-4 doses x 4-6 wks, then **Pen VK** 2-4 gm/day po x 3-6 wks	**Doxy** or **ceftriaxone** or **clinda**	Can use **Pen G** instead of AMP: 10-20 million units/day IV x 4-6 wks.
Anthrax **Inhalation** (applies to oro-pharyngeal & gastrointestinal forms): **Treatment** (Cutaneous: *See page 51)* Ref: *www.bt.cdc.gov; CDC panel recommendations for adults: Emerg Infect Dis 20(2). Doi: 10.3201/eid2002.130687. American Academy of Pediatrics recommendations for children: Pediatrics 133:e1411, 2014.*	Bacillus anthracis **To report possible bioterrorism event: 770-488-7100** Plague, tularemia: *See page 42.* Chest x-ray: mediastinal widening & pleural effusion	**Adults (including pregnancy): CIP** 400 mg IV q8h + (**Linezolid** 600 mg IV q12h or **Clindamycin** 900 mg IV q8h) + **Meropenem** 2 gm IV q8h *(see comments)* + **raxibacumab** 40 mg/kg IV over 2 hrs). Switch to po after 2 wks if stable: CIP 500 mg q12h or Doxy 100 mg q12h to complete 60 day regimen.	**Children: CIP** 10 mg/kg IV q8h (max 400 mg per dose) + [**Linezolid** 10 mg/kg IV q8h (age <12 yr) or **Linezolid** 15 mg/kg q12h (age >12 yr) (max 600 mg per dose)] + **Meropenem** 40 mg/kg IV q8h (max 2 gm per dose) *(see comments)* + **raxibacumab** 40 80 mg/kg IV over 2 hrs. Switch to po after 2 wks if stable: **CIP** 15 mg/kg q12h or **Doxy** 2.2 mg/kg q12h (<45 kg) or 100 mg q12h (>45 kg) q12h to complete 60-day regimen for oral dosage.	1. Meropenem if meningitis cannot be excluded; Linezolid preferred over Clinda for meningitis. 2. Pen G 4 million units IV (adults) or 67,000 units/kg (children, max 4 million units per dose) IV q4h can be substituted for Meropenem for pen-susceptible strain. 3. For children <8 years of age tooth staining likely with Doxy for 60 days. Alternatives for oral switch include Clinda 10 mg/kg q8h (max dose 600 mg) or Levo 8 mg/kg (max dose 250 mg) q12h for <50 kg, 500 mg q24h >50 kg or for pen-susceptible strains Amox 25 mg/kg (max dose 1 gm) q8h or Pen VK 25 mg/kg (max dose 1 gm) q8h. 4. Levo and Moxi are alternatives to CIP 5. For complete recommendations *see Emerg Infect Dis 20(2). doi: 10.3201/eid2002.130687 (adults)* and *Pediatrics 133:e1411, 2014 (children).* 6. Anthrax immune globulin (Anthrasil) FDA approved for emergency use (U.S. strategic national stockpile).
Anthrax, prophylaxis: *See: Emerg Infect Dis 20(2). doi: 10.3201/eid2002.130687.* 60 days of **antimicrobial prophylaxis** + 3-dose series of **Biothrax Anthrax Vaccine Adsorbed.**	Info: www.bt.cdc.gov	**Adults (including pregnancy): CIP** 500 mg po q12h or **Doxy** 100 mg po q12h x 60 days + 3 dose series of Biothrax Anthrax Vaccine Adsorbed	**Children: CIP** or **Doxy** *(see above for dosing)* x 60 days +3-dose series of Biothrax (not FDA approved, to be made available on investigational basis)	1. Consider alternatives to Doxy for pregnant adult. 2. Alternatives include Clinda, Levo, Moxi, and for pen-susceptible strains Amox or Pen VK.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (38)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
LUNG/Bronchi/Pneumonia/ Selected specific therapy after culture results (sputum, blood, pleural fluid, etc.) available. *(continued)*				
Burkholderia (Pseudomonas) pseudomallei (etiology of melioidosis) Can cause primary or secondary skin infection *See NEJM 367:1035, 2012*	Gram-negative	**Initial parenteral rx: Ceftazidime** 30–50 mg/kg IV q8h or **IMP** 20 mg/kg IV q8h. Rx minimum 10 days & improving, then po therapy → *see Alternative column*	**Post-parenteral po rx: Adults** *(see Comment for children)*: **TMP-SMX** 5 mg/kg (TMP component) bid + **Doxy** 2 mg/kg bid x 3 mos.	**Children ≤8 yrs old & pregnancy:** For oral regimen, use **AM-CL-ER** *1000/62.5*, 2 tabs po bid times 20 wks. Even with compliance, relapse rate is 10%. Max. daily ceftazidime dose: 6 gm. Tigecycline: No clinical data but active in vitro *(AAC 50:1555, 2006)*
Haemophilus influenzae	β-lactamase negative	**AMP** IV, **amox** po, **TMP-SMX**, **azithro/clarithro**, **doxy.**		25–35% strains β-lactamase positive. ↑ resistance to both TMP-SMX and doxy. *See Table 10A, page 102 for dosages.* High % of commensal H. hemolyticus misidentified as H. influenza *(JID 195:81, 2007).*
	β-lactamase positive	**AM-CL**, **O Ceph 2/3**, **P Ceph 3**, **FO** Dosage: *Table 10A*		
Klebsiella sp.—ESBL pos. & other coliforms[16]	β-lactamase positive	**IMP** or **MER**, if resistant, **Colistin** + **(IMP** or **MER)**		ESBL inactivates all cephalosporins, β-lactam/β-lactamase inhibitor drug activ not predictable; co-resistance to all FQs & often aminoglycosides.
Legionella species Relative bradycardia common feature	**Hospitalized/ immunocompromised**	**Azithro** 500 mg **IV** or **Levo** 750 mg **IV** or **Moxi** 400 mg **IV.** *See Table 10A, pages 108 & 111 for dosages.* Treat for 7–14 days *(CID 39:1734, 2004)*		Legionella website: www.legionella.org. Two studies support superiority of **Levo** over macrolides *(CID 40:794 & 800, 2005), although not FDA-approved.* Meta-analysis favors a FQ (*JAC 69:2354, 2014*).
Moraxella catarrhalis	93% β-lactamase positive	**AM-CL**, **O Ceph 2/3**, **P Ceph 2/3**, **macrolide**[17], **FQ**, **TMP-SMX**. **Doxy** another option. *See Table 10A, page 102 for dosages*		
Nocardia pneumonia Expert Help: Wallace Lab (+1) 903-877-7680; CDC (+1) 404-639-3158 Ref: *Medicine 88:250, 2009.*	N. asteroides, N. brasiliensis	**TMP-SMX** 15 mg/kg/day IV/po in 2-4 divided doses + **Imipenem** 500 mg IV q6h for first 3-4 weeks then **TMP-SMX** 10 mg/kg/day in 2-4 divided doses x 3-6 mos.	**IMP** 500 mg IV q6h + **amikacin** 7.5 mg/kg IV q12h x 3-4 wks & then po **TMP-SMX**	**Duration:** 3 mos. if immunocompetent; 6 mos. if immunocompromised. **Measure peak sulfonamide levels:** Target is 100-150 mcg/mL 2 hrs post po dose. **Linezolid** active in vitro *(Ann Pharmacother 41:1694, 2007).* In vitro resistance to TMP-SMX may be increasing *(Clin Infect Dis 51:1445, 2010),* but whether this is associated with worse outcomes is not known.
Pseudomonas aeruginosa Combination rx controversial: superior in animal model *(AAC 57:2788, 2013)* but no benefit in observational trials *(AAC 57:1270, 2013; CID 57:208, 2013).*	Often ventilator-associated	(**PIP-TZ** 3.375 gm IV q4h or prefer 4-hr infusion of 3.375 gm q8h) + **Tobra** 5 mg/kg IV once q24h *(see Table 10D, page 118).* Could substitute anti-pseudomonal **cephalosporin** or **carbapenem** (**IMP**, **MER**) for **PIP-TZ** if pt. strain is susceptible.		Options: **CFP** 2 gm IV q8h; **CIP** 400 mg IV q8h + **PIP-TZ**; **IMP** 500 mg IV q6h + **CIP** 400 mg IV q8h; if multi-drug resistant **[Polymyxin B** (preferred) OR **Colistin]**+ **(IMP or MER) +** consider **Colistin** by inhalation 80 mg bid *Expert Rev Antiinfect Ther 13:1237, 2015.* Also available for inhalation rx: **tobra** and **aztreonam**.
Q Fever Acute atypical pneumonia. *See MMWR 62 (3):1, 2013.*	Coxiella burnetii	No valvular heart disease: **Doxy** 100 mg po bid x 14 days	Valvular heart disease: (**Doxy** 100 mg po bid + **hydroxychloroquine** 200 mg tid) x 12 months (CID 57:836, 2013)	In pregnancy: **TMP-SMX DS** 1 tab po bid throughout pregnancy.

[16] Dogma on duration of therapy not possible with so many variables: i.e. certainty of diagnosis, infecting organism, severity of infection and number/severity of co-morbidities. Agree with efforts to de-escalate & shorten course. Treat at least 7-8 days. Need clinical evidence of response: fever resolution, improved oxygenation, falling WBC. Refs: *AJRCCM 171:388, 2005; CID 43:S75, 2006; COID 19:185, 2006.*

[17] **Macrolide** = azithromycin, clarithromycin and erythromycin.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (39)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
LUNG/Bronchi/Pneumonia/ Selected specitic therapy after culture results (sputum, blood, pleural fluid, etc.) available. *(continued)*				
Staphylococcus aureus Duration of treatment: 2-3 wks if just pneumonia; 4-6 wks if concomitant endocarditis and/or osteomyelitis. *IDSA Guidelines, CID 52 (Feb 1):1, 2011.*	Nafcillin/oxacillin susceptible	**Nafcillin/oxacillin** 2 gm IV q4h	**Vanco** 30-60 mg/kg/d iv in 2-3 divided doses or **linezolid** 600 mg IV q12h	Adjust dose of vancomycin to achieve target trough concentrations of 15-20 mcg/mL. Some authorities recommend a 25-30 mg/kg loading dose (actual body weight) in severely ill patients *(CID 49:325, 2009).*
	MRSA	**Vanco** 15-20 mg/kg q8-12h IV in 2-3 divided doses or **Linezolid** 600 mg IV/po q12h	**Dapto** not an option; pneumonia developed during dapto rx *(CID 49:1286, 2009).* **Ceftaroline** 600 mg IV q8h.	Prospective trial for MRSA pneumonia: cure rate with Linezolid (58%), Vanco (47%), p = 0.042; no difference in mortality *(CID 54:621, 2012).* **Telavancin** 10 mg/kg IV x 60 min q24h another option. Perhaps lower efficacy if CrCl < 50mL/min *(AAC 58:2030, 2014).*
Stenotrophomonas maltophilia		**TMP-SMX** 15-20 mg/kg/day div q8h (TMP component)	**FQ** (if susceptible in vitro)	Tigecycline only if no other option *(J Chemother 24:150, 2012)* but only if MIC < 2mcg/mL. Rarely may need to use polymyxin combination therapy.
Streptococcus pneumoniae	Penicillin-susceptible	**AMP** 2 gm IV q6h, **amox** 1 gm po tid, **pen G IV**[18], **doxy**, **O Ceph 2**, **P Ceph 2/3;** may add **Azithro** 500 mg IV/po qd *(JAC 69:1441, 2014).* *See Table 10A, page 102 for other dosages.* Treat until afebrile, (min. of 5 days) and/or until serum procalcitonin normal.		
	Penicillin-resistant, high level	**FQs** with enhanced activity: **Gemi**, **Levo**, **Moxi**; **P Ceph 3** (resistance rare); high-dose IV **AMP**; **vanco** IV—*see Table 5A, page 81 for more data.* If all options not possible (e.g., allergy), **linezolid** active: 600 mg IV or po q12h. *Dosages Table 10A.* Treat until afebrile, 3-5 days (min. of 5 days). In CAP trial, **Ceftaroline** 600 mg IV q12h superior to Ceftriaxone *(CID 51:641, 2010).*		
Tularemia **Inhalational tularemia** Ref.: *JAMA 285:2763, 2001 & www.bt.cdc.gov*	Francisella tularemia **Treatment**	(**Streptomycin** 15 mg per kg IV bid) or (**gentamicin** 5 mg per kg IV qd) times 10 days	**Doxy** 100 mg IV or po bid times 14-21 days or **CIP** 400 mg IV (or 750 mg po) bid times 14-21 days	Pregnancy: *as for non-pregnant adults.* **Tobramycin** should work.
	Postexposure prophylaxis	**Doxy** 100 mg po bid times 14 days	**CIP** 500 mg po bid times 14 days	Pregnancy: *As for non-pregnant adults*
Viral (interstitial) pneumonia suspected *See Influenza, Table 14A, page 173.* Ref: *Chest 133:1221, 2008.*	Consider: **Intluenza**, adenovirus, coronavirus (MERS/SARS), hantavirus, metapneumovirus, parainfluenza virus, respiratory syncytial virus	**Oseltamivir** 75 mg po bid for 5 days or **zanamivir** two 5 mg inhalations twice a day for 5 days.		No known efficacious drugs for adenovirus, coronavirus, hantavirus, metapneumovirus, parainfluenza or RSV. Need travel (MERS/SARS) & exposure (Hanta) history. RSV and human metapneumovirus as serious as influenza in the elderly *(NEJM 352:1749 & 1810, 2005; CID 44:1152 & 1159, 2007).*
Yersinia pestis (Plague) *CID 49:736, 2009; MMWR 64:918, 2015*	Y. pestis if aerosolized, suspect bioterror.	(**Gentamicin** 5 mg/kg IV q24h or **Streptomycin** 30 mg/kg/day in 2 div doses) x 10 days	**Doxy** 200 mg IV q12h x 1 day, then 100 mg po bid x 7-10 days	**Cipro** 500 mg po bid or 400 mg IV q12h also an option. **Chloramphenicol** also effective but potentially toxic. Consider if evidence of plague meningitis.

[18] **IV Pen G dosage:** no meningitis, 2 million units IV q4h. If concomitant meningitis, 4 million units IV q4h.

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (40)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
LUNG—Other Specific Infections				
Aspiration pneumonia/anaerobic lung infection/lung abscess	Transthoracic culture in 90 pts—% of total isolates: anaerobes 34%, Gm-pos. cocci 26%, S. milleri 16%, Klebsiella pneumoniae 25%, nocardia 3%	**Clindamycin** 300-450 mg po tid OR **Ampicillin-sulbactam** 3 g IV q6h OR **A carbapenem** (e.g., ertapenem 1 g IV q24h)	**Ceftriaxone** 1 gm IV q24h plus **metro** 500 mg IV q6h or 1 gm IV q12h	Typically anaerobic infection of the lung: aspiration pneumonitis, necrotizing pneumonia, lung abscess and empyema *(REF: Anaerobe 18:235, 2012)* Other treatment options: PIP-TZ 3.375 g IV q6h (for mixed infections with resistant Gram-negative aerobes) or Moxi 400 mg IV/po q24h *(CID 41:764, 2005).*
Chronic pneumonia with fever, night sweats and weight loss	M. tuberculosis, coccidioidomycosis, histoplasmosis	See *Table 11, Table 12.* For risk associated with TNF inhibitors, see *CID 41(Suppl 3):S187, 2005*		HIV+, foreign-born, alcoholism, contact with TB, travel into developing countries
Cystic fibrosis Acute exacerbation of pulmonary symptoms *BMC Medicine 9:32, 2011*	S. aureus or H. influenzae early in disease; P. aeruginosa later in disease Nontuberculous mycobacteria emerging as an important pathogen *(Semin Respir Crit Care Med 34:124, 2013)*	**For P. aeruginosa:** (Peds doses) **Tobra** 3.3 mg/kg q8h or 12 mg/kg IV q24h. Combine tobra with **PIP-TZ** 4.5 gm IV q6h **or ceftaz** 50 mg/kg IV q8h to max of 6 gm per day. If resistant to above, **CIP/Levo** used if P. aeruginosa susceptible. *See footnote[19] & Comment*	**For S. aureus: (1) MSSA—oxacillin/nafcillin** 2 gm IV q4h. **(2) MRSA—vanco** 15-20 mg/kg (actual wt) IV q8-12h (to achieve target trough concentration of 15-20 µg/mL.	Cystic Fibrosis Foundation Guidelines: 1. Combination therapy for P. aeruginosa infection. 2. Once-daily dosing for aminoglycosides. 3. Need more data on continuous infusion beta-lactam therapy. 4. Routine use of steroid not recommended. Inhalation options (P. aeruginosa suppression): 1) Nebulized tobra 300 mg bid x 28 days, no rx for 28 days, repeat; 2) Inhaled tobra powder-hand held: 4-28 mg cap bid x 28 days, no rx for 28 days, repeat; Nebulized aztreonam (Cayston): 75 mg tid after pre-dose bronchodilator. *Ref: Med Lett 56:51, 2014.*
	Burkholderia (Pseudomonas) cepacia. Mechanisms of resistance *(Sem Resp Crit Care Med 36:99, 2015)*	**TMP-SMX** 5 mg per kg (TMP) IV q6h	**Chloro** 15-20 mg per kg IV/po q6h	B. cepacia has become a major pathogen. Patients develop progressive respiratory failure, 62% mortality at 1 yr. **Fail to respond to aminoglycosides,** anti-pseudomonal beta-lactams. Patients with B. cepacia should be isolated from other CF patients.
		Need culture & sens results to guide rx.		
Empyema. *IDSA Treatment Guidelines for Children, CID 53:617, 2011;* exudative pleural effusion criteria *(JAMA 311:2422, 2014)*				
Neonatal	Staph. aureus	See *Pneumonia, neonatal, page 38*		Drainage indicated.
Infants/children (1 month–5 yrs)	Staph. aureus, Strep. pneumoniae, H. influenzae	See *Pneumonia, age 1 month–5 years, page 38*		Drainage indicated.
Child >5 yrs to ADULT—Diagnostic thoracentesis; chest tube for empyemas				
Acute, usually parapneumonic *For dosage, see Table 10B or footnote page 25*	Strep. pneumoniae, Group A strep	**Cefotaxime** or **ceftriaxone** *(Dosage, see footnote[11] page 25)*	**Vanco**	Tissue Plasminogen Activator (10 mg) + DNase (5 mg) bid x 3 days via chest tube improves outcome *(NEJM 365:518, 2011).*
	Staph. aureus: Check for MRSA	**Nafcillin** or **oxacillin** if MSSA	**Vanco** or **linezolid** if MRSA.	Usually complication of S. aureus pneumonia &/or bacteremia.
	H. influenzae	**Ceftriaxone**	**TMP-SMX** or **AM-SB**	Pleomorphic Gm-neg. bacilli. ↑ resistance to TMP-SMX.
Subacute/chronic	Anaerobic strep, Strep. milleri, Bacteroides sp., Enterobacteriaceae, M. tuberculosis	**Clinda** 450–900 mg IV q8h + **ceftriaxone**	**Cefoxitin** or **IMP** or **PIP-TZ** or **AM-SB** *(Dosage, see footnote[11] page 25)*	Intrapleural tissue plasminogen activator (t-PA) 10 mg + DNase 5 mg via chest tube twice daily for 3 days improved fluid drainage, reduced frequency of surgery, and reduced duration of the hospital stay; neither agent effective alone *(N Engl J Med 365:518, 2011).* Pro/con debate: *Chest 145:14, 17, 20, 2014.* Pleural biopsy with culture for mycobacteria and histology if TBc suspected.

[19] Other options: (Tobra + aztreonam 50 mg per kg IV q8h); (IMP 15–25 mg per kg IV q6h + tobra); **CIP commonly used in children**, e.g., CIP IV/po + ceftaz IV *(LnID 3:537, 2003).*

TABLE 1 (41)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
LUNG—Other Specific Infections *(continued)*				
Human Immunodeficiency virus infection (HIV+): See SANFORD GUIDE TO HIV/AIDS THERAPY				
CD4 T-lymphocytes <200 per mm³ or clinical AIDS Dry cough, progressive dyspnea, & diffuse infiltrate **Prednisone first if suspect pneumocystis** *(see Comment)*	Pneumocystis carinii most likely; also MTB, fungi, Kaposi's sarcoma, & lymphoma NOTE: AIDS pts may develop pneumonia due to DRSP or other pathogens—see *next box below*	*Rx listed here is for* **severe** *pneumocystis; see Table 11A, page 132 for po regimens for* **mild** *disease.* **Prednisone 1st** *(see Comment),* **then:** **TMP-SMX** [IV: 15 mg per kg per day div q8h (TMP component) or po: 2 DS tabs q8h], total of 21 days	(**Clinda** 600 mg IV q8h + **primaquine** 30 mg po q24h) or (**pentamidine isethionate** 4 mg per kg per day IV) times 21 days. See *Comment*	**Diagnosis (induced sputum or bronchial wash) for:** histology or monoclonal antibody strains or PCR. Serum beta-glucan (Fungitell) levels under study *(CID 46:1928 & 1930, 2008).* **Prednisone 40 mg bid po times 5 days then 40 mg q24h po times 5 days then 20 mg q24h po times 11 days is indicated with PCP (pO_2 <70 mmHg), should be given at initiation of anti-PCP rx; don't wait until pt's condition deteriorates.** If PCP studies negative, consider bacterial pneumonia, TBc, cocci, histo, crypto, Kaposi's sarcoma or lymphoma. **Pentamidine not active vs. bacterial pathogens.** **NOTE: Pneumocystis resistant to TMP-SMX, albeit rare, does exist.**
CD4 T-lymphocytes normal Acute onset, purulent sputum & pulmonary infiltrates ± pleuritic pain. **Isolate pt until TBc excluded: Adults**	Strep. pneumoniae, H. influenzae, aerobic Gm-neg. bacilli (including P. aeruginosa), Legionella rare, MTB.	Ceftriaxone 1 gm IV q24h (over age 65 1 gm IV q24h) + **azithro**. Could use **Levo,** or **Moxi** IV as alternative *(see Comment)*		If Gram stain of sputum shows Gm-neg. bacilli, options include **P Ceph 3 AP, PIP-TZ, IMP,** or **MER**. **FQs: Levo** 750 mg po/IV q24h; **Moxi** 400 mg po/IV q24h. Gati not available in US due to hypo- & hyperglycemic reactions.
As above: Children	Same as adult with HIV + lymphoid interstitial pneumonia (LIP)	As for HIV+ adults with pneumonia. If diagnosis is LIP, rx with steroids.		In children with AIDS, LIP responsible for 1/3 of pulmonary complications, usually >1 yr of age vs. PCP, which is seen at <1 yr of age. Clinically: clubbing, hepatosplenomegaly, salivary glands enlarged (take up gallium), lymphocytosis.
LYMPH NODES (approaches below apply to lymphadenitis without an obvious primary source)				
Lymphadenitis, acute **Generalized**	Etiologies: EBV, early HIV infection, syphilis, toxoplasma, tularemia, Lyme disease, sarcoid, lymphoma, systemic lupus erythematosus, **Kikuchi-Fujimoto** disease and others. For differential diagnosis of fever and lymphadenopathy see *NEJM 369:2333, 2013.*			
By Region:				
Cervical—see cat-scratch disease (CSD), below	CSD (B. henselae), Grp A strep, Staph. aureus, anaerobes, MTB (scrofula), M. avium, M. scrofutaceum, M. malmoense, toxo, tularemia		History & physical exam directs evaluation. If nodes fluctuant, aspirate and base rx on Gram & acid-fast stains. **Kikuchi-Fujimoto** disease causes fever and benign self-limited adenopathy; the etiology is unknown *(CID 39:138, 2004).*	
Inguinal Sexually transmitted	HSV, chancroid, syphilis, LGV			
Not sexually transmitted	GAS, SA, tularemia, CSD, Y. pestis (plague)		Consider bubonic plague & glandular tularemia.	
Axillary	GAS, SA, CSD, tularemia, Y. pestis, sporotrichosis		Consider bubonic plague & glandular tularemia.	
Extremity, with associated nodular lymphangitis	Sporotrichosis, leishmania, Nocardia brasiliensis, Mycobacterium marinum, Mycobacterium chelonae, tularemia		Treatment varies with specific etiology	A distinctive form of lymphangitis characterized by subcutaneous swellings along inflamed lymphatic channels. Primary site of skin invasion usually present; regional adenopathy variable.
Nocardia lymphadenitis & skin abscesses	N. asteroides, N. brasiliensis	**TMP-SMX** 5-10 mg/kg/day based on TMP IV/po div in 2-4 doses	**Sulfisoxazole** 2 gm po qid or **minocycline** 100-200 mg po bid.	**Duration:** 3 mos. if immunocompetent; 6 mos. if immunocompromised. **Linezolid:** 600 mg po bid reported effective *(Ann Pharmacother 41:1694, 2007).*

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (42)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
LYMPH NODES *(continued)*				
By Pathogen:				
Cat-scratch disease—Immunocompetent patient Axillary/epitrochlear nodes 46%, neck 26%, inguinal 17%. Ref: *Amer Fam Physician 83:152, 2011.*	Bartonella henselae	**Azithro** dosage—**Adults** (>45.5 kg): 500 mg po x 1, then 250 mg/day x 4 days. **Children** (<45.5 kg): liquid azithro 10 mg/kg x 1, then 5 mg/kg per day x 4 days.	Adult: Clarithro 500 mg po bid or RIF 300 mg po bid or TMP-SMX DS 1 tab po bid or CIP 500 mg po bid (duration at least 10 days)	**Dx:** Antibody titer; PCR increasingly available. Can spread. For hepatosplenic infection: (Doxy 100 mg po bid + RIF 300 mg po bid) x 10-14 days. For CNS or retinal infection: same as above, but treat for 4-6 wks.
Bubonic plague *(see also, plague pneumonia)* *Ref: MMWR 64:918, 2015*	Yersinia pestis	(**Streptomycin** 30 mg/kg/day IV in 2 div doses or Gentamicin 5 mg/kg/day IV single dose) x 10 days	**Doxy** 200 mg IV/po bid x 1 day, then 100 mg IV/po bid x 10 days	FOs effective in animals: [Levo 500 mg IV/po once daily or CIP 500 mg po (or 400 mg IV) q12h] x 10 days or Moxi 400 mg IV/po q24h x 10-14 days
MOUTH				
Aphthous stomatitis, recurrent	Etiology unknown	Topical steroids (Kenalog in Orabase) may ↓ pain and swelling; if AIDS, *see SANFORD GUIDE TO HIV/AIDS THERAPY.*		
Actinomycosis: "Lumpy jaw" after dental or jaw trauma	Actinomyces israelii	**AMP** 50 mg/kg/d IV div q6-8h x 4-6 wks, then **Pen VK** 2-4 gm/d x 3-6 mos	(**Ceftriaxone** 2 gm IV q24h or **Clinda** 600-900 mg IV q8h or **Doxy** 100 mg IV/po bid) x 4-6 wks, then **Pen VK** 2-4 gm/d x 3-6 mos	Note: Metro not active vs. actinomyces. Ref: *BMJ 343:d6099, 2011.*
Buccal cellulitis Children <5 yrs	H. influenzae	**Ceftriaxone** 50 mg/kg IV q24h	**AM-CL** 45-90 mg/kg po div bid or **TMP-SMX** 8-12 mg/kg (TMP comp) IV/po div bid	With Hib immunization, invasive H. influenzae infections have ↓ by 95%. Now occurring in infants prior to immunization.
Candida Stomatitis ("Thrush")	C. albicans	**Fluconazole**	Echinocandin	*See Table 11, page 122.*
Dental (Tooth) abscess	Aerobic & anaerobic Strep sp.	Mild: **AM-CL** 875/125 mg po bid	Severe: **PIP-TZ** 3.375 gm IV q6h	Surgical drainage / debridement. If Pen-allergic: **Clinda** 600 mg IV q6-8h
Herpetic stomatitis	Herpes simplex virus 1 & 2	*See Table 14*		
Submandibular space infection, bilateral (Ludwig's angina)	Oral anaerobes, facultative streptococci, S. aureus (rare)	**PIP-TZ** or (**Pen G** IV + **Metro** IV)	**Clinda** 600 mg IV q6-8h (for Pen-allergic pt)	**Ensure adequate airway** and early surgical debridement. Add Vanco IV if gram-positive cocci on gram stain.
Ulcerative gingivitis (Vincent's angina or Trench mouth)	Oral anaerobes + vitamin deficiency	**Pen G** 4 million units IV q4h or **Metro** 500 mg IV q6h	**Clinda** 600 mg IV q8h	Replete vitamins (A-D). Can mimic scurvy. Severe form is NOMA (Cancrum oris) *(Ln 368:147, 2006)*
MUSCLE				
"Gas gangrene". Contaminated traumatic wound. Can be spontaneous without trauma.	C. perfringens, other histotoxic Clostridium sp.	(**Clinda** 900 mg IV q8h) + (**pen G** 24 million units/day div. q4–6h IV)		Susceptibility of C. tertium to penicillins and metronidazole is variable; resistance to clindamycin and 3GCs is common, so vanco or metro (500 mg q8h) recommended. IMP or MER expected to have activity in vitro against Clostridium spp.
Pyomyositis	Staph. aureus, Group A strep, (rarely Gm-neg. bacilli), variety of anaerobic organisms	(**Nafcillin** or **oxacillin** 2 gm IV q4h) or **Cefazolin** 2 gm IV q8h if **MSSA**	**Vanco** 15-20 mg/kg q8-12h if **MRSA**	No benefit of prophylactic antibiotics in uncomplicated acute pancreatitis. Clinical deterioration in the presence of pancreatic necrosis raises concerns for infection. Empirical antibiotic therapy for suspicion of infected pancreatic necrosis: IMP 0.5-1 gm IV q6h; or MER 1 gm IV q8h; or Moxi 400 mg IV q24h. If patient worsens, CT-guided fine-needle aspiration for culture and sensitivity testing to re-direct therapy. Candida spp may complicate necrotizing pancreatitis.

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (43)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
PANCREAS: Review: *NEJM 354:2142, 2006.*				
Acute alcoholic (without necrosis) (idiopathic) pancreatitis	Not bacterial	None No necrosis on CT	1–9% become infected but prospective studies show no advantage of prophylactic antimicrobials. Observe for pancreatic abscesses or necrosis which require therapy.	
Post-necrotizing pancreatitis; infected pseudocyst; pancreatic abscess	Enterobacteriaceae, enterococci, S. aureus, S. epidermidis, anaerobes, candida	Need culture of abscess/infected pseudocyst to direct therapy; **PIP-TZ** is reasonable empiric therapy		Can often get specimen by fine-needle aspiration. **Moxi, MER, IMP, ERTA** are all options *(AAC 56:6434, 2012).*
Antimicrobic prophylaxis, necrotizing pancreatitis	As above	If > 30% pancreatic necrosis on CT scan (with contrast), initiate antibiotic therapy: **IMP** 0.5-1 gm IV q6h or **MER** 1 gm IV q8h. No need for empiric Fluconazole. If patient worsens CT guided aspiration for culture & sensitivity. Controversial: *Cochrane Database Sys Rev 2003: CD 002941; Gastroenterol 126:977, 2004; Ann Surg 245:674, 2007.*		
PAROTID GLAND				
"Hot" tender parotid swelling	S. aureus, S. pyogenes, oral flora, & aerobic Gm-neg. bacilli (rare), mumps, rarely enteroviruses/ influenza; parainfluenza: **Nafcillin** or **oxacillin** 2 gm IV q4h or cefazolin 2 gm IV q8h if MSSA; **vanco** if MRSA; **metro** or **clinda** for anaerobes			Predisposing factors: stone(s) in Stensen's duct, dehydration. Therapy depends on ID of specific etiologic organism.
"Cold" non-tender parotid swelling	Granulomatous disease (e.g., mycobacteria, fungi, sarcoidosis, Sjögren's syndrome), drugs (iodides, et al.), diabetes, cirrhosis, tumors			History/lab results may narrow differential; may need biopsy for diagnosis
PERITONEUM/PERITONITIS: *Reference—CID 50:133, 2010*				
Primary (spontaneous bacterial peritonitis, SBP) *Hepatology 49:2087, 2009.* Dx: Pos. culture & ≥ 250 neutrophils/μL of ascitic fluid	Enterobacteriaceae 63%, S. pneumo 9%, enterococci 6–10%, anaerobes <1%. Extended β-lactamase (ESBL) positive Klebsiella species.	**Cefotaxime** 2 gm IV q8h (if life-threatening, q4h) OR **PIP-TZ** OR **ceftriaxone** 2 gm IV q24h or **ERTA** 1 gm IV q24h **If resistant E. coli/Klebsiella species (ESBL+), then:** (**DORI, ERTA, IMP** or **MER**) or (**FQ: CIP, Levo, Moxi**) *(Dosage in footnote[20]).* Check in vitro susceptibility		One-year **risk of SBP** in pts with ascites and cirrhosis as high as 29% *(Gastro 104: 1133, 1993).* Diagnosis of SBP: 30–40% of pts have neg. cultures of blood and ascitic fluid. % pos. cultures ↑ if 10 mL of pt's ascitic fluid inoculated to blood culture bottles *(JAMA 299:1166, 2008).* **Duration of rx unclear.** Treat for at least 5 days, perhaps longer if pt has bacteremia: *(Pharm & Therapeutics 34:204, 2009).* **IV albumin** (1.5 gm/kg at dx & 1 gm/kg on day 3) may ↓ frequency of renal impairment (p 0.002) & ↓ hospital mortality (p 0.01) *(NEJM 341:403, 1999).*
Prevention of SBP *(Amer J Gastro 104:993, 2009)* Cirrhosis & ascites *For prevention after UGI bleeding, see Liver, page 36*		**TMP-SMX-DS** 1 tab po 5 / day / wk or **CIP** 750 mg po q wk		**TMP-SMX** ↓ peritonitis or spontaneous bacteremia from 27% to 3% *(AnIM 122:595, 1995).* Ref. for CIP: *Hepatology 22:1171, 1995*

[20] Parenteral **IV therapy** for peritonitis: **PIP-TZ** 3.375 gm q6h or 4.5 gm q8h or 4 hr infusion of 3.375 gm q8h *(See Table 10),* **Dori** 500 mg IV q8h (1-hr infusion), **IMP** 0.5–1 gm q6h, **MER** 1 gm q8h, **FQ** [**CIP** 400 mg q12h, **Oflox** 400 mg q12h, **Levo** 750 mg q24h, **Moxi** 400 mg q24h], **AMP** 1 gm q6h, **aminoglycoside** *(see Table 10D, page 118),* **cefotetan** 2 gm q12h, **cefoxitin** 2 gm q8h, **P Ceph 3** (**cefotaxime** 2 gm q4–8h, **ceftriaxone** 1–2 gm q24h, **ceftizoxime** 2 gm q4–8h), **P Ceph 4** (**CFP** 2 gm q12h, **cefpirome**[NUS] 2 gm q12h), ; (**Ceftolozane-tazobactam** 1.5 gm IV over 1 hr q8h + **Metro**); **Ceftazidime-avibactam** 2.5 gm IV over 2 hrs q8h + **Metro**) **clinda** 600–900 mg q8h, **Metronidazole** 1 gm (15 mg/kg) loading dose IV, then 1 gm IV q12h or 500 mg IV q8h (Some data supports once-daily dosing, *see Table 10A, page 112*), **AP Pen** (**aztreonam** 2 gm q8h)

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives: consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (44)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
PERITONEUM/PERITONITIS *(continued)*				
Secondary (bowel perforation, ruptured appendix, ruptured diverticula) Ref: *CID 50:133, 2010 (IDSA Guidelines)* **Antifungal rx?** No need if successful uncomplicated 1st surgery for viscus perforation. Treat for candida if: pure culture from abdomen or blood. In controlled study, no benefit from preemptive rx to prevent invasive candidiasis *(CID 61:1671, 2015)*.	Enterobacteriaceae, Bacteroides sp., enterococci, P. aeruginosa (3-15 %). C. albicans *(see Comment)* If VRE documented, dapto may work *(Int J Antimicrob Agents 32:369, 2008)*.	**Mild-moderate disease—Inpatient—parenteral rx:** (e.g., focal periappendiceal peritonitis, perdiverticular abscess). **Usually need surgery for source control.** **PIP-TZ** 3.375 gm IV q6h or 4.5 gm IV q8h or 4-hr infusion of 3.375 gm q8h **OR ERTA** 1 gm IV q24h **OR MOXI** 400 mg IV q24h	[(**CIP** 400 mg IV q12h or **Levo** 750 mg IV q24h) + (**metro** 1 gm IV q12h) or (**CFP** 2 gm q12h + **metro**) Note: avoid tigecycline unless no other alternative due to increased mortality risk (FDA warning)]	Must "cover" both Gm-neg. aerobic & Gm-neg. anaerobic bacteria. Empiric coverage of MRSA, enterococci and candida not necessary unless culture indicates infection. Cover enterococci if valvular heart disease. **Drugs active only vs. anaerobic Gm-neg. bacilli:** metro. **Drugs active only vs. aerobic Gm-neg. bacilli:** aminoglycosides, P Ceph 2/3/4, aztreonam, AP Pen, CIP, Levo. **Drugs active vs. both aerobic/anaerobic Gm-neg. bacteria:** TC-CL, PIP-TZ, DORI, IMP, MER. Increasing resistance (R) of Bacteroides species *(Anaerobe 17:147, 2013; AAC 56:1247, 2012)* to: **Cefoxitin** **Cefotetan** **Clindamycin** **% R** 5-30 17–87 19-35 Essentially no resistance of Bacteroides to: **metro, PIP-TZ, TC-CL, Carbapenems.** Case report of B. fragilis resistant to all drugs except tmnocycline, tigecycline & linezolid *(MMWR 62:694, 2013)*. **Ertapenem** not active vs. P. aeruginosa/ Acinetobacter species. In absence of ongoing fecal contamination, **aerobic/anaerobic culture** of peritoneal exudate/abscess may be of help in guiding specific therapy. Data need for aminogfycosides. **With severe pen allergy,** can "cover" Gm-neg. aerobes with **CIP** or **aztreonam. Remember DORI/IMP/MER are β-lactams.** IMP dose increased to 1 gm q6h if suspect P. aeruginosa and pt. is critically ill. Resistance to Moxi increasing. See CID 59:698, 2014 (suscept. of anaerobic bacteria). Recent data suggest that short course antibiotic Rx (approx 4 days) may be sufficient where there is adequate source control of complicated intra-abdominal infections (NEJM 372:21, 2015).
		Severe life-threatening disease—ICU patient: Surgery for source control ! **IMP** 500 mg IV q6h or **MER** 1 gm IV q8h or **DORI** 500 mg IV q8h (1-hr infusion) or (**Ceftolozone-tazobactam** 1.5 gm IV q8h + **Metro** 500 mg q8h) or (**Ceftazidime-avibactam** 2.5 gm IV over 2 hrs q8h + **Metro** 500 mg q8h) **Concomitant surgical management important.**	[**AMP** + **metro** + (**CIP** 400 mg IV q8h or **Levo** 750 mg IV q24h)] **OR** [**AMP** 2 gm IV q6h + **metro** 500 mg IV q6h + **aminoglycoside** *(see Table 100, page 118)*]	
Abdominal actinomycosis	A. Israelii and rarely others	**AMP** 50 mg/kg/day IV div in 3-4 doses x 4-6 wks, then **Pen VK** 2-4 gm/day po x 3-6 mos.	**Doxy** or **ceftriaxone** or **clinda**	Presents as mass +/- fistula tract after abdominal surgery, e.g., for inflamed appendix. Can use IV Pen G instead of AMP: 10-20 million units/day IV x 4-6 wks.
Associated with chronic ambulatory peritoneal dialysis (Abdominal pain, cloudy dialysate, dialysate WBC >100 cell/μL with >50% neutrophils; normal = <8 cells/μL. Ref: *Perit Dial Int 30:393, 2010.*)	Gm+ 45%, Gm- 15%, Multiple 1%, Fungi 2%, MTB 0.1% *(Perit Dial Int 24:424, 2004)*.	**Empiric therapy:** Need activity vs. MRSA **(Vanco)** & aerobic gram-negative bacilli (**Ceftaz, CFP, Carbapenem, CIP, Aztreonam, Gent**). Add **Fluconazole** if gram stain shows yeast. Use intraperitoneal dosing, unless bacteremia (rare). For bacteremia, IV dosing. For dosing detail, *see Table 19, page 231.*		**For diagnosis:** concentrate several hundred mL of removed dialysis fluid by centrifugation. Gram stain concentrate and then inject into aerobic/anaerobic blood culture bottles. A positive Gram stain will guide initial therapy. If culture shows Staph. epidermidis and no S. aureus, good chance of "saving" dialysis catheter; **if multiple Gm-neg. bacilli cultured, consider catheter-induced bowel perforation and need for catheter removal.** *See Perit Dialysis Int 29:5, 2009.* Other indications for catheter removal: relapsing/refractory peritonitis, fungal peritonitis, catheter tunnel infection.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (45)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
PHARYNX				
Pharyngitis/Tonsillitis: "Strept throat"				
Exudative or Diffuse Erythema				
Associated cough, rhinorrhea, hoarseness and/or oral ulcers suggest viral etiology. IDSA Guidelines on Group A Strep: *CID 55:1279, 2012; CID* 55:e86, *2012.* PCR for diagnosis of *F. necrophorum* not yet commercially available (12/2015)	Group A, C, G Strep.; Fusobacterium (in research studies); EBV; Primary HIV; *N. gonorrhea*; Respiratory viruses. Student health clinic pts: *F. necrophorum* found in 20%, Gp A Strep in 10% *(AnIM 162:241, 311 & 876, 2015)*	**For Strep pharyngitis: (Pen V** or **Benzathine Pen)** or **Cefdinir** or **Cefpodoxime**). **If suspect F. necrophorum: AM-CL** or **Clinda** *Doses in footnote 21*	**For Strep pharyngitis: Clinda** or **Azithro** or **Clarithro. If suspect F. necrophorum: Metro. Resistant to macrolides** *Doses in footnote 21.*	**Do not use: sulfonamides (TMP-SMX), tetracyclines or FQs due to resistance, clinical failures.** **Dx: Rapid Strep test.** If rapid test neg., do culture (*CID 59:643, 2014*). No need for post-treatment test of cure rapid strep test or culture. **Complications of Strep pharyngitis**: 1) Acute rheumatic fever 48 – follows Grp A *S. pyogenes* infection, rare after Grp *C/G* infection. See *footnote*[22]. For prevention, start treatment within 9 days of onset of symptoms. 2) Children age < 7 yrs at risk for post-streptococcal glomerulonephritis. 3) Pediatric autoimmune neuropsychiatric disorder associated with Grp A Strep (PANDAS) infection. 4) Peritonsillar abscess; Suppurative phlebitis are potential complications.
	Gonococcal pharyngitis	**Ceftriaxone** 250 mg IM x 1 dose + **Azithro** 1 gm po x 1 dose	FQs not recommended due to resistance	Not effective for pharyngeal GC: spectinomycin, cefixime, cefpodoxime and cefuroxime. Ref: *MMWR 61:590, 2012.* **See** *MMWR 64(RR-03):1, 2015 for most recent CDC STD guidelines.*
	Proven *S. pyogenes* recurrence or documented relapse	**Cefdinir** or **Cefpodoxime**	**AM-CL** or **Clinda**	*Doses in footnote 21.*
	Grp A infections: 6 in 1 yr; 4 in 2 consecutive yrs	Tonsillectomy may be reasonable		Hard to distinguish true Grp A Strep infection from chronic Grp A Strep carriage and/or repeat viral infections.
Peritonsillar abscess – Sometimes a serious complication of exudative pharyngitis ("Quinsy") *(JAC 68:1941, 2013)*	**F. necrophorum** (44%) Grp A Strep (33%) Grp *C/G* Strep (9%) Strep anginosus grp	**Surgical drainage plus**		**Avoid macrolides: Fusobacterium is resistant.** Reports of beta-lactamase production by oral anaerobes *(Anaerobe 9:105, 2003).* *See jugular vein suppurative phlebitis, page 49.* *See JAC 68:1941, 2013. Etiologies ref: CID 49:1467, 2009.*
		PIP-TZ 3.375 gm IV q6h or (**Metro** 500 mg IV/po q6-8h + **Ceftriaxone** 2 gm IV q24h)	Pen allergic: **Clinda** 600-900 mg IV q6-8h	
Other complications	*See parapharyngeal space infection and jugular vein suppurative phlebitis (see next page)*			

[21] **Treatment of Group A, C & G strep: Treatment durations are from approved package inserts. Subsequent studies indicate efficacy of shorter treatment courses. All po unless otherwise indicated. PEDIATRIC DOSAGE; Benzathine penicillin** 25,000 units per kg IM to max. 1.2 million units; **Pen V** 25–50 mg per kg per day div. q6h x 10 days; **amox** 1000 mg po once daily x 10 days; **AM-CL** 45 mg per kg per day div. q12h x 10 days; **cephalexin** 20 mg/kg/dose bid (max 500 mg/dose) x 10 days; **cefuroxime axetil** 20 mg per kg per day div. bid x 10 days; **cefpodoxime proxetil** 10 mg per kg div. bid x 10 days; **cefdinir** 7 mg per kg q12h x 5–10 days or 14 mg per kg q24h x 10 days; **cefprozil** 15 mg per kg per day div. bid x 10 days; **cefadroxil** 30 mg/kg once daily (max 1 gm/day) x 10 days; **clarithro** 15 mg per kg per day div. bid or 250 mg qid x 10 days; **azithro** 12 mg per kg once daily x 5 days; clinda 20–30 mg per kg per day div. q8h x 10 days. **ADULT DOSAGE; Benzathine** penicillin 1.2 million units IM x 1; **Pen V** 500 mg bid or 250 mg qid x 10 days; **cefditoren** 200 mg bid x 10 days; **cefuroxime axetil** 250 mg bid x 4 days; **cefpodoxime proxetil** 100 mg bid x 5 days; **cefdinir** 300 mg q12h x 5–10 days or 600 mg q24h x 10 days; **cefditoren** 200 mg bid; **cefprozil** 500 mg q24h x 10 days; **NOTE:** All **O Ceph 2** drugs approved for 10-day rx of strep pharyngitis; increasing number of studies show efficacy of 4–6 days; **clarithro** 250 mg bid x 10 days; **azithro** 500 mg x **1** and then 250 mg q24h x 4 days or 500 mg q24h x 3 days; Clinda 300 mg po tid x 10 days.

[22] Primary rationale for therapy is eradication of Group A strep (GAS) and prevention of acute rheumatic fever (ARF). Benzathine penicillin G has been shown in clinical trials to ↓ rate of ARF from 2.8 to 0.2%. This was associated with clearance of GAS on pharyngeal cultures *(CID 19:1110, 1994).* Subsequent studies have been based on cultures, not actual prevention of ARF. Treatment decreases duration of symptoms.

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (46)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
PHARYNX/Pharyngitis/Tonsillitis/Exudative or Diffuse Erythema *(continued)*				
Membranous pharyngitis: due to **Diphtheria** Respiratory isolation, nasal & pharyngeal cultures (special media), obtain antitoxin. **Place pt in respiratory droplet isolation.**	*C. diphtheriae* (human to human), *C. ulcerans* and *C. pseudotuberculosis* (animal to human) (rare)	**Treatment: antibiotics + antitoxin** **Antibiotic therapy:** **Erythro** 500 mg IV qid OR **Pen G** 50,000 units/kg (max 1.2 million units) IV q12h. Can switch to Pen VK 250 mg po qid when able. Treat for 14 days	**Diphtheria antitoxin:** Horse serum obtain from CDC, (+1 404 639 3889) Do scratch test before IV therapy. Dose depends on stage of illness: < 48hrs: 20,000 40,000 units; if NP membranes: 40,000 60,000 units; > 3 days & bull neck: 80,000 120,000 units	**Ensure adequate airway.** EKG & cardiac enzymes. F/U cultures 2 wks post-treatment to document cure. Then, diphtheria toxoid immunization. Culture contacts; treat contacts with either single dose of **Pen G** IM: 600,000 units if age < 6 yrs, 1.2 million units if age > 6 yrs. If Pen-allergic, **Erythro** 500 mg po qid x 7-10 days. Assess immunization status of close contacts: toxoid vaccine as indicated. In vitro, C. diphtheriae suscept. to clarithro, azithro, clinda, FQs, TMP/SMX.
Vesicular, ulcerative pharyngitis (viral)	Coxsackie A9, B1-5, ECHO (multiple types), Enterovirus 71, Herpes simplex 1,2	Antibacterial agents not indicated. For HSV-1, 2: **acyclovir** 400 mg tid po x 10 days.	HIV: Famciclovir 250 mg po tid x 7-10 days; or Valacyclovir 1000 mg po bid x 7-10 days	Small vesicles posterior pharynx suggests enterovirus. Viruses are most common etiology of acute pharyngitis. **Suspect viral if concurrent conjunctivitis, coryza, cough, skin rash, hoarseness.**
Epiglottitis (Supraglottis): Concern in life-threatening obstruction of the airway				
Children	H. influenzae (rare), S. pyogenes, S. pneumoniae, S. aureus (includes MRSA), viruses	**Peds dosage:** (**Cefotaxime** 50 mg per kg IV q8h or **ceftriaxone** 50 mg per kg IV q24h) + **Vanco**	**Peds dosage**: **Levo** 10 mg/kg IV q24h + **Clinda** 7.5 mg/kg IV q6h	Have tracheostomy set "at bedside". **Levo** use in children is justified as emergency empiric therapy in pts with severe beta-lactam allergy. *Ref: Ped Clin No Amer 53:215, 2006.* Use of steroids is controversial; do not recommend.
Adults	Group A strep, H. influenzae (rare) & many others	Same regimens as for children. **Adult dosage:** *See footnote*[23]		
Parapharyngeal space infection [Spaces include: sublingual, submandibular (Ludwig's angina), *(see page 45)* lateral pharyngeal, retropharyngeal, pretracheal]				
Poor dental hygiene, dental extractions, foreign bodies (e.g., toothpicks, fish bones) Ref: *CID 49:1467, 2009*	Polymicrobic: Strep sp., anaerobes, Eikenella corrodens. Anaerobes outnumber aerobes 10:1.	[(**Clinda** 600–900 mg IV q8h) or (**pen G** 24 million units/day by cont. infusion or div. q4–6h IV]+ **metro** 1 gm load and then 0.5 gm IV q6h)	**PIP-TZ** 3.375 gm IV q6h or **AM-SB** 3 gm IV q6h	Close observation of airway, 1/3 require intubation. MRI or CT to identify abscess; **surgical drainage. Metro** may be given 1 gm IV q12h. Complications: infection of carotid (rupture possible) & jugular vein phlebitis.
Jugular vein suppurative phlebitis (Lemierre's syndrome) *LnID 12:808, 2012.*	Fusobacterium necrophorum in vast majority	**PIP-TZ** 4.5 gm IV q8h or **IMP** 500 mg IV q6h or (**Metro** 500 mg po/IV q8h + **ceftriaxone** 2 gm IV once daily)	**Clinda** 600–900 mg IV q8h. **Avoid macrolides: fusobacterium are resistant**	Emboli: pulmonary and systemic common. Erosion into carotid artery can occur. Lemierre described F. necrophorum in 1936; other anaerobes & Gm-positive cocci are less common etiologies of suppurative phlebitis post-pharyngitis.
Laryngitis (hoarseness)	Viral (90%)	Not indicated		

[23] Parapharyngeal space infection: **Ceftriaxone** 2 gm IV q24h; **cefotaxime** 2 gm IV q4–8h; **PIP-TZ** 3.375 gm IV q6h or 4-hr infusion of 3.375 gm q8h; **TMP-SMX** 8–10 mg per kg per day (based on TMP component) div q6h, q8h, or q12h ; **Clinda** 600-900 mg IV q6-8h; **Levo** 750 mg IV q24h; **vanco** 15 mg/kg IV q12h.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (47)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SINUSES, PARANASAL				
Sinusitis, acute *(Ref: CID 54:e72, 2012). Guidelines: Pediatrics 132:e262 & 284, 2013 (American Academy of Pediatrics)*				
Treatment goals: • Speed resolution • Prevent bacterial complications *(see Comment)* • Prevent chronic sinusitis • Avoid unnecessary use of antibiotics	S. pneumonia 33% H. influenza 32% M. catarrhalis 9% Anaerobes 6% Grp A strep 2% Viruses 15-18% S. aureus 10% *(see Comment)*	Most common: obstruction of sinus ostia by inflammation from virus or allergy. Treatment: Saline irrigation **Antibiotics for bacterial sinusitis if:** 1) fever, pain, purulent nasal discharge; 2) still symptomatic after 10 days with no antibiotic; 3) clinical failure despite antibiotic therapy *No penicillin allergy* **Peds: Amox** 90 mg/kg/day divided q12h or **Amox-Clav** suspension 90 mg/kg/day (Amox comp) divided q12h. Treat for 10-14 days **Adult: Amox-Clav** 1000/62.5-2 tabs po bid x 5-7 days	*Penicillin allergy* **Peds (if anaphylaxis): Clinda** 30-40 mg/kg/day divided tid or qid x 10-14 days (see Comment) **Peds (no anaphylaxis): Cefpodoxime** 10 mg/kg/day po div q12h **Adult (if anaphylaxis): Levo** or doxy. Adult (no anaphylaxis): **Cefpodoxime** 200 mg po bid	**Treatment:** • Clinda. Haemophilus & Moraxella sp. are resistant; may need 2nd drug • Duration of rx: 5-7 days *(IDSA Guidelines)*, 10-14 days *(Amer Acad Ped Guidelines)* • Adjunctive rx: 1) do not use topical decongestant for > 3 days; 2) no definite benefit from nasal steroids & antihistamines; 3) saline irrigation may help • Avoid macrolides & TMP-SMX due to resistance • Empiric rx does not target S. aureus; incidence same in pts & controls *(CID 45:e121, 2007)* Potential complications: transient hyposmia, orbital infection, epidural abscess, brain abscess, meningitis, cavernous sinus thrombosis. For other adult drugs and doses, *see footnote[24].*
Clinical failure after 3 days	As above; consider diagnostic tap/aspirate	**Mild/Mod. Disease: AM-CL-ER** OR (**cefpodoxime**, **cefprozil**, or **cefdinir** *Treat 5-10 days. Adult doses in footnote[24]*	**Severe Disease: Gati[NUS], Gemi, Levo, Moxi**	Severe/hospitalized: **AM-SB** 3 gm IV q6h or **Ceftriaxone** 1-2 gm IV q24h or **Levo** 750 mg IV/po q24h.If no response in 48 hrs, CT sinus & surgical consult.
Diabetes mellitus with acute keto-acidosis; neutropenia; deferox-amine rx: Mucormycosis	Rhizopus sp., (mucor), aspergillus	*See Table 11, pages 121 & 131.*		
Hospitalized + nasotracheal or nasogastric intubation	Gm-neg. bacilli 47% (pseudomonas, enterobacter, E. coli common), Gm+ (S. aureus) 38%, yeasts 18% Polymicrobial in 80%	Remove nasotracheal tube: if fever persists and ENT available, recommend sinus aspiration for C/S & S. aureus PCR prior to empiric therapy **IMP** 0.5 gm IV q6h or **MER** 1 gm IV q8h. Add vanco for MRSA if Gram stain suggestive.	(**Ceftaz** 2 gm IV q8h + **vanco**) or (**CFP** 2 gm IV q12h + **vanco**).	After 7 days of nasotracheal or nasogastric tubes, 95% have x-ray "sinusitis" (fluid in sinuses), but on transnasal puncture only 38% culture + *(AJRCCM 150:776, 1994)*. For pts requiring mechanical ventilation with nasotracheal tube for >1 wk, bacterial sinusitis occurs in <10% *(CID 27:851, 1998)* May need linezolid/vanco if yeast on Gram stain of sinus aspirate.
Sinusitis, chronic Adults Defined: (drainage, blockage, facial pain, ↓ sense of smell) + (Polyps, purulence or abnormal endoscopy or sinus CT scan: *JAMA 314:926, 2015*)	Multifactorial inflammation of upper airways	Standard maintenance therapy: Saline irrigation + topical corticosteroids	Intermittent/Rescue therapy: For symptomatic nasal polyps: oral steroid x 1-3 wks. For polyps + purulence: Doxy 200 mg po x 1 dose, then 100 mg po once daily x 20 days	Leukotriene antagonists: considered only for pts with nasal polyps. No antihistamines: unless clearly allergic sinusitis. Some suggest > 12 wks of macrolide rx, data only somewhat supportive; worry about AEs.

[24] **Adult doses for sinusitis (all oral): AM-CL-ER** 2000/125 **mg** bid, **amox high-dose (HD)** 1 gm tid, **clarithro** 500 mg bid or **clarithro ext. release** 1 gm q24h, **doxy** 100 mg bid, **respiratory FQs** (**Gati** 400 mg q24hNUS due to hypo/hyperglycemia; **Gemi** 320 mg q24h *(not FDA indication but should work)*, **Levo** 750 mg q24h x 5 days, **Moxi** 400 mg q24h); **O Ceph** (**cefdinir** 300 mg q12h or 600 mg q24h, **cefpodoxime** 200 mg bid, **cefprozil** 250–500 mg bid, **cefuroxime** 500 mg bid), **TMP-SMX** 1 double-strength (TMP 160 mg) bid (results after 3- and 10-day rx similar).

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (48)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
SKIN *See* IDSA Guideline: *CID 59:147, 2014.*				
Acne vulgaris *(Med Lett Treatment Guidelines 11 (Issue 125): 1, 2013).*				
Comedonal acne, "blackheads", "whiteheads", earliest form, no inflammation	Excessive sebum production & gland obstruction. No Propionibacterium acnes	Once-q24h: Topical **tretinoin** (cream 0.025 or 0.05%) or (gel 0.01 or 0.025%)	All once q24h topical **adapalene** 0.1% gel OR **azelaic acid** 20% cream or **tazarotene** 0.1% cream	Goal is prevention, ↓ number of new comedones and create an environment unfavorable to P. acnes. Adapalene causes less irritation than tretinoin. Azelaic acid less potent but less irritating than retinoids. **Tazarotene: Do not use in pregnancy.**
Mild inflammatory acne: small papules or pustules	Proliferation of P. acnes + abnormal desquamation of follicular cells	Topical **erythro** 3% + **benzoyl peroxide** 5%, bid	Can substitute **clinda** 1% gel for erythro	In random. controlled trial, topical benzoyl peroxide + erythro of equal efficacy to oral minocycline & tetracycline and not affected by antibiotic resistance of propionibacteria *(Ln 364:2188, 2004).*
Inflammatory acne: comedones, papules & pustules. Less common: deep nodules (cysts) Isotretinoin ref: *JAMA 311: 2121, 2133, 2014.*	Progression of above events. Also, drug induced, e.g., glucocorticoids, phenytoin, lithium, INH & others.	(Topical **erythro** 3% + **benzoyl peroxide** 5% bid) ± oral antibiotic. *See Comment for mild acne*	Oral drugs: (**doxy** 50 mg bid) or (**minocycline** 50 mg bid). Others: **tetracycline, erythro, TMP-SMX, clinda.** Expensive extended release **once-daily minocycline** (Solodyn) 1 mg/kg/d	Systemic **isotretinoin** reserved for pts with severe widespread nodular cystic lesions that fail oral antibiotic rx; 4–5 mos. course of 0.1–1 mg per kg per day. Aggressive/violent behavior reported. **Teratogenic (Preg category X). Tetracyclines** stain developing teeth. **Doxy** can cause photosensitivity. **Minocycline** side-effects: urticaria, vertigo, pigment deposition in skin or oral mucosa. Rare induced autoimmunity in children: fever; polyarthralgia, positive ANCA *(J Peds 153:314, 2008).*
Acne rosacea Ref: *NEJM 352:793, 2005.*	Skin mite: Demadex folliculorum *(Arch Derm 146:896, 2010)*	Facial erythema: Brimonidine gel (Mirvaso) applied to affected area bid *(J Drugs Dermatol 12:650, 2013)*	Papulopustular rosacea: **Azelaic acid** gel bid, topical or **Metro** topical cream once daily or q24h	Avoid activities that provoke flushing, e.g., alcohol, spicy food, sunlight.
Anthrax, cutaneous **To report bioterrorism event: 770-488-7100;** **For info: www.bt.cdc.gov** Treat as inhalation anthrax if systemic illness. *Refs: AJRCCM 184:1333, 2011* (Review); *CID 59:147, 2014* (Clinical Prac Guideline); Pediatrics 133:e1411, 2014.	B. anthracis Spores are introduced into/under the skin by contact with infected animals/animal products. *See Lung, page 40.*	**Adults: CIP** 500 mg po q12h or **Doxy** 100 mg po q12h. **Children: CIP** 15 mg/kg (max dose 500 mg) po q12h or for pen-susceptible strain **Amox** 25 mg/kg (max dose 1 gm) po q8h For bioterrorism exposure, 3-dose series of Biothrax Anthrax Vaccine Adsorbed is indicated.		1. Duration of therapy 60 days for bioterrorism event because of potential inhalational exposure and 7-10 days for naturally acquired disease. 2. Consider alternative to Doxy for pregnancy. 3. Alternatives for adults: Levo 750 mg q24h or Moxi 400 mg q24h or Clinda 600 mg q8h or for pen-susceptible strains Amox 1 gm q8h or Pen VK 500 mg q6h 4. Alternatives for children: Doxy 2.2 mg/kg (max dose 100 mg) q12h (tooth staining likely with 60-day regimen age < 8 years) or Clindamycin 10 mg/kg (max dose 600 mg) q8h or Levo 8 mg/kg q12h (max dose 250 mg) if < 50 kg and 500 mg q24h if > 50 kg
Bacillary angiomatosis: For other Bartonella infections, see *Cat-scratch disease lymphadenitis, page 45, and Bartonella systemic infections, page 57*				
In immunocompromised (HIV-1, bone marrow transplant) patients *Also see SANFORD GUIDE TO HIV/AIDS THERAPY*	Bartonella henselae and quintana	**Clarithro** 500 mg po bid or ext. release 1 gm po q24h or **azithro** 250 mg po q24h *(see Comment)*	**Erythro** 500 mg po qid or **doxy** 100 mg po bid or (**Doxy** 100 mg po bid + **RIF** 300 mg po bid)	For AIDS pts, continue suppressive therapy until HIV treated and CD > 200 cells/μL for 6 mos.

**NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (49)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
SKIN *(continued)*				
Bite: Remember tetanus prophylaxis— See *Table 20B, page 233 for rabies prophylaxis.* Review: *CMR 24:231, 2011.* **Avoid primary wound closure.**				
Alligator *(Alligator mississippiensis)*	Gram negatives including Aeromonas hydrophila, Clostridia sp.	Severe wound: Surgical debridement + (**CIP** 400 mg IV /750 mg po bid or **Levo** 750 mg IV qd)	Severe wound: Surgical debridement + (**TMP-SMX** 8-10 mg/kg/day IV div q6h or q8h or **Cefepime** 2 gm IV q8h)	Oral flora of American alligator isolated: anaerobes, including Aeromonas hydrophila and Clostridia sp. *(S Med J 82:262, 1989).*
Bat, raccoon, skunk	Strep & staph from skin; rabies	**AM-CL** 875/125 mg po bid or 500/125 mg po tid	**Doxy** 100 mg po bid	In Americas, **anti-rabies rx indicated:** rabies immune globulin + vaccine. *(See Table 20B, page 233)*
Camel	S. aureus, P. aeruginosa, Other Gm-neg bacilli	**Diclox** 250-500 mg po q6h + **CIP** 750 mg po bid	**Cephalexin** 500 mg po qid + **CIP** 750 mg po bid	See *EJCMID 18:918, 1999.*
Cat: 80% get infected, culture & treat empirically. Cat-scratch disease: *page 45*	**Pasteurella multocida**, Streptococci, Staph. aureus, Neisseria, Moraxella	**AM-CL** 875/125 mg po bid 1000/62.5 mg 2 tabs po bid	**Cefuroxime axetil** 0.5 gm po q12h or **doxy** 100 mg po bid. **Do not use cephalexin.** Sens. to FQs in vitro.	**P. multocida resistant to dicloxacillin, cephalexin, clinda; many strains resistant to erythro** (most sensitive to azithro but no clinical data). P. multocida infection develops within 24 hrs. Observe for osteomyelitis. If culture + for only P. multocida, can switch to pen G IV or pen VK po. See Dog Bite
Catfish sting	Toxins	See *Comments*		Presents as immediate pain, erythema and edema. Resembles strep cellulitis. May become secondarily infected; AM-CL is reasonable choice for prophylaxis
Dog: Only 5% get infected; treat only if bite severe or bad co-morbidity (e.g. diabetes).	**Pasteurella canis**, S. aureus, Streptococci, Fusobacterium sp., Capnocytophaga canimorsus	**AM-CL** 875/125 mg po bid or 1000/62.5 mg 2 tabs po bid	Adult: **Clinda** 300 mg po q6h + **FQ** Child: **Clinda** + **TMP-SMX**	Consider anti-rabies prophylaxis: rabies immune globulin + vaccine *(see Table 20B).* Capnocytophaga in splenectomized pts may cause local eschar, sepsis with DIC. **P. canis resistant to diclox, cephalexin, clinda and erythro;** sensitive to ceftriaxone, cefuroxime, cefpodoxime and FQs.
Human For bacteriology, see *CID 37:1481, 2003*	Viridans strep 100%, Staph epidermidis 53%, corynebacterium 41%, **Staph. aureus 29%, eikenella 15%,** bacteroides 82%, peptostrep 26%	**Early** (not yet infected): **AM-CL** 875/125 mg po bid times 5 days. **Later:** Signs of infection (usually in 3–24 hrs): (**AM-SB** 1.5 gm IV q6h or **cefoxitin** 2 gm IV q8h) or (**PIP-TZ** 3.375 gm IV q6h or 4.5 gm q8h or 4-hr infusion of 3.375 gm q8h). Pen allergy: **Clinda** + (either **CIP** or **TMP-SMX**)		**Cleaning, irrigation and debridement most important.** For clenched fist injuries, x-rays should be obtained. Bites inflicted by hospitalized pts, consider aerobic Gm-neg. bacilli. **Eikenella resistant to clinda, nafcillin/oxacillin, metro, P Ceph 1, and erythro; susceptible to FQs and TMP-SMX.**
Leech (Medicinal) *(Ln 381:1686, 2013)*	Aeromonas hydrophila	**CIP** (400 mg IV or 750 mg po) bid	**TMP-SMX DS** 1 tab po bid	Aeromonas found in GI tract of leeches. Some use prophylactic antibiotics when leeches used medicinally, but not universally accepted or necessary.
Pig (swine)	Polymicrobic: Gm + cocci, Gm-neg. bacilli, anaerobes, Pasteurella sp.	**AM-CL** 875/125 mg po bid	**P Ceph 3** or **AM-SB** or **IMP**	Information limited but infection is common and serious *(Ln 348:888, 1996).*
Prairie dog	Monkeypox	*See Table 14A, page 174.* No rx recommended		
Primate, non-human	Microbiology. Herpesvirus simiae	**Acyclovir:** *See Table 14B, page 177*		*CID 20:421, 1995*
Rat	Spirillum minus & Streptobacillus moniliformis	**AM-CL** 875/125 mg po bid	**Doxy**	Anti-rabies rx not indicated. Causes rat bite fever (Streptobacillus moniliformis): Pen G or doxy, alternatively erythro or clinda.
Seal	Marine mycoplasma	Tetracycline times 4 wks		Can take weeks to appear after bite *(Ln 364:448, 2004).*
Snake: pit viper (Ref.: *NEJM 347:347, 2002*)	Pseudomonas sp., Enterobacteriaceae, Staph. epidermidis, Clostridium sp.	**Primary therapy is antivenom**. Penicillin generally used but would not be effective vs. organisms isolated. Ceftriaxone should be more effective. Tetanus prophylaxis indicated. Ref: *CID 43:1309, 2006.*		

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives: consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (50)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SKIN/Bite *(continued)*				
Spider bite: Most necrotic ulcers attributed to spiders are probably due to another cause, e.g., cutaneous anthrax *(Lancet 364:549, 2004)* or **MRSA infection** (spider bite painful; anthrax not painful.)				
Widow (Latrodectus)	Not infectious	None	May be confused with "acute abdomen". Diazepam or calcium gluconate helpful to control pain, muscle spasm. Tetanus prophylaxis.	
Brown recluse (Loxosceles) *NEJM 352:700, 2005*	Not infectious. Overdiagnosed! Spider distribution limited to S. Central & desert SW of US	Bite usually self-limited & self-healing. No therapy of proven efficacy.	**Dapsone** 50 mg po q24h often used despite marginal supportive data	Dapsone causes hemolysis (check for G6PD deficiency). Can cause hepatitis; baseline & weekly liver panels suggested.
Boils—Furunculosis				
Active lesions *See Table 6, page 82*	Staph. aureus, both MSSA & MRSA *IDSA Guidelines: CID 59:147, 2014; CID 59147, 2014.*	**Boils and abscesses** uncomplicated patient (e.g., no immunosuppression, diabetes) **I&D** + **TMP/SMX** 1 DS (2 DS for BMI > 40) bid or **I&D** + **Clinda** 300 mg tid equally efficacious *(NEJM 372:1093, 2015)*		Other options: **Doxy** 100 mg po bid or **Minocycline** 100 mg po bid for 5-10 days; **Fusidic acid**[NUS] 250-500 mg po q8-12h ± **RIF**; **cephalexin** 500 mg po tid-qid or dicloxacillin 500 mg po tid-qid, only in low prevalence setting for MRSA. If dx uncertainty or for assessing adequacy of I&D, ultrasound is helpful *(NEJM 370:1039, 2014)*. **Note: needle aspiration is inadequate.**
		Incision and Drainage mainstay of therapy!		
To lessen number of furuncle recurrences --decolonization *For surgical prophylaxis, see Table 15B, page 200.*	MSSA & MRSA. *IDSA Guidelines, CID 59:e10, 2014*	7-day therapy: **Chlorhexidine** (2%) washes daily; 2% **mupirocin ointment** anterior nares 2x daily + (**rifampin** 300 mg bid + **doxy** 100 mg bid).	**Mupirocin ointment** in anterior nares bid x 7 days + **chlorhexidine** (2%) washes daily x 7 days + (**TMP-SMX DS** 1 tab po bid + **RIF** 300 mg po bid) x 7 days	Optimal regimen uncertain. Can substitute bleach baths for chlorhexidine *(Inf Control Hosp Epidemiol 32:872, 2011) but only modest effect (CID 58:679, 2014).* In vitro resistance of mupirocin & retapamulin roughly 10% *(AAC 58:2878, 2014).* One review found mupirocin resistance ranging from 1.81% *(JAC 70:2681, 2015).*
Hidradenitis suppurativa Not infectious disease, but bacterial superinfection occurs	Lesions secondarily infected: S. aureus, Enterobacteriaceae, pseudomonas, anaerobes	Clinda 1% topical cream	**Clinda** 300 mg po bid + **RIF** 300 mg po bid x 6 mos *(NEJM 366: 158, 2012)*	Caused by keratinous plugging of apocrine glands of axillary, inguinal, genital, perineal, infra-mammary areas. Other therapy: antiperspirants, loose clothing and anti-androgens. *Dermatol Clin 28:779, 2010.*
		Adalimumab 40 mg once weekly beneficial *(AnIM 157:846, 2012)*		
Burns. Overall management: *NEJM 350:810, 2004 – step-by-step case outline*				
Initial wound care Use burn unit, if available Topical rx options *(NEJM 359:1037, 2008; Clin Plastic Surg 36:597, 2009)*	**Not Infected** Prophylaxis for potential pathogens: Gm-pos cocci Gm-neg bacilli Candida	Early excision & wound closure. Variety of skin grafts/substitutes. Shower hydrotherapy. Topical antimicrobials	**Silver sulfadiazine** cream 1% applied 1-2 x daily. Minimal pain. Transient reversible neutropenia due to margination in burn – not marrow toxicity	Mafenide acetate cream is an alternative but painful to apply. Anti-tetanus prophylaxis indicated.
Burn wound sepsis Proposed standard def: *J Burn Care Res 28:776, 2007.* Need quantitative wound cultures	Strep. pyogenes, Enterobacter sp., S. aureus, S. epidermidis, E. faecalis, E. coli, P. aeruginosa. Fungi (rare). Herpesvirus (rare).	**Vanco** high dose to rapidly achieve trough concentration of 15-20 µg/mL + (**MER** 1 gm IV q8h or **cefepime** 2 gm IV q8h) + **Fluconazole** 6 mg/kg IV qd See *Comments for alternatives*		Vanco allergic/intolerant: **Dapto** 6-10 mg/kg IV qd IgE mediated allergy to beta lactams: **Aztreonam** 2 gm IV q6h. ESBL- or carbapenemase-producing MDR gm-neg bacilli: only option is **[Polymyxin B** (preferred) or **Colistin]** + (**MER** or **IMP**)

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (51)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
SKIN *(continued)*				
Cellulitis, erysipelas: NOTE: Consider diseases that masquerade as cellulitis *(Clev Clin J Med 79:547, 2012)*				
Extremities, non-diabetic *For diabetes, see below.* Practice guidelines: *CID 59:147, 2014.*	Streptococcus sp., Groups A, B, C & G. Staph. aureus, including MRSA (but rare). Strept sp: No purulence Staph sp: Purulence	**Inpatients: Elevate legs. Pen G** 1–2 million units IV q6h or **cefazolin** 1 gm IV q8h. If Pen-allergic: **Vanco** 15 mg/kg IV q12h. When afebrile: **Pen VK** 500 mg po qid ac & hs. Total therapy: 10 days.	**Outpatient: Elevate legs. Pen VK** 500 mg po qid ac & hs x 10 days. If Pen-allergic: **Azithro** 500 mg po x 1 dose, then 250 mg po once daily x 4 days (total 5 days). Rarely, **Linezolid** 600 mg po bid or **Tedizolid** 200 mg po q24h.	•Erysipelas: elevation, IV antibiotic, treat T. pedis if present, if no purulence, no need for culture, TMP-SMX may fail but TMP-SMX was equivalent to clinda in clinical trial of cellulitis treatment *(NEJM 372: 1093, 2015).* •If unsure as to presence of deep abscess, bedside ultrasound can help. If present: furunculosis (boils) • **TMP-SMX** 1 DS bid OR **Clinda** 300 mg tid effective for uncomplicated cellulitis in non-diabetic outpatients *(NEJM 372:2460, 2015)* • **Oritavancin** 1500 mg IV x1 OR **Dalbavancin** 1000 mg IV x1 then 500 mg x1 a week later also effective for outpatient therapy of more severe infections in patients who might otherwise be admitted to the hospital *(see NEJM 370:2180, 2014, NEJM 370:2169, 2014).*
Facial, adult (erysipelas)	Strep. sp. (Grp A, B, C & G), Staph. aureus (to include MRSA), S. pneumo	**Vanco** 15 mg/kg (actual wt) IV q8-12h (to achieve target trough concentration of 15-20 µg/mL x 7-10 days	**Dapto** 4 mg/kg IV q 24h **or Linezolid** 600 mg IV q 12h. Treat 7-10 days if not bacteremic.	**Choice of empiric therapy must have activity vs. S. aureus.** S. aureus erysipelas of face can mimic streptococcal erysipelas of an extremity. Forced to treat empirically for MRSA until in vitro susceptibilities available.
Diabetes mellitus and erysipelas *(See Foot, "Diabetic", page 16)*	Strep. sp. (Grp A, B, C & G), Staph. aureus, Enterobacteriaceae; Anaerobes	**Early mild: TMP-SMX-DS** 1-2 tabs po bid + (**Pen VK** 500 mg po qid or **cephalexin** 500 mg po qid). **For severe disease: IMP, MER, ERTA** or **DORI** IV + (**linezolid** 600 mg IV/po bid or **vanco** IV or **dapto** 4 mg/kg IV q 24h). *Dosage, see page 16, Diabetic foot*		Prompt surgical debridement indicated to rule out necrotizing fasciitis and to obtain cultures. If septic, consider x-ray of extremity to demonstrate gas. **Prognosis dependent on blood supply: assess arteries.** *See diabetic foot, page 16.* For severe disease, use regimen that targets both aerobic gram-neg bacilli & MRSA.
Erysipelas 2° to lymphedema (congenital = Milroy's disease); post-breast surgery with lymph node dissection	Streptococcus sp., Groups A, C, G	**Benzathine pen G** 1.2 million units IM q4 wks or **Pen VK** 500 mg po bid or **azithro** 250 mg po qd		Indicated only if pt is having frequent episodes of cellulitis. Benefit in controlled clinical trial *(NEJM 368:1695, 2013).*
Dandruff (seborrheic dermatitis)	Malassezia species	**Ketoconazole shampoo** 2% or **selenium sulfide** 2.5% *(see page 10, chronic external otitis)*		
Erythema multiforme	H. simplex type 1, mycoplasma, Strep. pyogenes, drugs (sulfonamides, phenytoin, penicillins)			Treat underlying disorder / Remove offending drug; symptomatic Rx.
Erythema nodosum	Sarcoidosis, inflammatory bowel disease, MTB, coccidioidomycosis, yersinia, sulfonamides, Whipple's disease			**Rx: NSAIDs; glucocorticoids** if refractory. Identify and treat precipitant disease if possible
Erythrasma	Corynebacterium minutissimum	Localized infection: **Topical Clinda** 2-3 x daily x 7–14 days	Widespread infection: **Clarithro** 500 mg po bid or **Erythro** 250 mg po bid) x 14 days	Dx: Coral red fluorescence with Wood's lamp. If infection recurs, prophylactic bathing with anti bacterial soap or wash with benzyl peroxide. One-time dose of Clari 1 gm po reported to be effective *(Intl J Derm 52:516, 2013, J Derm Treatm 24:70, 2013).*
Folliculitis	S. aureus, candida, P. aeruginosa common	Usually self-limited, no Rx needed. Could use topical mupirocin for Staph and topical antifungal for Candida.		
Furunculosis	Staph. aureus	*See Boils, page 53*		
Hemorrhagic bullous lesions Hx of sea water-contaminated abrasion or eating raw seafood in cirrhotic pt.	**Vibrio vulnificus** *(CID 52:788, 2011; JAC 67:488, 2012)*	**Ceftriaxone** 2 gm IV q24h + (**Doxy** or **Minocycline**) 100 mg po/IV bid	**CIP** 750 mg po bid or 400 mg IV bid	Wound infection in healthy hosts, but bacteremia mostly in cirrhotics. Pathogenesis: Open wound exposure to contaminated seawater. Can cause necrotizing fasciitis *(JAC 67:488, 2012).* Surgical debridement *(Am J Surg 206:32, 2013).*
Herpes zoster (shingles): *See Table 14*				

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (52)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
SKIN *(continued)*				
Impetigo—*See CID 59:147, 2014.*				
"Honey-crust" lesions (non-bullous). Ecthyma is closely related. Causes "punched out" skin lesions.	**Group A strep impetigo** (rarely Strept. sp. Groups B, C or G); crusted lesions can be Staph. aureus + strepto-cocci. Staph. aureus may be secondary colonizer.	Few lesions: (Mupirocin ointment 2% tid or fusidic acid cream[NUS] 2%, or retapamulin ointment, 1% bid. Treat for 5 days	Numerous lesions: **Pen VK** 250-500 mg po q6h x 5 days or **Benzathine Pen** 600,000 units IM x 1 or **TMP-SMX** po x 5 days	Topical rx: OTC ointments (bacitracin, neomycin, polymyxin B not as effective as prescription ointments. For mild disease, topical rx as good as po antibiotics *(Cochrane Database Syst Rev CD003261, 2012).* **Ecthyma:** Infection deeper into epidermis than impetigo. May need parenteral penicillin. Military outbreaks reported: *CID 48: 1213 & 1220, 2009 (good images).*
Bullous (if ruptured, thin "varnish-like" crust)	**Staph. aureus** MSSA & MRSA: strains that produce exfoliative toxin A.	**For MSSA**: po therapy with **dicloxacillin**, **oxacillin**, **cephalexin**, **AM-CL**, **clinda**, **TMP-SMX-DS**, or **mupirocin** ointment or **retapamulin** ointment	**For MRSA**: **Mupirocin** ointment or po therapy with, **TMP-SMX-DS**, **minocycline**, **doxy**, **clinda**. **Treat for 7 days**	
		For dosages, see Table 10A		
Infected wound, extremity —Post-trauma *(for bites, see page 52; for post-operative, see below)*— **Gram stain negative**				
Mild to moderate; uncomplicated Debride wound, if necessary.	Polymicrobic: S. aureus (MSSA & MRSA), aerobic & anaerobic strep, Enterobacteriaceae, C. perfringens, C. tetani; if water exposure, Pseudomonas sp., Aeromonas sp. Acinetobacter in soldiers in Iraq *(see CID 47:444, 2008).*	**Clinda** 300-450 mg po tid	**Minocycline** 100 mg po bid or **linezolid** 600 mg po bid	**Culture & sensitivity, check Gram stain. Tetanus toxoid if indicated.** **Mild infection:** Suggested drugs focus on S. aureus & Strep species. If suspect Gm-neg. bacilli, add **AM-CL-ER** 1000/62.5 two tabs po bid. If MRSA is erythro-resistant, may have inducible resistance to clinda. **Fever—sepsis:** Another alternative is **linezolid** 600 mg IV/po q12h. If Gm-neg. bacilli & severe pen allergy, **CIP** or **Levo**
Febrile with sepsis—hospitalized Debride wound, if necessary.		[**PIP-TZ** or **DORI**[NAI] or **IMP** or **MER** or **ERTA** *(Dosage, page 25)*] + **vanco** 15-20 mg/kg q8-12h	(**Vanco** 15-20 mg/kg IV q8-12h or **dapto** 6 mg/kg IV q 24h or **ceftaroline** 600 mg IV q12h or **telavancin** 10 mg/kg IV q24h) + (**CIP** 400 mg IV q12h (q8h if P. aeruginosa) or Levo 750 mg IV q24h)	
Infected wound, post-operative—Gram stain negative: for Gram stain positive cocci – see below				
Surgery not involving GI or female genital tract				
Without sepsis (mild, afebrile)	Staph. aureus, Group A, B, C or G strep sp.	**Clinda** 300–450 mg po tid		Check Gram stain of exudate. If Gm-neg. bacilli, **add** β-lactam/β-lactamase inhibitor: **AM-CL-ER** po or (**ERTA** or **PIP-TZ**) IV. *Dosage on page 25.*
With sepsis (severe, febrile)		**Vanco** 15-20 mg/kg (actual wt) IV q8-12h (to achieve target trough concentration of 15-20 μg/mL	**Dapto** 6 mg per kg IV q24h or **telavancin** 10 mg/kg IV q24h	
Surgery involving GI tract (includes oropharynx, esophagus) or female genital tract—fever, neutrophilia	MSSA/MRSA, coliforms, bacteroides & other anaerobes	[**PIP-TZ** or (**P Ceph 3** + **metro**) or **DORI** or **ERTA** or **IMP** or **MER**] + (**vanco** 1 gm IV q12h or **dapto** 6 mg/kg IV q 24h) **if severely ill.** **Mild infection: AM-CL-ER** 1000/62.5 mg 2 tabs po bid + **TMP-SMX-DS** 1-2 tabs po bid if Gm+ cocci on Gram stain. *Dosages Table 10A & footnote 26, page 63.*		For all treatment options, *see Peritonitis, page 46.* Most important: Drain wound & get cultures. Can sub **linezolid** for vanco. Can sub **CIP or Levo** for β-lactams if local susceptibility permits.
Meleney's synergistic gangrene	*See Necrotizing fasciitis, page 56*			

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (53)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SKIN/Infected wound, post-operative—Gram stain negative *(continued)*				
Infected wound, post-op, febrile patient— Positive gram stain: Gram-positive cocci in clusters	S. aureus, possibly MRSA	**Do culture & sensitivity; open & drain wound** **Oral: TMP-SMX-DS** 1 tab po bid or **clinda** 300–450 mg po tid *(see Comment)*	**IV: Vanco** 15-20 mg/kg q8-12h or **dapto** 4-6 mg/kg IV q24h or **ceftaroline** 600 mg IV q12h or **telavancin** 10 mg/kg IV q24h	Need culture & sensitivity to verify MRSA. Other po options for CA-MRSA include minocycline 100 mg po q12h or **Doxy** 100 mg po bid (inexpensive) & linezolid 600 mg po q12h (expensive). If MRSA clinda-sensitive but erythro-resistant, watch out for inducible clinda resistance. Dalbavancin and oritavancin recently FDA approved for treatment of acute bacterial skin and skin structure infections.
Necrotizing fasciitis ("flesh-eating bacteria") Post-surgery, trauma, or strepto-coccal skin infections *See Gas gangrene, page 45, & Toxic shock, page 65.* Refs: *CID 59:147, 2014; NEJM 360:281, 2009.*	**5 types:** (1) Strep sp., Grp A, C, G; (2) Clostridia sp.; (3) polymicrobic: aerobic + anaerobic (if S. aureus + anaerobic strep = Meleney's synergistic gangrene); (4) Community- associated MRSA *(NEJM 352:1445, 2005)*; (5) K. pneumoniae *(CID 55:930 & 946, 2012)*	*For treatment of clostridia, see Muscle, gas gangrene, page 45.* The terminology of **polymicrobic** wound infections is not precise: Meleney's synergistic gangrene, Fournier's gangrene, necrotizing fasciitis have common pathophysiology. **All require prompt surgical debridement** + antibiotics. Dx of necrotizing fasciitis req incision & probing. If no resistance to probing subcut with fascial plane involvement. (fascial plane), diagnosis = necrotizing fasciitis. **Need Gram stain/culture** to determine if etiology is strep, clostridia, polymicrobial, or S. aureus. **Treatment: Pen G** if strep or clostridia; **IMP** or **MER** if polymicrobial, add **vanco OR dapto** if MRSA suspected. **NOTE:** If strep necrotizing fasciitis, reasonable to treat with penicillin & clinda; if clostridia ± gas gangrene, add clinda to penicillin *(see page 45)*. ***See toxic shock syndrome, streptococcal, page 65.*** Use of hyperbaric oxygen (HBO) for necrotizing soft tissue infection long debated, *see Arch Surgery 139:1339, 2004.* Recent study limited to centers with on-site HBO found survival benefit for those in most extremely ill category *(Surg Infect (Larchmt) 15:328, 2014)*.		
Puncture wound—nail, toothpick	Through tennis shoe: P. aeruginosa	Local debridement to remove foreign body & tetanus prophylaxis; no antibiotic therapy.		Osteomyelitis evolves in only 1–2% of plantar puncture wounds. Consider x-ray if chance of radio-opaque foreign body.
Staphylococcal scalded skin syndrome Ref.: *PIDJ 19:819, 2000*	Toxin-producing S. aureus	**Nafcillin** or **oxacillin** 2 gm IV q4h (children: 150 mg/kg/day div. q6h) x 5–7 days for MSSA; **vanco** 15-20 mg/kg q8-12h (children 40–60 mg/kg/day div. q6h) for MRSA		Toxin causes **intraepidermal spitt** and positive Nikolsky sign. Biopsy differentiates: drugs cause epidermal/dermal split, **called toxic epidermal necrolysis**—more serious.
Ulcerated skin lesions: Differential Dx	Consider: anthrax, tularemia, P. aeruginosa (ecthyma gangrenosum), plague, blastomycosis, spider (rarely), mucormycosis, mycobacteria, leishmania, YAWS, arterial insufficiency, venous stasis, and others.			
Ulcerated skin: venous/arterial insufficiency; pressure with secondary infection (infected decubiti) Care of non-healing, non-infected ulcers *(AnIM 159:532, 2013)*.	Polymicrobic: Streptococcus sp. (Groups A, C, G), enterococci, anaerobic strep, Enterobacteriaceae, Pseudomonas sp., Bacteroides sp., Staph. aureus	Severe local or possible bacteremia: **IMP** or **MER** or **DORI** or **PIP-TZ** or **ERTA**. If Gm pos cocci on gram stain, add **Vanco**.	[(**CIP** or **Levo**) + **Metro**] or [(**CFP** or **Ceftaz**) + **Metro**]. If Gm-pos cocci on gram stain, add **Vanco**.	If ulcer clinically inflamed, treat IV with no topical rx. If not clinically inflamed, consider debridement, removal of foreign body, lessening direct pressure for weight-bearing limbs & leg elevation (if no arterial insufficiency). Topical rx to reduce bacterial counts: silver sulfadiazine 1% or combination antibiotic ointment. **Chlorhexidine & povidone iodine may harm "granulation tissue"–Avoid.** If not inflamed, healing improved on air bed, protein supplement, radiant heat, electrical stimulation *(AnIM 159:39, 2013)*.
		Dosages, see footnotes [5, 6, 7, 11, 14, 26]		
Whirlpool: (Hot Tub) folliculitis	Pseudomonas aeruginosa	Usually self-limited, treatment not indicated		Decontaminate hot tub: drain and chlorinate. Also associated with exfoliative beauty aids (loofah sponges).
Whirlpool: Nail Salon, soft tissue infection	Mycobacterium (fortuitum or chelonae)	**Minocycline**, **doxy** or **CIP**		Ref: *CID 38:38, 2004.*
SPLEEN. For post-splenectomy prophylaxis, *see Table 15A, page 199, for Septic Shock Post-Splenectomy, see Table 1, pg 64. Vaccines: CID 58:309, 2014.*				
Splenic abscess Endocarditis, bacteremia	Staph. aureus, streptococci	**Nafcillin** or **oxacillin** 2 gm IV q4h or **cefazolin** 2 gm IV q8h if MSSA	**Vanco** 15-20 mg/kg IV q8-12h (to achieve target trough concentration of 15–20 µg/mL).	Burkholderia (Pseudomonas) pseudomallei is common cause of splenic abscess in SE Asia. Presents with fever and LUQ pain. Usual treatment is antimicrobial therapy and splenectomy.
Contiguous from intra-abdominal site	Polymicrobic	*Treat as Peritonitis, secondary, page 46*		
Immunocompromised	Candida sp.	**Amphotericin B** *(Dosage, see Table 11, page 122)*	**Fluconazole, caspofungin**	

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (54)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SYSTEMIC SYNDROMES (FEBRILE/NON-FEBRILE) Spread by infected TICK, FLEA, or LICE				
Epidemiologic history crucial. **Babesiosis, Lyme disease, & Anaplasma (Ehrlichiosis)** have same reservoir & tick vector.				
Babesiosis: *see NEJM 366:2397, 2012.* Do not treat if asymptomatic, young, has spleen, and immunocompetent; can be fatal in lymphoma pts.	Etiol.: B. microti et al. Vector: Usually Ixodes ticks Host: White-footed mouse & others	[(**Atovaquone** 750 mg po q12h) + (**azithro** 600 mg po day 1, then 500-1000 mg per day) times 7-10 days]. If severe infection [**clinda** 1.2 gm IV bid or 600 mg po tid times 7 days + **quinine** 650 mg po tid times 7 days. **Ped. dosage: Clinda** 20–40 mg per kg per day and **quinine** 25 mg per kg per day] **Exchange transfusion**--See *Comment*		**Seven diseases where pathogen visible in peripheral blood smear:** African/American trypanosomiasis; babesia; bartonellosis; filariasis; malaria; relapsing fever. **Dx:** Giemsa-stained blood smear; antibody test available. PCR if available. **Rx: Exchange transfusions successful adjunct if used early, in severe disease.** May need treatment for 6 or more wks if immunocompromised. Look for Lyme and/or Anaplasma co-infection.
Bartonella infections: Review *EID 12:389, 2006*				
Bacteremia, asymptomatic	B. quintana, B. henselae	**Doxy** 100 mg po/IV times 15 days		Can lead to endocarditis &/or trench fever: found in homeless, alcoholics, esp. if lice/leg pain. Often missed since asymptomatic.
Cat-scratch disease	B. henselae	**Azithro** 500 mg po x 1 dose, then 250 mg/day po x 4 days. **Or** symptomatic only—see *Lymphadenitis, page 45:* usually lymphadenitis, hepatitis, splenitis, FUO, neuroretinitis, transverse myelitis, oculoglandular syndrome.		
Bacillary angiomatosis; Peliosis hepatis—pts with AIDS *MMWR 58(RR-4):39, 2009; AAC 48:1921, 2004.*	B. henselae, B. quintana	**Erythro** 500 mg po qid or **Doxy** 100 mg po bid x 3 months or longer. If CNS involvement: **Doxy** 100 mg IV/po bid + **RIF** 300 mg po bid	**Azithro** 250 mg po once daily x 3 months or longer	**Do not use:** TMP-SMX, CIP, Pen, Ceph. **Manifestations of Bartonella infections:** **HIV/AIDS Patient:** Bacillary angiomatosis; Bacillary peliosis; Bacteremia/endocarditis/FUO. **Immunocompetent Patient:** Bacteremia/endocarditis/FUO/ encephalitis; Cat scratch disease; Vertebral osteo; Trench fever; Parinaud's oculoglandular syndrome
		Regardless of CD4 count, DC therapy after 3-4 mos. & observe. If no relapse, no suppressive rx. If relapse, **doxy**, **azithro** or **erythro** x 3 mos. Stop when CD4 >200 x 6 mos.		
Endocarditis *(see page 28) (Circ 111:3167, 2005; AAC 48:1921, 2004)*	B. henselae, B. quintana	Surgical removal of infected valve		**Gentamicin toxicity:** If Gent toxicity, substitute Rifampin 300 mg IV/po bod x 14 days. Role of valve removal surgery to cure unclear. Presents as SBE. Diagnosis: ECHO, serology & PCR of resected heart valve.
		If suspect endocarditis: **Ceftriaxone** 2 gm IV once daily x 6 weeks + **Gent** 1 mg/kg IV q8h x 14 days + **Doxy** 100 mg IV/po bid x 6 wks	*If proven endocarditis:* **Doxy** 100 mg IV/po bid x 6 wks + **Gent** 1 mg/kg IV q8h x 11 days	
Oroya fever (acute) & Verruga peruana (chronic) *(AAC 48:1921, 2004)*	B. bacilliformis	**Oroya fever:** (**CIP** 500 mg po bid or **Doxy** 100 mg po bid) x 14 d. Alternative: **Chloro** 500 mg IV/po q6h + (**beta lactam** or **Doxy** 100 mg po bid) x 14 days	**Verruga peruana: RIF** 10 mg/kg po once daily x 14 d or **Streptomycin** 15-20 mg/kg IM/IV once daily x 10 days or **Azithro** 500 mg po q24h x 7 days	Oroya fever transmitted by sand-fly bite in Andes Mtns. Related Bartonella (B. rochalimae) caused bacteremia, fever and splenomegaly *(NEJM 356:2346 & 2381, 2007).* **CIP and Chloro preferred due to prevention of secondary Salmonella infections.**
Trench fever (FUO) *(AAC 48:1921, 2004)*	B. quintana	No endocarditis: **Doxy** 100 mg po bid x 4 wks + **Gentamicin** 3 mg/kg once daily for 1st 2 wks of therapy *(AAC 48:1921, 2004).*		Vector is body louse. Do not use: TMP-SMX, FQs, cefazolin or Pen. If endocarditis, need longer rx. See *Emerg ID 2:217, 2006).*

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (55)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE[§]	
SYSTEMIC SYNDROMES (FEBRILE/NON-FEBRILE)/Spread by infected TICK, FLEA, or LICE *(continued)*				
Ehrlichiosis[25]. CDC def. is one of: (1) 4x ↑ IFA antibody, (2) detection of Ehrlichia DNA in blood or CSF by PCR, (3) visible morulae in WBC and IFA ≥1:64. New species in *WI, MN (NEJM 365:422, 2011).*				
Human monocytic ehrlichiosis (HME) *(MMWR 55(RR-4), 2006; CID 43:1089, 2006)*	Ehrlichia chaffeensis (Lone Star tick is vector)	**Doxy** 100 mg po/IV bid times 7–10 days	**Tetracycline** 500 mg po qid x 7–10 days. No current rec. for children or pregnancy	30 states: mostly SE of line from NJ to Ill. to Missouri to Oklahoma to Texas. History of outdoor activity and tick exposure. April-Sept. Fever, rash (36%), leukopenia and thrombocytopenia. Blood smears no help. PCR for early dx.
Human Anaplasmosis (formerly known as Human granulocytic ehrlichiosis)	Anaplasma (Ehrlichia) phagocytophilum (Ixodes sp. ticks are vector). Dog variant is Ehrlichia ewingii *(NEJM 341:148 & 195, 1999)*	**Doxy** 100 mg bid po or IV times 7–14 days	**Tetracycline** 500 mg po qid times 7–14 days. Not in children or pregnancy. *See Comment*	Upper Midwest, NE, West Coast & Europe. H/O tick exposure. April-Sept. Febrile flu-like illness after outdoor activity. No rash. Leukopenia/ thrombocytopenia common. **Dx:** PCR best; blood smear insensitive *(Am J Trop Med Hyg 93:66, 2015).* **Rx:** RIF active in vitro *(IDCNA 22:433, 2008)* but worry about resistance developing. Minocycline should work if doxy not available.
Lyme Disease NOTE: Think about concomitant tick-borne disease e.g., babesiosis and ehrlichiosis. **Guidelines:** *CID 51:1, 2010; NEJM 370:1724, 2014.*				
Bite by ixodes-infected tick in an endemic area -- **Postexposure prophylaxis**	Borrelia burgdorferi **IDSA guidelines:** *CID 43:1089, 2006; CID 51:1, 2010*	**If endemic area,** if nymphal partially engorged deer tick: **doxy** 200 mg po times 1 dose with food	**If not endemic area,** not engorged, not deer tick: No treatment	Prophylaxis study in endemic area: erythema migrans developed in 3% of the control group and 0.4% doxy group *(NEJM 345:79 & 133, 2001).* Can substitute **Minocycline** for Doxy, if Doxy is unavailable.
Early (erythema migrans) *See Comment*	Western blot diagnostic criteria: **IgM**—Need 2 of 3 positive of kilodaltons (KD): 23, 39, 41 **IgG**—Need 5 of 10 positive of KD: 18, 21, 28, 30, 39, 41, 45, 58, 66, 93 Interest in 2 tier diagnostic approach: 1) standard Lyme ELISA & if positive; 2) C6 peptide ELISA. Better sensitivity/specificity. Applicable to European cases *(CID 57:333 & 341, 2013)*	**Doxy** 100 mg po bid. or **amoxicillin** 500 mg po tid or **cefuroxime axetil** 500 mg po bid or **erythro** 250 mg po qid. All regimens for 14–21 days. (10 days as good as 20: *AnIM 138:697, 2003)* *See Comment for peds doses*		High rate of clinical failure with azithro & erythro *(Drugs 57:157, 1999).* **Peds** (all po for 14–21 days): **Amox** 50 mg per kg per day in 3 div. doses or **cefuroxime axetil** 30 mg per kg per day in 2 div. doses or **erythro** 30 mg per kg per day in 3 div. doses. Lesions usually homogenous—not target-like *(AnIM 136:423, 2002).*
Carditis *See Comment*		(**Ceftriaxone** 2 gm IV q24h) or (**cefotaxime** 2 gm IV q4h) or (**Pen G** 3 million units IV q4h) times 14–21 days	**Doxy** *(see Comments)* 100 mg po bid times 14–21 days or **amoxicillin** 500 mg po tid times 14–21 days.	First degree AV block: Oral regimen. Generally self-limited. High degree AV block (PR >0.3 sec.): IV therapy—permanent pacemaker not necessary, but temporary pacing in 39% *(CID 59:996, 2014).*
Facial nerve paralysis (isolated finding, early)		(**Doxy** 100 mg po bid) or (**amoxicillin** 500 mg po) tid times 14–21 days	**Ceftriaxone** 2 gm IV q24h times 14–21 days	LP suggested excluding central neurologic disease. If LP neg., oral regimen OK. If abnormal or not done, suggest parenteral Ceftriaxone.
Meningitis, encephalitis *For encephalopathy, see Comment*		**Ceftriaxone** 2 gm IV q24h times 14–28 days	(**Pen G** 20 million units IV q24h in div. dose) or (**cefotaxime** 2 gm IV q8h) times 14–28 days	Encephalopathy: memory difficulty, depression, somnolence, or headache, CSF abnormalities. 89% had objective CSF abnormalities. 18/18 pts improved with ceftriaxone 2 gm per day times 30 days *(JID 180:377, 1999).* No compelling evidence that prolonged treatment has any benefit in post-Lyme syndrome *(Neurology 69:91, 2007).*
Arthritis		(**Doxy** 100 mg po bid) or (**amoxicillin** 500 mg po tid), both times 30–60 days	(**Ceftriaxone** 2 gm IV q24h) or (**pen G** 20–24 million units per day IV) times 14–28 days	Start with 1 mo of therapy; if only partial response, treat for a second mo.
Pregnancy		**Amoxicillin** 500 mg po tid times 21 days.	**If pen. allergic:** (**azithro** 500 mg po q24h times 7–10 days) or (**erythro** 500 mg po qid times 14–21 days). Choice should not include doxy.	
Post-Lyme Disease Syndromes		None indicated		No benefit from rx *(AJM 126:665, 2013; CID 51:1, 2010; AAC 58:6701, 2014; NEJM 345:85, 2001).* Constructive review: *CID 58:1267, 2014.*

[25] In endemic area (New York), high % of both adult ticks and nymphs were jointly infected with both Anaplasma (HGE) and B. burgdorferi *(NEJM 337:49, 1997).*

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (56)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
SYSTEMIC SYNDROMES (FEBRILE/NON-FEBRILE)/Spread by infected TICK, FLEA, or LICE *(continued)*				
Plague, bacteremic *(see also Bubonic plague and plague pneumonia)*	Yersinia pestis	(**Streptomycin** 30 mg/kg/day IV in 2 div doses or **Gentamicin** 5 mg/kg/day IV single dose) x 10 days	**Doxy** 200 mg IV/po bid x 1 day, then 100 mg IV/po bid x 7-10 days	FQs effective in animals: [**Levo** 500 mg IV/po once daily or **CIP** 500 mg po (or 400 mg IV) q12h] x 10 days or **Moxi** 400 mg IV/po q24h x 10-14 days
Relapsing fever				
Louse-borne (LBRF)	*Borrelia recurrentis* Reservoir: human Vector: Louse pediculus humanus	**Tetracycline** 500 mg IV/po x 1 dose	**Erythro** 500 mg IV/po x 1 dose	Jarisch-Herxheimer (fever, ↑ pulse, ↑ resp., ↓ blood pressure) in most patients (occurs in ~2 hrs). Not prevented by prior steroids. **Dx: Examine peripheral blood smear during fever for spirochetes.** Can relapse up to 10 times. Postexposure **doxy** pre-emptive therapy highly effective *(NEJM 355:148, 2006)* *B. miyamoto:* Dx by ref lab serum PCR. Fever, headache, thrombocytopenia & tick exposure (NE USA). Seems to respond to Doxy, Amox, Ceftriaxone *(AnIM 163:91 & 141, 2015; NEJM 373:468, 2015).*
Tick-borne (TBRF)	No Amer: *B. hermsii, B. turicata;* Africa: *B. hispanica, B. crocidurae, B. duttonii;* Russia: *B. miyamoto (see Comment)*	**Doxy** 100 mg po bid x 7-10 days	**Erythro** 500 mg po qid x 7-10 days	

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (57)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
SYSTEMIC SYNDROMES (FEBRILE/NON-FEBRILE)/Spread by infected TICK, FLEA, or LICE *(continued)*				
Rickettsial diseases. Review—Disease in travelers *(CID 39:1493, 2004)*				
Spotted fevers (NOTE: Rickettsial pox not included)				
Rocky Mountain spotted fever (RMSF) *(LnID 8:143, 2008 and MMWR 55 (RR-4), 2007)*	R. rickettsii (Dermacentor tick vector)	**Doxy** 100 mg po/IV bid times 7 days or for 2 days after temp. normal. Do not use in pregnancy. Some suggest loading dose: 200 mg IV/po q 12h x 3 days, then 100 mg po bid	**Pregnancy: Chloro** 50 mg/kg/day in 4 div doses. If cannot obtain Chloro, no choice but Doxy despite risks (fetal bone & teeth malformation, maternal toxicity).	Fever, rash (88%), petechiae 40–50%. **Rash spreads from distal extremities to trunk.** Rash in <50% pts in 1st 72 hrs. Dx: Immunohistology on skin biopsy; confirmation with antibody titers. Highest incidence in SE and South Central states; also seen in Oklahoma, S. Dakota, Montana. Cases reported from 42 U.S. states. **NOTE: Only 3–18% of pts present with fever, rash, and hx of tick exposure; many early deaths in children & empiric doxy reasonable** *(MMWR 49: 885, 2000).*
NOTE: Can mimic ehrlichiosis. Pattern of rash important—*see Comment*				
Other spotted fevers, e.g., Rickettsial pox, African tick bite fever	At least 8 species on 6 continents *(CID 45 (Suppl 1) S39, 2007).*	**Doxy** 100 mg po bid times 7 days	**Chloro** 500 mg po/IV qid times 7 days Children <8 y.o.: **azithro** or **clarithro** *(if mild disease)*	Clinical diagnosis suggested by: 1) fever, intense myalgia, headache; 2) exposure to mites or ticks; 3) localized eschar (tache noire) or rash. Definitive Dx: PCR of blood, skin biopsy or sequential antibody tests.
Typhus group—Consider in returning travelers with fever				
Louse-borne: epidemic typhus Ref: *LnID 8:417, 2008.*	R. prowazekii (vector is body or head louse)	**Doxy** 100 mg IV/po bid times 7 days; single 200 mg dose 95% effective.	**Chloro** 500 mg IV/po qid times 5 days	**Brill-Zinsser disease** *(Ln 357:1198, 2001)* is a relapse of typhus acquired during WWII. Truncal rash (64%) spreads centrifugally—opposite of RMSF. Louse borne typhus is a winter disease. Diagnosis by serology. R. prowazekii found in flying squirrels in SE US. Delouse clothing of infected pt.
Murine typhus (cat flea typhus): *EID 14:1019, 2008.*	R. typhi (rat reservoir and flea vector): *CID 46:913, 2008*	**Doxy** 100 mg IV/po bid times 7 days	**Chloro** 500 mg IV/po qid times 5 days	Rash in 20-54%, not diagnostic. Without treatment most pts recover in 2 wks. Faster recovery with treatment. Dx based on suspicion; confirmed serologically.
Scrub typhus	O. tsutsugamushi [rodent reservoir; vector is larval stage of mites (chiggers)]	**Doxy** 100 mg po/IV bid x 7 days. In pregnancy: **Azithro** 500 mg po x one dose	**Chloro** 500 mg po/IV qid x 7 days	Asian rim of Pacific. Confirm with serology. If Doxy resistance suspected, alternatives are **Doxy** + **RIF** 900 or 600 mg once daily *(Ln 356:1057, 2000)* or **Azithro** 500 mg q24h *(AAC 58:1488, 2014).*
Tularemia, typhoidal type Ref. **bioterrorism**: see *JAMA 285:2763, 2001; ID Clin No Amer 22:489, 2008; MMWR 58:744, 2009.*	Francisella tularensis. (Vector depends on geography: ticks, biting flies, mosquitoes identified)	Moderate/severe: [(**Gentamicin** or **tobra** 5 mg per kg per day div. q8h IV) or (**Streptomycin** 10 mg/kg IV/IM q12h)] x 10 days	Mild: [**CIP** 400 mg IV (or 750 mg po) bid or **Doxy** 100 mg IV/po bid] x 14-21 days	Diagnosis: Culture on cysteine-enriched media & serology. Dangerous in the lab. Hematogenous meningitis is a complication: treatment is **Streptomycin** + **Chloro** 50-100 mg/kg/day IV in 4 divided doses *(Arch Neurol 66:523, 2009).*

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (58)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SYSTEMIC SYNDROMES (FEBRILE/NON-FEBRILE)/Spread by infected TICK, FLEA, or LICE *(continued)*				
Other Zoonotic Systemic Bacterial Febrile Illnesses (not spread by fleas, lice or ticks): Obtain careful epidemiologic history				
Brucellosis *Refs: NEJM 352:2325, 2005; CID 46:426, 2008; MMWR 57:603, 2008; BMJ 336:701, 2008; PLoS One 7:e32090, 2012.*	B. abortus–cattle B. suis–swine B. melitensis–goats B canis–dogs	**Non focal disease:** [**Doxy** 100 mg po bid x 6 wks + **Gent** 5 mg/kg once daily for 1st 7 days	(**Doxy** 100 mg po bid + **RIF** 600-900 mg po once daily) x 6 wks. Less optimal: **CIP** 500 mg po bid + (**Doxy** or **RIF**) x 6 wks	Bone involvement, esp. sacroiliitis in 20-30%. **Neurobrucellosis:** Usually meningitis. 1% of all pts with brucellosis. Role of corticosteroids unclear; not recommended. **Endocarditis:** Rare but most common cause of death. Need surgery + antimicrobials. **Pregnancy:** TMP-SMX may cause kernicterus if given during last week of pregnancy.
		Spondylitis, Sacroiliitis: [**Doxy** + **Gent** (as above) + **RIF**] x min 3 mos	(**CIP** 750 mg po bid + **RIF** 600-900 mg po once daily) x min 3 mos	
		Neurobrucellosis: [**Doxy** + **RIF** (as above) + **ceftriaxone** 2 gm IV q12h until CSF returned to normal *(AAC 56:1523, 2012)*		
		Endocarditis: Surgery + [(**RIF** + **Doxy** + **TMP-SMX**) x 1-1/2 to 6 mos + **Gent** for 2-4 wks *(CID 56:1407, 2013)*		
		Pregnancy: Not much data. **RIF** 900 mg po once daily x 6 wks	**RIF** 900 mg po once daily + **TMP-SMX** 5 mg/kg (TMP comp) po bid x 4 wks.	
Leptospirosis *(CID 36:1507 & 1514, 2003; LnID 3:757, 2003)*	Leptospira—in urine of domestic livestock, dogs, small rodents	Severe illness: **Pen G** 1.5 million units IV q6h or **ceftriaxone** 2 gm q24h. Duration: 7 days	Mild illness: (**Doxy** 100 mg IV/po q12h **Amoxicillin** 500 mg po tid x 7 days	**Severity varies**. Varies from mild anicteric illness to severe icteric disease (Weil's disease) with renal failure and myocarditis. AST/ALT do not exceed 5x normal. **Rx:** Azithro 1 gm once, then 500 mg daily x 2 days: non-inferior to, and fewer side effects than, doxy in standard dose *(AAC 51:3259, 2007)*. Jarisch-Herxheimer reaction can occur post-Pen therapy.
Salmonella bacteremia other than S. typhi–non-typhoidal)	Salmonella enteritidis— a variety of serotypes from animal sources	It NOT acquired in Asia: (**CIP** 400 mg IV q12h or **Levo** 750 mg po once daily) x 14 days *(See Comment)*	It acquired in Asia: **Ceftriaxone** 2 gm IV q24h or **Azithro** 1 gm po x 1 dose, then 500 mg po once daily x 5-7 days. Do NOT use FQs until susceptibility determined. *(See Comment)*	In vitro resistance to nalidixic acid indicates relative resistance to FQs. Bacteremia can infect any organ/tissue: look for infection of atherosclerotic aorta, osteomyelitis in sickle cell pts. Rx duration range 14 days (immunocompetent) to ≥6 wks if mycotic aneurism or endocarditis. Alternative, if susceptible: **TMP-SMX** 8-10 mg/kg/day (TMP comp) divided q8h. CLSI has established new interpretive breakpoints for susceptibility to Ciprotloxacin: susceptible strains, MIC ≤ 0.06 µg/mL *(CID 55:1107, 2012)*.

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (59)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SYSTEMIC SYNDROMES (FEBRILE/NON-FEBRILE) *(continued)*				
Miscellaneous Systemic Febrile Syndromes				
Fever in Returning Travelers Etiology by geographic exposure & clinical syndrome *(AnIM 158:456, 2013).*	Dengue (Flavivirus)	Supportive care; *see Table 14A, page 166*		Average incubation period 4 days; serodiagnosis.
	Malaria (Plasmodia sp)	Diagnosis: peripheral blood smear		*See Table 13A, page 153*
	Typhoid (Salmonella sp)	*See Table 1, page 61.*		Average incubation 7-14 days; diarrhea in 45%.
Kawasaki syndrome 6 weeks to 12 yrs of age, peak at 1 yr of age; 85% below age 5. *Pediatrics 124:1, 2009.* Tongue image *(NEJM 373:467, 2015)*	Self-limited vasculitis with ↑ temp., rash, conjunctivitis, strawberry tongue, cervical adenitis, red hands/feet & coronary artery aneurysms	**IVIG** 2 gm per kg over 8-12 hrs x 1 + **ASA** 20-25 mg per kg qid THEN **ASA** 3–5 mg per kg per day po q24h times 6–8 wks	If still febrile after 1st dose of IVIG, some give 2nd dose. In Japan: **IVIG** + prednisolone 2 mg/kg/day. Continue steroid until CRP normal for 15 days *(Lancet 379:1571, 2012).*	IV gamma globulin (2 gm per kg over 10 hrs) in pts rx before 10th day of illness ↓ coronary artery lesions. *See Table 14A, page 175* for IVIG adverse effects. In children, wait until 11+ months after IVIG before giving live virus vaccines.
Rheumatic Fever, acute Ref.: *Ln 366:155, 2005*	Post-Group A strep pharyngitis (not Group B, C, or G)	(1) Symptom relief: **ASA** 80–100 mg per kg per day in children; 4–8 gm per day in adults. (2) Eradicate Group A strep: **Pen** times 10 days *(see Pharyngitis, page 48).* (3) Start prophylaxis: *see below*		
Prophylaxis				
Primary prophylaxis: Treat S. pyogenes pharyngitis	**Benzathine pen G** 1.2 million units IM *(see Pharyngitis, pg. 48)*		**Penicillin** for 10 days prevents rheumatic fever even when started 7–9 days after onset of illness *(see page 48).* **Alternative: Penicillin V** 250 mg po bid or **sulfadiazine (sulfisoxazole)** 1 gm po q24h or **erythro** 250 mg po bid.	
Secondary prophylaxis (previous documented rheumatic fever)	**Benzathine pen G** 1.2 million units IM q3–4 wks *(AAC 58:6735, 2014).*		**Duration?** No carditis: 5 yrs or until age 21, whichever is longer; carditis without residual heart disease: 10 since last attack; carditis with residual valvular disease: 10 yrs since last episode or until age 40 whichever is longer *(PEDS 96:758, 1995).*	
Typhoidal syndrome (typhoid fever, enteric fever) Global susceptibility results: *CID 50:241, 2010. Treatment: BMJ 338:b1159 & b1865, 2009.*	Salmonella typhi, S. paratyphi A, B, C & S. choleraesuis. **NOTE: In vitro resistance to nalidixic acid predicts clinical failure of CIP (FQs).** Do not use empiric FQs if Asia-acquired infection. Need susceptibility results.	**If NOT acquired in Asia:** (**CIP** 400 mg IV q12h or **Levo** 750 mg po/IV q24h) x 7-14 days. *(See Comment)*	**If acquired in Asia:** (**Ceftriaxone** 2 gm IV daily x 7-14 d) or (**Azithro** 1 gm po x 1 dose, then 500 mg po daily x 7 days) or (**Chloro** 500 mg po/IV q6h x 14 d) *(See Comment)*	**Dexamethasone: Use in severely ill pts: 1st dose just prior to antibiotic, 3 mg/kg IV, then 1 mg/kg q6h x 8 doses.** **Complications:** perforation of terminal ileum &/or cecum, osteo, septic arthritis, **mycotic aneurysm**, meningitis, hematogenous pneumonia. FQs, including Gati, remain best treatment if isolate susceptible *(BMJ 338:b1159 & 1865, 2009; LnID 11:445, 2011).* CLSI has established new interpretive breakpoints for susceptibility to Ciprofloxacin: susceptible strains, MIC < 0.06 µg/mL *(CID 55:1107, 2012).*
		In children, azithro 10 mg/kg once daily x 7 days *(AAC 51:819, 2007).*		
Sepsis: Following suggested **empiric** therapy assumes pt is bacteremic; mimicked by viral, fungal, rickettsial infections and pancreatitis *(Intensive Care Medicine 34:17, 2008; IDC No Amer 22:1, 2008).*				
Neonatal—early onset <1 week old	Group B strep, E. coli, klebsiella, enterobacter, Staph. aureus (uncommon), listeria (rare in U.S.)	**AMP** 25 mg/kg IV q8h + **cefotaxime** 50 mg/kg q12h	(**AMP** + **gent** 2.5 mg/kg IV/IM q12h) or (**AMP** + **ceftriaxone** 50 mg/kg IV/IM q24h)	Blood cultures are key but only 5–10% +. Discontinue antibiotics after 72 hrs if cultures and course do not support diagnosis. In Spain, listeria predominates; in S. America, salmonella. If Grp B Strep infection + severe beta-lactam allergy, alternatives include: erythro & clinda; report of clinda resistance at 38% & erythro resistance at 51% *(AAC 56:739, 2012).*
Neonatal—late onset 1–4 weeks old	As above + H. influenzae & S. epidermidis	(**AMP** 25 mg/kg IV q6h + **cefotaxime** 50 mg/kg q8h) or (**AMP** + **ceftriaxone** 75 mg/kg IV q24h)	**AMP** + **gent** 2.5 mg/kg q8h IV or IM	**If MSSA/MRSA a concern, add vanco.**

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (60)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
SYSTEMIC SYNDROMES (FEBRILE/NON-FEBRILE)/Sepsis *(continued)*				
Child; not neutropenic	Strep. pneumoniae, meningococci, Staph. aureus (MSSA & MRSA), H. influenzae now rare	(**Cefotaxime** 50 mg/kg IV q8h or **ceftriaxone** 100 mg/kg IV q24h) + **vanco** 15 mg/kg IV q6h	**Aztreonam** 7.5 mg/kg IV q6h ± **linezolid**	Major concerns are S. pneumoniae & community-associated MRSA. Coverage for Gm-neg. bacilli included but H. influenzae infection now rare. Meningococcemia mortality remains high *(Ln 356:961, 2000)*.
Adult; not neutropenic; NO HYPOTENSION but LIFE-THREATENING!—*For Septic shock, see page 64*				Systemic inflammatory response syndrome **(SIRS):** 2 or more of the following: 1. Temperature >38°C or <36°C 2. Heart rate >*90* beats per min. 3. Respiratory rate >*20* breaths per min. 4. WBC >12,*000* per mcL or >10% bands **Sepsis:** SIRS + a documented infection (+ culture) **Severe sepsis:** Sepsis + organ dysfunction: hypotension or hypoperfusion abnormalities (lactic acidosis, oliguria, ↓ mental status) **Septic shock:** Sepsis-induced hypotension (systolic BP <90 mmHg) not responsive to *500* mL IV fluid challenge + peripheral hypoperfusion.
Source unclear—consider primary bacteremia, intra-abdominal or skin source. May be **Life-threatening.** Survival greater with quicker, effective empiric antibiotic Rx *(CCM 38:1045 & 1211, 2010)*.	Aerobic Gm-neg. bacilli; S. aureus; streptococci; others	(**IMP** or **MER**) + **vanco**] or (**PIP-TZ** + **vanco**)	(**Dapto** 6 mg/kg IV q24h) + (**cefepime** or **PIP-TZ**)	
		If ESBL and/or carbapenemase-producing GNB. Empiric options pending clarification of clinical syndrome/culture results: **Low prevalence: Vanco + PIP-TZ** **High prevalence: Colistin + (MER** or **IMP)** *(See Table 5B, page 81)* *Dosages in footnote*[26] For **Colistin combination dosing**, *see Table 10A, page 112.*		
If suspect biliary source *(see Gallbladder pg. 17)*	Enterococci + aerobic Gm-neg. bacilli	**PIP-TZ** or **TC-CL**	**Ceftriaxone** + **metro** or (**CIP** or **Levo**) + **metro** *Dosages-footnote*[26]	If enterococci a concern, add ampicillin or vanco to metro regimens
If community-acquired pneumonia *(see page 39 and following pages)*	**S. pneumoniae**; MRSA, **Legionella, Gm-neg. bacillus, others**	(**Levo** or **moxi**) + (**PIP-TZ**) + **Vanco**	**Aztreonam** + (**Levo** or **moxi**) + **linezolid**	Many categories of CAP, *see material beginning at page 39*. Suggestions based on most severe CAP, e.g., MRSA after influenza or Klebsiella pneumonia in an alcoholic.
If illicit use IV drugs	S. aureus	**Vanco if high prevalence of MRSA. Do NOT use empiric vanco + oxacillin pending organism ID.** In vitro nafcillin increased production of toxins by CA-MRSA *(JID 195:202, 2007)*. *Dosages—footnote 26, page 63*		
If suspect intra-abdominal source	Mixture aerobic & anaerobic Gm-neg. bacilli	*See secondary peritonitis, page 47.*		
If petechial rash	Meningococcemia	**Ceftriaxone** 2 gm IV q12h (until sure no meningitis); consider Rocky Mountain spotted fever—*see page 60*		
If suspect urinary source, e.g. pyelonephritis	Aerobic Gm-neg. bacilli & enterococci	*See pyelonephritis, page 34*		
Neutropenia: Child or Adult (absolute PMN count <500 per mm³) in cancer and transplant patients. Guideline: *CID 52:427, 2011 (inpatients); J CLin Oncol 31:794, 2013 (outpatients)*				
Prophylaxis *(J Clin Oncol 31:794, 2013)*				
Post-chemotherapy—impending neutropenia	Pneumocystis (PCP), Viridans strep	In patients expected to have PMN · t00 lor · 7 days consider Levo *500-750* mg po q24h. Acute leukemics undergoing intensive induction consider addition of Fluc 400 mg q24h. In patients with AML or MDS who have prolonged neutropenia, consider Posa instead at 200 mg TID *(N Engl J Med 356:348, 2007)*.		
Post allogeneic stem cell transplant	Aerobic Gm-neg bacilli, ↑ risk pneumocystis, herpes viruses, candida aspergillus	**TMP-SMX** (vs. PCP) + **Acyclovir** (vs. HSV/VZV)+ **pre-emptive** monitoring for **CMV** + **Posa** (vs. mold)		In autologous HCT, not active prophylaxis nor CMV screening is recommended. Fluc OK with TMP-SMX and acyclovir.

[26] **P Ceph 3** (**cefotaxime** 2 gm IV q8h, use q4h if life-threatening; **ceftizoxime** 2 gm IV q4h; **ceftriaxone** 2 gm IV q12h), **PIP-TZ** 3.375 gm IV q4h or 4-hr infusion of 3.375 gm q8h, **Aminoglycosides** *(see Table 10D, page 118)*, **AMP** 200 mg/kg/day divided q6h, **clinda** *900* mg IV q8h, **IMP** *0.5* gm IV q6h, **MER** 1 gm IV q8h, **ERTA** 1 gm IV q24h, **DORI** 500 mg IV q8h (1-hr infusion), **Nafcillin** or **oxacillin** 2 gm IV q4h, **aztreonam** 2 gm IV q8h, **metro** 1 gm loading dose then 0.5 gm q6h or 1 gm IV q12h, **vanco** loading dose 25-*30* mg/kg IV, then 15-*20* mg/kg IV q8-12h (dose in obese pt, *see Table 17C, page 229*), **ceftazidime** 2 gm IV q8h, [**Cefepime** 2 gm IV q12h (q8h if neutropenic), **cefpirome**[NUS] 2 gm IV q12h], **CIP** 400 mg IV q12h, **levo** 750 mg IV q24h, **linezolid** 600 mg IV q12h.

TABLE 1 (61)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
SYSTEMIC SYNDROMES (FEBRILE/NON-FEBRILE)/Neutropenia *(continued)*				
Empiric therapy—febrile neutropenia (≥38.3°C for > 1 hr or sustained >38°C and absolute neutrophil count <500 cells/μL) (IDSA Guidelines: *CID 52:427, 2012*). *(Outpatients: J CLin Oncol 31:794, 2013).*				
Low-risk adults Anticipate < 7 days neutropenia, no co-morb, can take po meds	Aerobic Gm-neg bacilli, Viridans strep	**CIP** 750 mg po bid + **AM-CL** 875 /125 mg po bid. Treat until absolute neutrophil count ≥ 1000 cells/μL	Treat as outpatients with 24/7 access to inpatient care if: no focal findings, no hypotension, no COPD, no fungal infection, no dehydration, age range 16-60 yrs; motivated and compliant pts & family. If pen allergy: can substitute clinda 300 mg po qid for AM-CL	
High-risk adults and children (Anticipate > 7 days profound neutropenia, active co-morbidities)	**Aerobic Gm-neg. bacilli; to include P. aeruginosa; cephalosporin-resistant viridans strep; MRSA**	**Empiric therapy: CFP**, **IMP**, **MERO**, **DORI**, or **PIP-TZ**. Consider addition of **Vanco** as below. *Dosages: Footnote[26] and Table 10B*	**Combination therapy:** If pt has severe sepsis/shock, consider add **Tobra** AND **Vanco** AND **Echinocandin**	Increasing resistance of viridans streptococci to penicillins, cephalosporins & FQs *(CID 34:1469 & 1524, 2002).* **What if severe IgE-mediated β-lactam allergy?** Aztreonam plus Tobra. Work-up should include blood, urine, CXR with additional testing based on symptoms. Low threshold for CT scan. If cultures remain neg, but pt afebrile, treat until absolute neutrophil count ≥ *500* cells/μL.
		Include empiric vanco if: Suspected CLABSI, severe mucositis, SSTI, PNA, or hypotension		
Persistent fever and neutropenia after 5 days of empiric antibacterial therapy—*see CID 52:427, 2011.*				
	Candida species, aspergillus, VRE, resistant GNB	Add either (**caspofungin** 70 mg IV day 1, then 50 mg IV q24h or **Micafungin** 100 mg IV q24h or **Anidulafungin** 200 mg IV x 1 dose, then 100 mg IV q24h) **OR voriconazole** 6 mg per kg IV q12h times 2 doses, then 4 mg per kg IV q12h		Conventional **ampho B** causes more fever & nephrotoxicity & lower efficacy than lipid-based ampho B; both **caspofungin** & **voriconazole** better tolerated & perhaps more efficacious than lipid-based ampho B *(NEJM 346:225, 2002 & 351:1391 & 1445, 2005).*
Shock syndromes				
Septic shock: Fever & hypotension Bacteremic shock, endotoxin shock *Goals:* *1. Effective antibiotics* *2. Fluid resuscitation* *3. Vasoactive drugs, if needed* *4. Source control* *Refs: Chest 145:1407, 2014; NEJM 369:840, 2013; CCM 188:77, 2013*	Bacteremia with aerobic Gm-neg. bacteria or Gm + cocci	Lower mortality with **sepsis treatment "bundle"** *(AJRCCM 188:77, 2013)* • Blood cultures & serum lactate • Initiate effective antibiotic therapy: o No clear source & MDR GNB are rare: **PIP-TZ** + **Vanco** o No clear source but high prevalence of MDR GNB: [**Polymyxin B** (preferred) or **Colistin** + (**MER** or **IMP**)] • IV crystalloid: 20-40 mL/kg for hypotension or elevated lactate; prefer lactated Ringers *(AnIM 161:347 & 372, 2014)* • If hypolensive after fluids, nor-epinephrine • Attempt to identify & correct source of bacteremia • Monitor lactate, CVP (target ≥ 8 cm H_2O) & central venous O_2 sat (target ≥ 70%) • Low tidal volume (6 mL/kg) mechanical ventilation *(NEJM 369:2126, 2013)* • Transfuse if hematocrit < 30% *(NEJM 371:1381, 2014)* • *See Comment* for continuation		• Hydrocortisone in stress dose: 100 mg IV q8h if BP still low after fluids and one vasopressor *(ARJCCM 185:135, 2012).* Benefit in pts with severe shock *(CCM 42:333, 2014).* • Insulin Rx: Current target is glucose level of 140-180 mg/dL. Attempts at tight control (80-110 mg/dL) resulted in excessive hypoglycemia *(NEJM 363:2540, 2010).* • Impact of early effective antibiotic therapy *(CCM 38:1045 & 1211, 2010)* • Bacteremia due to carbapenemase-producing K. pneumoniae: lowest mortality with combination rx: carbapenem + Polymyxin B (preferred over Colistin) *(AAC 58:2322, 2014).* • Number of pts needed to treat with appropriate antimicrobial rx to prevent one pt death reported as 4 *(CCM 42:2342 & 2444, 2014).* • Shock associated with leaky capillaries which results in increased volume of drug distribution. Hence, need loading dose of antibiotics and, early in treatment, larger maintenance dose *(AAC 59:2995, 2015).*
Septic shock: post-splenectomy or functional asplenia Asplenic pt care: *NEJM 371:349, 2014*	S. pneumoniae, N. meningitidis, H. influenzae, Capnocytophaga (DF-2)	No dog bite: **Ceftriaxone** 2 gm IV q24h (↑ to 2 gm q12h if meningitis)	No dog bite: (**Levo** 750 mg or **Moxi** 400 mg) once IV q24h	Howell-Jolly bodies in peripheral blood smear confirm absence of functional spleen. Often results in **symmetrical peripheral gangrene of digits** due to severe DIC. For prophylaxis, see Table 15A, page 199. Vaccines: *CID 58:309, 2014.*
		Post-dog bite: (**PIP-TZ** 3.375 gm IV q6h OR **MER** 1 gm IV q8h) + **Clinda** 900 mg IV q8h		

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (62)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SYSTEMIC SYNDROMES (FEBRILE/NON-FEBRILE)/Shock syndromes *(continued)*				
Toxic shock syndrome, Clostridium sordellii				
Clinical picture: shock, capillary leak, hemoconcentration, leukemoid reaction, afebrile Ref: CID 43:1436 & 1447, 2006.	Clostridium sordellii–hemorrhagic & lethal toxins	Ffuids, aq. **penicillin G** 18–20 million units per day div. q4–6h + **clindamycin** 900 mg IV q8h. **Surgical debridement is key.**	Occurs in variety of settings that produce anaerobic tissue, e.g., illicit drug use, post-partum. Several deaths reported after use of abortifacient regimen of mifepristone (RU486) & misoprostol. *(NEJM 363:2540, 2010).* 2001-2006 standard medical abortion: po mifepristone & then vaginal misoprostof. Since 2006, switch to buccal, instead of vaginal misoprostof, pfus prophylactic Doxy resulted in dramatic decrease in TSS *(NEJM 361:145, 2009).* Mortality nearly 100% if WBC >50,000/μL.	
Toxic shock syndrome, staphylococcal. Review: *LnID 9:281, 1009*				
Colonization by toxin-producing Staph. aureus of: vagina (tampon-assoc.), surgical/traumatic wounds, endometrium, burns	Staph. aureus (toxic shock toxin-mediated)	(**Nafcillin** or **oxacillin** 2 gm IV q4h) or (if MRSA, **vanco** 15-20 mg/kg q8-12h) + **Clinda** 600-900 mg IV q8h + **IVIG** (Dose in Comment)	(**Cefazolin** 1–2 gm IV q8h) or (if MRSA, **vanco** 15-20 mg/kg q8-12h OR **dapto** 6 mg/kg IV q24h) **Clinda** 600-900 mg IV q8h+ **IVIG** (Dose in Comment)	**IVIG reasonable** *(see Streptococcal TSS)* — dose 1 gm per kg on day 1, then 0.5 gm per kg days 2 & 3 — antitoxin antibodies present. If suspect TSS, "turn off" toxin production with clinda; report of success with **linezolid** *(JID 195:202, 2007). Exposure of MRSA to nafcillin increased toxin production in vitro: JID 195:202, 2007.*
Toxic shock syndrome, streptococcal. NOTE: For Necrotizing fasciitis without toxic shock, *see page 56.* Ref: *LnID 9:281, 2009.*				
Associated with **invasive disease**, i.e., erysipelas, necrotizing fasciitis; secondary strep infection of varicella. Secondary household contact TSS cases reported *(NEJM 335:547 & 590, 1996; CID 27:150, 1998).*	Group A, B, C, & G Strep. pyogenes, Group B strep ref: *EID 15:223, 2009.*	(**Pen G** 24 million units per day IV in div. doses) + (**clinda** 900 mg IV q8h)	**Ceftriaxone** 2 gm IV q24h + **clinda** 900 mg IV q8h	**Definition:** Isolation of Group A strep, hypotension and ≥2 of: renal impairment, coagulopathy, liver involvement, ARDS, generalized rash, soft tissue necrosis. Associated with invasive disease. **Surgery usually required.** Mortality with fasciitis 30–50%, myositis 80% even with early rx *(CID 14:2, 1992).* Clinda ↓ toxin production. Use of NSAID may predispose to TSS. For reasons pen G may fail in fulminant S. pyogenes infections *(see JID 167:1401, 1993).*
		Prospective observational study *(CID 59:358, 366 & 851, 2014)* indicates: • Clinda decreases mortality • IVIG perhaps of benefit: 1 gm/kg on day 1, then 0.5 gm/kg days 2, 3 • High incidence of secondary cases in household contacts		
Toxin-Mediated Syndromes—no fever unless complicated				
Botulism *(CID 41:1167, 2005. As* **biologic weapon:** *JAMA 285:1059, 2001; www.bt.cdc.gov)*				
Food-borne Dyspnea at presentation bad sign *(CID 43:1247, 2006)*	Clostridium botulinum	For all types: Follow vital capacity; other supportive care If no ileus, purge GI tract	Heptavalent equine serum antitoxin—CDC *(see Comment)*	**Equine antitoxin:** Heptavalent currently only antitoxin available (U.S) for non-infant botulism: *CDC (+1 404-639-2206 M-F OR +1 404-639-2888 evenings/weekends).* For infants, *use Baby BIG (human botulism immune globulin): California Infant Botulism Treat & Prevent Program.*
Infant (Adult intestinal botulism is rare variant: EID 18:1, 2012).		Human botulinum immunoglobufin (BIG) IV, single dose. Call (+1) 510-540-2646. Do not use equine antitoxin.	**No antibiotics;** may lyse C. botulinum in gut and ↑ load of toxin	**Antimicrobials:** May make infant botulism worse. Untested in wound botulism. When used, pen G 10–20 million units per day usual dose. If complications (pneumonia, UTI) occur, avoid antimicrobials with assoc. neuromuscular blockade, i.e., aminoglycosides, tetracycline, polymyxins. **Differential dx:** Guillain-Barré, myasthenia gravis, tick paralysis, organophosphate toxicity, West Nile virus
Wound		Debridement & anaerobic cultures. No proven value of local antitoxin. Role of antibiotics untested.	Trivalent equine antitoxin *(see Comment)*	Wound botulism can result from spore contamination of tar heroin. *Ref: CID 31:1018, 2000.* Mouse bioassay failed to detect toxin in 1/3 of patients *(CID 48:1669, 2009).*

Abbreviations on page 2.

**NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (63)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
SYSTEMIC SYNDROMES/Toxin-Mediated Syndromes *(continued)*				
Tetanus: Trismus, generalized muscle rigidity, muscle spasm Ref: *AnIM 154:329, 2011.*	C. tetani–production of tetanospasmin toxin	**Six treatment steps:** 1–Urgent endotracheal intubation to protecl the airway. Laryngeal spasm is common. Early tracheostomy. 2–Eliminate reflex spasms with diazepam, 20 mg/kg/day IV or midazolam. Reports of benefit combining diazepam with magnesium sulfate *(Ln 368:1436, 2006)*. Worsl cases: need neuromuscular blockade with vecuronium. 3–Neutralize toxin: Human hyperimmune globulin IM; start tetanus immunization–no immunity from clinical tetanus. 4–Surgically debride infected source tissue. Start antibiotic: (**Pen G** 3 million units IV q4h or **Doxy** 100 mg IV q12h or **Metro** 1000 mg IV q12h) x 7-10 days. 5–Avoid light as may precipitate muscle spasms. 6–Use beta blockers, e.g., short acting esmolol, to control sympathetic hyperactivity.		
VASCULAR				
IV line Infection *(See IDSA Guidelines CID 49:1, 2009).*				
Heparin lock, midline catheter, **non-tunneled** central venous catheter (subclavian, internal jugular), peripherally inserted central catheter (PICC) *2008 study found ↑ infection risk/thrombosis if femoral vein used, esp. if BMI >28.4 (JAMA 299:2413, 2008).* *See Comment*	Staph. epidermidis, Staph. aureus (MSSA/MRSA). **Diagnosis:** Fever & either + blood cult from line & peripheral vein **OR** >15 colonies on tip of removed line **OR** culture from catheter positive 2 hrs earlier than peripheral vein culture.	**Vanco** 15-20 mg/kg q8-12h. **Other alternatives—see Comment.** Other rx and duration: **(1) If S. aureus,** remove catheter. Can use TEE result to determine if 2 or 4 wks of therapy *(JAC 57:1172, 2006)*. **(2) If S. epidermidis,** can try to "save" catheter. *80%* cure after 7–10 days of therapy. With only systemic antibiotics, high rate of recurrence *(CID 49:1187, 2009)*. If **leuconostoc** or **lactobacillus**, which are **Vanco** resistant, need **Pen G**, **Amp** or **Clinda**.	For documented MSSA **nafcillin** or **oxacillin** 2 gm IV q4h or **cefazolin** 2 gm IV q8h, if no response to, or intolerant of, **vanco**: switch to **daptomycin** 6 mg per kg IV q24h. Culture removed catheter. With "roll" method, >15 colonies *(NEJM 312:1142, 1985)* suggests infection. Lines do not require "routine" changing when not infected. When infected, do not insert new catheter over a wire. Antimicrobial-impregnated catheters may ↓ infection risk; the debate is lively *(CID 37:65, 2003 & 38:1287, 2004 & 39:1829, 2004)*. Are femoral lines more prone to infection than subclavian or internal jugular lines? Meta-analysis: no difference *(CCM 40:2479, 2012)*. In random trial, subclavian site had lowest risk of infection & thrombosis *(NEJM 373:1220, 2015)*.
Tunnel type indwelling venous catheters and ports (Broviac, Hickman, Groshong, Quinton), dual lumen hemodialysis catheters (Permacath). *For prevention, see below.*	Staph. epidermidis, Staph. aureus, (Candida sp.). Rarely: leuconostoc or lacto-bacillus—both resistant to vanco *(see Table 2, page 69) (Dx, see above)*			If subcutaneous tunnel infected, very low cure rates; need to remove catheter. Beware of silent infection in clotted hemodialysis catheters. Indium scans detect *(Am J Kid Dis 40:832, 2002)*.
Impaired host (burn, neutropenic)	As above + Pseudomonas sp., Enterobacteriaceae, Corynebacterium jeikeium, aspergillus, rhizopus	[**Vanco** + (**Cefepime** or **Ceftaz**) or (**Vanco** + **PIP-TZ**) or **IMP** or [(**Cefepime** or **Ceftaz**) + **Aminoglycoside**]. *(Dosage in footnotes**,¶, pages 46 and 63).*		Usually have associated septic thrombophlebitis: biopsy of vein to rule out fungi. If fungal, surgical excision + amphotericin B. Surgical drainage, ligation or removal often indicated.
Hyperalimentation	As with tunnel, Candida sp. common *(see Table 11, resistant Candida species)*	If candida, **voriconazole or an echinocandin** (**anidulafungin**, **micafungin**, **caspofungin**) if clinically stable. Dosage: *see Table 11B, page 134.*		Remove venous catheter and discontinue antimicrobial agents if possible. Ophthalmologic consultation recommended. **Rx all patients with + blood cultures.** *See Table 11A, Candidiasis, page 122*
Intravenous lipid emulsion	Staph. epidermidis	**Vanco** 1 gm IV q12h		Discontinue intralipid
	Malassezia furfur	**Fluconazole** 400 mg IV q24h		

 **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (64)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
VASCULAR/IV line infection *(continued)*				
Prevention of Infection of Long-Term IV Lines *CID 52:1087, 2011*	To minimize risk of infection: **Hand washing and** **1.** Maximal sterile barrier precautions during catheter insertion **2.** Use >0.5% chlorhexidine prep with alcohol for skin antisepsis **3.** If infection rate high despite #1 & 2, use either chlorhexidine/silver sulfadiazine or minocycline/rifampin-impregnated catheters or "lock" solutions *(see Comment)*. **4.** If possible, use subclavian vein, avoid femoral vessels. Lower infection risk in jugular vs. femoral vein if BMI >28.4 *(JAMA 299:2413, 2008)*.			**IV line "lock" solutions under study. No FDA-approved product.** Reports of the combination of TMP, EDTA & ethanol *(AAC 55:4430, 2011)*. Trials to begin in Europe. Another report: lock soln of sodium citrate, methylene blue, methylparabens *(CCM 39:613, 2011)*. Recent meeting abstracts support 70% ethanol.
Mycotic aneurysm	S. aureus (28-71%), S. epidermidis, Salmonella sp. (15-24%), M.TBc, S. pneumonia, many others	**Vanco** (dose sufficient to achieve trough level of 15-20 μg/mL) + (**ceftriaxone** or **PIP-TZ** or **CIP**)	**Dapto** could be substituted for Vanco. For GNB: **cefepime** or **carbapenems**. For MDR-GNB, **[Polymyxin B** (preferred) or **Colistin] + MER** **Treatment is combination of antibiotic + surgical resection with revascularization.**	No data for ceftaroline or telavancin. Best diagnostic imaging: CT angiogram. Blood cultures positive in 50-85%. **De-escalate to specific therapy when culture results known.** Treatment duration varies but usually 6 wks from date of definitive surgery.
Suppurative (Septic) Thrombophlebitis				
Cranial dural sinus: **Cavernous Sinus**	S. aureus (70%) Streptococcus sp. Anaerobes (rare) Mucormycosis (diabetes)	[**Vanco** (dose for trough conc of 15-20 mcg/mL) + **Ceftriaxone** 2 gm IV q12h], add **Metro** 500 mg IV q8h if dental/sinus source	(**Dapto** 8-12 mg/kg IV q24h OR **Linezolid** 600 mg IV q12h), add **Metro** 500 mg IV q8h if dental/sinus source	• Diagnosis: CT or MRI • Treatment: 1) obtain specimen for culture; 2) empiric antibiotics; 3) may need adjunctive surgery; 4) heparin until afebrile, then coumadin for several weeks
Lateral Sinus: Complication of otitis media/mastoiditis	Polymicrobial (often) Aerobes Anaerobes S. aureus P. aeruginosa B. fragilis Other GNB	**Cefepime** 2 gm IV q8h + **Metro** 500 mg IV q8h + **Vanco** (dose for trough conc of 15-20 mcg/mL)	**Meropenem** 1-2 gm IV q8h + **Linezolid** 600 mg IV q12h	• Diagnosis: CT or MRI • Treatment: 1) consider radical mastoidectomy; 2) obtain cultures; 3) antibiotics; 4) anticoagulation controversial • Prognosis: favorable
Superior Sagittal Sinus: Complication of bacterial meningitis or bacterial frontal sinusitis	S. pneumoniae N. meningitides H. influenzae (rare) S. aureus (very rare)	As for meningitis: **Ceftriaxone** 2 gm IV q12h + **Vanco** (dose for trough conc of 15-20 mcg/mL) + **dexamethasone**	As for meningitis: **Meropenem** 1-2 gm IV q8h + **Vanco** (dose for trough conc of 15-20 mcg/mL) + **dexamethasone**	• Diagnosis: MRI • Prognosis: bad; causes cortical vein thrombosis, hemorrhagic infarcts and brainstem herniation. • Anticoagulants not recommended

Abbreviations on page 2.

**NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 1 (65)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*		ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
		PRIMARY	ALTERNATIVE§	
VASCULAR/Suppurative (Septic) Thrombophlebitis *(continued)*				
Jugular Vein, Lemierre's Syndrome: Complication of pharyngitis, tonsillitis, dental infection, EBV. Ref: *NEJM 371:2018, 2015.*	Fusobacterium necrophorum (anaerobe) Less often: Other Fusobacterium S. pyogenes Bacteroides sp.	(**PIP-TZ** 3.375 gm IV q6h OR **Amp-Sulb** 3 gm IV q6h) x 4 weeks	[**Imipenem** 500 mg IV q6h OR (**Metro** 500 mg IV q8h + **Ceftriaxone** 2 gm IV once daily)] x 4 weeks. Another option: **Clinda** 600-900 mg IV q8h	• Diagnosis: Preceding pharyngitis and antibiotics therapy, persistent fever and pulmonary emboli • Imaging: Hi-res CT scan • Role of anticoagulants unclear
Pelvic Vein: Includes ovarian vein and deep pelvic vein phlebitis	Aerobic gram-neg bacilli Streptococcus sp. Anaerobes	Antibiotics + anticoagulation (heparin, then coumadin) *Low prevalence of MDR GNB:* **PIP-TZ** 3.375 gm IV q6h or 4.5 gm IV q8h OR (**Ceftriaxone** 2 gm IV once daily + **Metro** 500 mg IV q8h)	*High prevalence of MDR GNB:* **Meropenem** 1 gm IV q8h. If severe beta-lactam allergy: (**CIP** 400 mg IV q12h + **Metro** 500 mg IV q8h)	• Diagnosis: ovarian vein infection presents 1 week post-partum with fever & local pain; deep pelvic vein presents 3-5 days post-delivery with fever but no local pain. CT or MRI may help. • Treat until afebrile for 48 hrs & WBC normal • Coumadin for 6 weeks
Portal Vein (Pylephlebitis): Complication of diverticulitis, appendicitis and (rarely) other intra-abdominal infection	Aerobic gram-neg bacilli: E. coli, Klebsiella & Proteus most common Other: aerobic/anaerobic streptococci, B. fragilis, Clostridia	*Low prevalence of MDR GNB* (<20%): **PIP-TZ** 4.5 gm IV q8h OR (**CIP** 400 mg IV q12h + **Metro** 500 mg IV q8h)	*High prevalence of MDR GNB* (>20%): If ESBL producer: **Meropenem** 1 gm IV q8h. If carbapenemase producer: **[Polymyxin B** (preferred) or **Colistin] + MER**	• Diagnosis: Pain, fever, neutrophilia in pt with intra-abdominal infection. Abdominal CT scan • Pyogenic liver abscess is a complication • No anticoagulants unless hypercoagulable disease (neoplasm) • Surgery on vein not indicated

Abbreviations on page 2. **NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. § Alternatives consider allergy, PK, compliance, local resistance, cost*

TABLE 2 – RECOMMENDED ANTIMICROBIAL AGENTS AGAINST SELECTED BACTERIA

BACTERIAL SPECIES	ANTIMICROBIAL AGENT *(See page 2 for abbreviations)*		
	RECOMMENDED	ALTERNATIVE	ALSO EFFECTIVE[1] (COMMENTS)
Achromobacter xylosoxidans spp xylosoxidans (formerly Alcaligenes)	IMP, MER, DORI (no DORI for pneumonia)	TMP-SMX. Some strains susc. to ceftaz, PIP-TZ	Resistant to aminoglycosides, most cephalosporins & FQs.
Acinetobacter calcoaceticus—baumannii complex	If suscept: IMP or MER or DORI. For MDR strains: (Polymyxin B + Colistin) + (IMP or MER)	AM-SB used for activity of sulbactam *(CID 51:79, 2010).* Perhaps Minocycline IV	Resistant to aminoglycosides, FQs. Minocycline, effective against many strains *(CID 51:79, 2010) (See Table 5A, pg 81)*
Actinomyces israelii	AMP or Pen G	Doxy, ceftriaxone	Clindamycin, erythro
Aeromonas hydrophila & other sp.	CIP or Levo	TMP-SMX or (P Ceph 3, 4)	See *AAC 56:1110, 2012.*
Arcanobacterium (C.) haemolyticum	Erythro; azithro	Benzathine Pen G, Clinda	Sensitive to most drugs, resistant to TMP-SMX *(AAC 38:142, 1994)*
Bacillus anthracis (anthrax): inhalation	See *Table 1, page 40*		
Bacillus cereus, B. subtilis	Vancomycin, clinda	FQ, IMP	
Bacteroides sp., B. fragilis & others	Metronidazole or PIP-TZ	DORI, ERTA, IMP, MER, AM-CL	Increasing resistance to: clinda, cefoxitin, cefotetan, moxi. Ref: *CID 59:698, 2014.*
Bartonella henselae, quintana See *Table 1, pages 30, 45, 51, 57*	Varies with disease entity & immune status. Active: Azithro, clarithro, erythro, doxy & in combination: RIF, gent, ceftriaxone. Not active: CIP, TMP-SMX, Pen, most cephalosporins, aztreonam		
Bordetella pertussis	Azithro or clarithro	TMP-SMX	*See PIDJ 31:78, 2012.*
Borrelia burgdorferi, B. afzelii, B. garinii (Lyme & relapsing fever)	*See specific disease entity*		
Brucella sp.	Drugs & duration vary with localization or non-localization. *See specific disease entities. PLoS One 7:e32090, 2012.*		
Burkholderia (Pseudomonas) cepacia	TMP-SMX or MER or CIP	Minocycline or chloramphenicol	Multiple mechanisms of resistance. Need C/S to guide therapy *(Sem Resp Crit Care Med 36:99, 2015)*
Burkholderia (Pseudomonas) pseudomallei *Curr Opin Infect Dis 23:554. 2010; CID 41:1105, 2005*	Initially, IV ceftaz or IMP or MER, then po (TMP-SMX + Doxy x 3 mos) ± Chloro *(AAC 49:4010, 2005).*		(Thai, 12–80% strains resist to TMP-SMX). FQ active in vitro. MER also effective *(AAC 48: 1763, 2004)*
Campylobacter jejuni	Azithro	Erythro or CIP	TMP-SMX, Pen & cephalosporins not active.
Campylobacter fetus	Gentamicin	IMP or ceftriaxone	AMP, chloramphenicol
Capnocytophaga ochracea (DF-1)	Dog bite: Clinda or AM-CL	Septic shock, post-splenectomy: PIP-TZ, Clinda, IMP, DORI, MER	FQ activity variable; aminoglycosides, TMP-SMX & Polymyxins have limited activity. *LN ID 9:439, 2009.*
Capnocytophaga canimorsus (DF-2)	Dog bite: AM-CL		
Chlamydophila pneumoniae	Doxy	Erythro, FQ	Azithro, clarithro
Chlamydia trachomatis	Doxy or azithro	Erythro	
Citrobacter diversus (koseri), C. freundii	Life threatening illness: IMP, MER, DORI	Non-life threatening illness: CIP or Gent	Emergence of resistance: *AAC 52:995, 2007.*
Clostridium difficile	Mild illness: Metronidazole (po)	Moderate/severe illness: Vancomycin (po) or Fidaxomicin *(CID 51:1306, 2010).*	*See also Table 1, page 18 re severity of disease.*
Clostridium perfringens	Pen G ± clindamycin	Doxy	Erythro, chloramphenicol, cefazolin, cefoxitin, PIP-TZ, carbapenems
Clostridium tetani	Metronidazole	Doxy	Role of antibiotics unclear.
Corynebacterium. diphtheriae	Erythro + antitoxin	Pen G + antitoxin	RIF reported effective *(CID 27:845, 1998)*
Corynebacterium jeikeium	Vancomycin + aminoglycoside	Pen G + aminoglycoside	Many strains resistant to Pen *(EJCMID 25:349, 2006).*
Corynebacterium minutissimum	Clinda 1% lotion	Clarithro or Erythro	Causes erythrasma
Coxiella burnetii (Q fever) acute disease *(CID 52:1431, 2011).*	Doxy, FQ *(see Table 1, page 31)*	Erythro, Azithro, Clarithro	Endocarditis: doxy + hydroxychloroquine *(JID 188:1322, 2003; LnID 3:709, 2003; LnID 10:527, 2010).*
chronic disease, e.g., endocarditis	Doxy + hydroxy chloroquine	TMP-SMX, Chloro	

TABLE 2 (2)

BACTERIAL SPECIES	ANTIMICROBIAL AGENT *(See page 2 for abbreviations)*		
	RECOMMENDED	ALTERNATIVE	ALSO EFFECTIVE[1] (COMMENTS)
Ehrlichia chaffeensis, Ehrlichia ewubguum Anaplasma (Ehrlichia) phagocytophillium	Doxy	RIF *(CID 27:213, 1998)*, Levo *(AAC 47:413, 2003)*.	CIP, oflox, chloramphenicol also active in vitro. Resist to clinda, TMP-SMX, IMP, AMP, erythro, & azithro *(AAC 41:76, 1997)*.
Eikenella corrodens	AM-CL, IV Pen G	TMP-SMX, FO	Resistant to clinda, cephalexin, erythro, metro, diclox
Elizabethkingae meningosepticum (formerly Chryseobacterium)	Levo or TMP-SMX	CIP, Minocycline	Resistant to Pen, cephalosporins, carbapenems, aminoglycosides, vancomycin *(JCM 44:1181, 2006)*
Enterobacter species	Recommended agents vary with clinical setting and degree and mechanism of resistance.		
Enterococcus faecalis	Highly resistant. *See Table 5A, page 81*		
Enterococcus faecium	Highly resistant. *See Table 5A, page 81*		
Erysipelothrix rhusiopathiae	Penicillin G or amox	P Ceph 3, FO	IMP, PIP-TZ (vancomycin, APAG, TMP-SMX resistant)
Escherichia coli	Highly resistant. Treatment varies with degree & mechanism of resistance. *see TABLE 5B.*		
Francisella tularensis (tularemia) *See Table 1, page 42*	Gentamicin, tobramycin, or streptomycin	Mild infection: Doxy or CIP	Chloramphenicol, RIF. Doxy/chloro bacteriostatic → relapses *CID 53:e133, 2011.*
Gardnerella vaginalis (bacterial vaginosis)	Metronidazole or Tinidazole	Clindamycin	*See Table 1, pg 26 for dosage*
Helicobacter pylori	*See Table 1, pg 21*		Drugs effective in vitro often fail in vivo.
Haemophilus aphrophilus (Aggregatibacter aphrophilus)	[(Penicillin or AMP) + gentamicin] or [AM- SB ± gentamicin]	(Ceftriaxone + Gent) or CIP or Levo	Resistant to vancomycin, clindamycin, methicillin
Haemophilus ducreyi (chancroid)	Azithro or ceftriaxone	Erythro, CIP	Most strains resistant to tetracycline, amox, TMP-SMX
Haemophilus influenzae Meningitis, epiglottitis & other life-threatening illness	Cefotaxime, ceftriaxone	AMP if susceptible and ß-lactamase neg, FOs	Chloramphenicol (downgrade from 1st choice due to hematotoxicity).
non-life threatening illness	AM-CL, O Ceph 2/3		Azithro, clarithro, telithro
Klebsiella ozaenae/ rhinoscleromatis	CIP	Levo	*Acta Otolaryngol 131:440, 2010.*
Klebsiella species	Treatment varies with degree & mechanism of resistance, *see Table 5B.*		
Lactobacillus species	Pen G or AMP	Clindamycin	**May be resistant to vancomycin**
Legionella sp.	Levo or Moxi	Azithro	Telithro active in vitro.
Leptospira interrogans	Mild: Doxy or amox	Severe: Pen G or ceftriaxone	
Leuconostoc	Pen G or AMP	Clinda	**NOTE: Resistant to vancomycin**
Listeria monocytogenes	AMP + Gent for synergy	TMP-SMX	Erythro, penicillin G (high dose), APAG may be synergistic with β-lactams. Meropenem active in vitro. **Cephalosporin-resistant!**
Moraxella (Branhamella) catarrhalis	AM-CL or O Ceph 2/3, TMP-SMX	Azithro, clarithro, dirithromycin, telithro	Erythro, doxy, FOs
Mycoplasma pneumoniae	Doxy	Azithro, Minocycline	Clindamycin & ß lactams NOT effective. Increasing macrolide resistance *(JAC 68:506, 2013; AAC 58:1034, 2014).*
Neisseria gonorrhoeae (gonococcus)	Ceftriaxone,	Azithro (high dose)	FOs and oral cephalosporins no longer recommended: high levels of resistance.
Neisseria meningitidis (meningococcus)	Ceftriaxone	Chloro, MER	(Chloro less effective than other alternatives: *see JAC 70:979, 2015*)
Nocardia asteroides or **Nocardia brasiliensis**	TMP-SMX + IMP	Linezolid	Amikacin + (IMP or ceftriaxone or cefotaxime) *(AAC 58:795, 2014).*
Pasteurella multocida	Pen G, AMP, amox, cefuroxime, cefpodoxime	Doxy, Levo, Moxi, TMP-SMX	Resistant to cephalexin, oxacillin, clindamycin, erythro, vanco.
Plesiomonas shigelloides	CIP	TMP-SMX	AM-CL, Ceftriaxone & Chloro active. Resistant to: Amp, Tetra, aminoglycosides
Propionibacterium acnes (not acne)	Penicillin, Ceftriaxone	Vanco, Dapto, Linezolid	May be resistant to Metro.
Proteus sp, **Providencia sp**, Morganella sp. (Need in vitro susceptibility)	CIP, PIP-TZ; avoid cephalosporins	May need carbapenem if critically ill	Note: Proteus sp. & Providencia sp. have intrinsic resistance to Polymyxins.
Pseudomonas aeruginosa *(ID Clin No Amer 23:277, 2009).* Combination therapy? *See Clin Micro Rev 25:450, 2012.*	No in vitro resistance: PIP-TZ, AP Ceph 3, DORI, IMP, MER, tobramycin, CIP, aztreonam. For serious inf., use AP ß-lactam + (tobramycin or CIP)	For UTI, if no in vitro resistance, single drugs effective: PIP-TZ, AP Ceph 3, cefepime, IMP, MER, aminoglycoside, CIP, aztreonam	If resistant to all beta lactams, FOs, aminoglycosides: Colistin + MER or IMP. Do not use DORI for pneumonia.

TABLE 2 (3)

BACTERIAL SPECIES	ANTIMICROBIAL AGENT *(See page 2 for abbreviations)*		
	RECOMMENDED	ALTERNATIVE	ALSO EFFECTIVE[1] (COMMENTS)
Rhodococcus (C. equi)	Two drugs: Azithro, Levo or RIF	(Vanco or IMP) + (Azithro, Levo or RIF)	Vancomycin active in vitro; intracellular location may impair efficacy *(CID 34:1379, 2002)*. Avoid Pen, cephalosporins, clinda, tetra, TMP-SMX.
Rickettsia species (includes spotted fevers)	Doxy	Chloramphenicol (in pregnancy), azithro (age < 8 yrs)	See *specific infections* (*Table 1*).
Salmonella typhi *(CID 50:241, 2010; AAC 54:5201, 2010; BMC ID 51:37, 2005)*	If FQ & nalidixic acid susceptible: CIP	Ceftriaxone, cefixime, azithro, chloro	Concomitant steroids in severely ill. Watch for relapse (1-6%) & ileal perforation. FQ resistance reported with treatment failures *(AAC 52:1278, 2008)*. Chloro less effective than other alternatives: *see JAC 70:979, 2015).*
Serratia marcescens	If no in vitro resistance: PIP-TZ, CIP, LEVO, Gent	If in vitro resistance: Carbapenem	Avoid extended spectrum Ceph if possible *Table 5A.*
Shigella sp.	FQ or azithro	Ceftriaxone is alternative; TMP-SMX depends on susceptibility.	
Staph. aureus, methicillin-susceptible	Oxacillin/nafcillin	P Ceph 1, vanco, teicoplanin[NUS], clinda ceftaroline	ERTA, IMP, MER, BL/BLI, FQ, PIP-TZ, linezolid, dapto, telavancin.
Staph. aureus, methicillin-resistant (health-care associated) *IDSA Guidelines: CID 52 (Feb 1):1, 2011.*	Vancomycin	Teicoplanin[NUS], TMP-SMX (some strains resistant), linezolid, daptomycin, telavancin, ceftaroline	Fusidic acid[NUS]. >60% CIP-resistant in U.S. (Fosfomycin + RIF). Partially vancomycin-resistant strains (GISA, VISA) & highly resistant strains now described—*see Table 6, pg 82.*
Staph. aureus, methicillin-resistant [community- associated (CA-MRSA)]			CA-MRSA usually not multiply-resistant. Qft resist. to erythro & variably to FQ. Vanco, teico[NUS], telavancin, daptomycin, ceftaroline can be used in pts requiring hospitalization *(see Table 6, pg 82)*. Also, ceftaroline.
Mild-moderate infection	(TMP-SMX or doxy or mino)	Clinda (if D-test neg—*see Table 5A & 6).*	
Severe infection	Vanco or teico[NUS]	Linezolid or daptomycin	
Staph. epidermidis	Vancomycin ± RIF	RIF + (TMP-SMX or FQ), daptomycin *(AAC 51:3420, 2007)*	Cephalothin or nafcillin/oxacillin if sensitive to nafcillin/oxacillin but 75% are resistant. FQs. *(See Table 5A).*
Staph. haemolyticus	TMP-SMX, FQ, nitrofurantoin	Oral cephalosporin	Recommendations apply to UTI only.
Staph. lugdunensis	Oxacillin/nafcillin or penicillin G (if β-lactamase neg.)	P Ceph 1 or vancomycin or teico[NUS]	Approx. 75% are penicillin-susceptible.
Staph. saprophyticus (UTI)	Oral cephalosporin or AM-CL	FQ	Almost always methicillin-susceptible
Stenotrophomonas (Xanthomonas, Pseudo-monas) maltophilia	TMP-SMX	FQ (AAC 58:176, 2014) if suscept in vitro	*JAC 62:889, 2008*
Streptobacillus moniliformis	Penicillin G	Doxy	Maybe erythro, clinda, ceftriaxone
Streptococcus, anaerobic (Peptostreptococcus)	Penicillin G	Clindamycin	Doxy, vancomycin, linezolid, ERTA *(AAC 51:2205, 2007).*
Streptococcus anginosus group	Penicillin	Vanco or Ceftriaxone	Avoid FQs; macrolide resistance emerging
Streptococcus pneumoniae penicillin-susceptible	Penicillin G, Amox	Multiple agents effective, e.g., Ceph 2/3, Clinda	If meningitis, higher dose, see *Table 1, page 9.*
penicillin-resistant (MIC ≥2.0)	Vancomycin, Levo, ceftriaxone, Amox (HD), Linezolid		
Streptococcus pyogenes, (Grp A). **Streptococcus sp** (Grp B, C, G). Erysipelas, bacteremia, TSS	Penicillin G + Clinda	Pen (alone) or Clinda (alone- low incidence of resistance)	*JCM 49:439, 2011.* Pockets of macrolide resistance. Do not use: FQs, TMP-SMX or tetracyclines
Tropheryma whipplei	Doxy + Hydroxychloroquine	None	Clinical failures with TMP-SMX
Vibrio cholerae	Doxy, FQ	Azithro, erythro	Maybe CIP or Levo; some resistance.
Vibrio parahaemolyticus	Doxy	Azithro, CIP	If bacteremic, treat as for V. vulnificus
Vibrio vulnificus, alginolyticus, damsela	Doxy + ceftriaxone	Levo	*CID 52:788, 2011*
Yersinia enterocolitica	CIP or ceftriaxone	TMP-SMX; CIP (if bacteremic)	CIP resistance *(JAC 53:1068, 2004)*, also resistant to Pen, AMP, erythro.
Yersinia pestis (plague)	Streptomycin or Gent	Doxy or CIP	Levo, Moxi

[1] Agents are more variable in effectiveness than "Recommended" or "Alternative". Selection of "Alternative" or "Also Effective" based on in vitro susceptibility testing, pharmacokinetics, host factors such as auditory, renal, hepatic function, & cost.

TABLE 3 – SUGGESTED DURATION OF ANTIBIOTIC THERAPY IN IMMUNOCOMPETENT PATIENTS[1,2]

CLINICAL SITUATION		DURATION OF THERAPY (Days)
SITE	**CLINICAL DIAGNOSIS**	
Bacteremia	Bacteremia with removable focus (no endocarditis)	10–14 *(See Table 1)*
Bone	Osteomyelitis, adult; acute	*42 (Ln 385:875, 2015)*
	adult; chronic	Until ESR normal (often > 3 months)
	child; acute; staph. and enterobacteriaceae[3]	21
	child; acute; strep, meningococci, haemophilus[3]	14
Ear	Otitis media with effusion	<2 yrs: 10; ≥2 yrs: 5–7
Endo-cardium	Infective endocarditis, native valve	
	Viridans strep	14 or 28 *(See Table 1, page 28)*
	Enterococci	28 or 42 *(See Table 1, page 29)*
	Staph. aureus	14 (R-sided only) or 28 *(See Table 1, page 29)*
GI *Also see Table 1*	Bacillary dysentery (shigellosis)/traveler's diarrhea	3
	Typhoid fever (S. typhi): Azithro	7 (children/adolescents)
	Ceftriaxone	7-14 [Short course * effective *(AAC 44:450, 2000)*]
	FQ	5–7
	Chloramphenicol	14
	Helicobacter pylori	10–14. For triple-drug regimens, 7 days.
	Pseudomembranous enterocolitis (C. difficile)	10
Genital	Non-gonococcal urethritis or mucopurulent cervicitis	7 days doxy or single dose azithro
	Pelvic inflammatory disease	14
Heart	Pericarditis (purulent)	28
Joint	Septic arthritis (non-gonococcal) Adult	14–28
	Infant/child	Rx as osteomyelitis above.
		10-14 days of therapy sufficient *(CID 48:1201, 2009)*, but not complete agreement on this *(CID 48:1211, 2009)*.
	Gonococcal arthritis/disseminated GC infection	7 *(See Table 1, page 23)*
Kidney	Cystitis (bladder bacteriuria)	3 (Single dose extended-release cipro also effective) *(AAC 49:4137, 2005)*
	Pyelonephritis *(Ln 380:484, 2012)*	7 (7 days if CIP used; 5 days if levo 750 mg)
Lung *(Curr Op ID 28:177, 2015)*	Pneumonia, pneumococcal	Until afebrile 3–5 days (minimum 5 days).
	Community-acquired pneumonia	Minimum 5 days and afebrile for 2-3 days *(Pediatr. PIDJ 33:136, 2014).*
	Pneumonia, enterobacteriaceae or pseudomonal	21, often up to 42
	Pneumonia, staphylococcal	21–28
	Pneumocystis pneumonia (PCP) in AIDS;	21
	other immunocompromised	14
	Legionella, mycoplasma, chlamydia	7–14
	Lung abscess	Usually 28–42[4]
Meninges[5]	N. meningitidis	7
	H. influenzae	–
	S. pneumoniae	10–14
	Listeria meningoencephalitis, gp B strep, coliforms	21 (longer in immunocompromised)
Multiple systems	Brucellosis *(See Table 1, page 61)*	42 (add SM or gent for 1st 7–14 days) *(PLoS One 7:e32090, 2012)*
	Tularemia *(See Table 1, pages 44, 60)*	7–14 *(MMWR 58:744, 2009)*
Muscle	Gas gangrene (clostridial)	10
Pharynx	Group A strep pharyngitis	10 PO Ceph 2/3, azithro, one effective at 5 days
	Also see Pharyngitis, *Table 1, page 48*	*(CID 55:1279, 2012)*
	Diphtheria (membranous)	7–14
	Carrier	7
Prostate	Chronic prostatitis (TMP-SMX)	30–90
	(FQ)	28–42
Sinuses	Acute sinusitis	5–14[6]
Skin	Cellulitis	Until 3 days after acute inflamm disappears
Systemic	Lyme disease	*See Table 1, page 58*
	Rocky Mountain spotted fever *(See Table 1, page 60)*	Until afebrile 2 days

[1] Early change from IV to po regimens (about 72 hrs) is cost-effective with many infections, i.e., intra-abdominal. There is emerging evidence that dc of antibiotic rx concomitant with normalization of serum procalcitonin level shortens treatment duration for pneumonia and peritonitis *(JAMA 309:717, 2013)*.

[2] The recommended duration is a minimum or average time and should not be construed as absolute.

[3] These times are with proviso: sx & signs resolve within 7 days and ESR is normalized.

[4] After patient afebrile 4-5 days, change to oral therapy.

[5] In children relapses seldom occur until 3 days or more after termination of rx. For meningitis in children, see *Table 1, page 8*.

[6] Duration of therapy dependent upon agent used and severity of infection. Longer duration (10-14 days) optimal for beta-lactams and patients with severe disease. For sinusitis of mild-moderate severity shorter courses of therapy (5-7 days) effective with "respiratory FQs" (including gemifloxacin, levofloxacin 750 mg), azithromycin. Courses as short as 3 days reported effective for TMP-SMX and azithro and one study reports effectiveness of single dose extended-release azithro. Authors feel such "super-short" courses should be restricted to patients with mild-mod disease *(Otolaryngol-Head Neck Surg 134:10, 2006)*.

TABLE 4A – ANTIBACTERIAL ACTIVITY SPECTRA

The data provided are intended to serve as a general guide to antibacterial usefulness based on Ireatmenl guidelines and recommendations, in vitro activity, predominant patterns of susceptibility or resistance and/or demonstrated clinical effectiveness. Variability in resistance patlerns due to regional differences or as a consequent of clinical setting (e.g., community-onset vs. ICU-acquired infection) should be taken into account when using this table because activities of certain agents can differ significantly from what is shown in the table, which are by necessity based on aggregate information. We have revised and expanded the color / symbol key to provide a more descriptive categorization of the table data.

++ = **Recommended:** Agent is a first line therapy: reliably active in vitro, clinically effective, guideline recommended, recommended as a first-line agent or acceptable alternative agent in the Sanford Guide

\+ = **Active**: Agent is a potential alternative agent (active in vitro, possesses class activity comparable to known effective agents or a therapeutically interchangeable agents and hence likely to be clinically effective, but second line due to overly broad spectrum, toxicity, limited clinical experience, or paucity of direct evidence of effectiveness)

± = **Variable**: Variable activity such that the agent, although clinically effective in some settings or types of infections is not reliably effective in others, or should be used in combination with another agent, and/or its efficacy is limited by resistance which has been associated with treatment failure

0 = **Not recommended**: Agent is a poor alternative to other agents because resistance to likely to be present or occur, due to poor drug penetration to site of infection or an unfavorable toxicity profile, or limited or anecdotal clinical data to support effectiveness

? = **Insufficient Data** to recommend use

NA = **No activity**: Agent has no activity against this pathogen

	Penicillins												Carbapenems					Fluoroquinolone						Parenteral Cephalosporins											
	Penicillin G	Penicillin VK	Nafcillin	Oxacillin	Cloxacillin	Flucloxacillin	Dicloxacillin	Ampicillin	Amoxicillin	Amox-Clav	Amp-Sulb	Pip-Tazo	Doripenem	Ertapenem	Imipenem	Meropenem	Aztreonam	Ciprofloxacin	Ofloxacin	Levofloxacin	Moxifloxacin	Gemifloxacin	Gatifloxacin	Cefazolin	Cefotetan	Cefoxitin	Cefuroxime	Cefotaxime	Ceftizoxime	Ceftriaxone	Ceftazidime	Cefepime	Ceftaz-Avibac	Ceftaroline	Ceftol-Tazo
Aerobic gram-pos cocci																																		
E. faecalis	++	0	0	0	0	0	0	++	++	+	+	+	±	±	±	±	0	±	±	+	+	+	+	0	0	0	0	0	0	±	0	0	0	0	0
E. faecium	±	0	0	0	0	0	0	±	±	±	±	±	0	0	0	0	0	0	0	0	±	±	±	0	0	0	0	0	0	0	0	0	0	0	0
VRE faecalis	±	0	0	0	0	0	0	±	±	±	±	±	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
VRE faecium	±	0	0	0	0	0	0	±	±	±	±	±	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
S. aureus MSSA	±	±	++	++	++	++	++	±	±	+	+	+	+	+	+	+	0	+	+	+	+	+	+	++	+	+	+	+	+	+	±	+	±	+	?
S. aureus HA-MRSA	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	0
S. aureus CA-MRSA	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	±	±	±	±	±	±	0	0	0	0	0	0	0	0	0	0	+	0
Staph coag-neg (S)	±	±	++	++	++	++	++	±	±	+	+	+	+	+	+	+	0	+	+	+	+	+	+	++	+	+	+	+	+	+	±	+	±	+	?
Staph coag-neg (R)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	±	±	0	0	0	0	0	0	0	0	0	0	0	0	+	0
S. lugdunensis	±	±	++	++	++	++	++	±	±	+	+	+	+	+	+	+	0	+	+	+	+	+	+	++	+	+	+	+	+	+	±	+	±	+	?
S. saprophyticus	±	±	+	+	+	+	+	±	±	++	+	+	+	+	+	+	0	+	+	+	+	+	+	++	+	+	+	+	+	+	±	+	±	+	?
Strep. anginosus gp	++	++	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	±	±	±	±	±	±	+	+	+	+	+	+	+	+	+	+	+	+
Strep. gp A,B,C,F,G	++	++	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	±	±	±	±	±	±	+	+	+	+	+	+	+	+	+	+	+	+
Strep. pneumoniae	++	++	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	±	±	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Viridans Strep.	±	±	±	±	±	±	±	±	±	±	±	±	+	+	+	+	0	0	0	+	+	+	+	+	+	+	+	++	+	++	±	+	±	+	+
Aerobic gram-pos bacilli																																		
Arcanobacter. sp	+	+	?	?	?	?	?	+	+	+	+	+	+	+	+	+	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	?
C. diphtheriae	++	++	0	0	0	0	0	+	+	+	+	+	?	?	?	?	0	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
C. jeikeium	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	±	±	0	0	0	0	0	0	0	0	0	0	0	0	0
L. monocytogenes	+	0	0	0	0	0	0	++	+	+	+	+	?	?	?	+	0	0	0	+	+	+	+	0	0	0	0	0	0	0	0	0	0	0	0
Nocardia sp.	0	0	0	0	0	0	0	0	0	±	?	?	?	0	++	+	0	0	0	0	0	0	0	0	0	0	0	±	0	±	0	0	0	0	0

TABLE 4A (2)

	Penicillins												Carbapenems					Fluoroquinolone						Parenteral Cephalosporins											
	Penicillin G	Penicillin VK	Nafcillin	Oxacillin	Cloxacillin	Flucloxacillin	Dicloxacillin	Ampicillin	Amoxicillin	Amox-Clav	Amp-Sulb	Pip-Tazo	Doripenem	Ertapenem	Imipenem	Meropenem	Aztreonam	Ciprofloxacin	Ofloxacin	Levofloxacin	Moxifloxacin	Gemifloxacin	Gatifloxacin	Cefazolin	Cefotetan	Cefoxitin	Cefuroxime	Cefotaxime	Ceftizoxime	Ceftriaxone	Ceftazidime	Cefepime	Ceftaz-Avibac	Ceftaroline	Ceftol-Tazo
Aerobic gram-neg bacilli - Enterobacteriaceae																																		
Aeromonas sp.	0	0	0	0	0	0	0	0	0	±	±	+	+	+	+	+	+	+	+	+	+	+	+	0	0	0	?	+	+	+	+	+	+	?	?
C. jejuni	0	0	0	0	0	0	0	0	0	+	0	0	+	+	+	+	?	+	+	+	+	+	+	0	0	0	0	+	+	+	+	+	+	?	?
Citrobacter sp.	0	0	0	0	0	0	0	0	0	0	0	++	+	+	++	++	±	+	+	+	+	+	+	0	0	0	0	±	±	±	±	++	+	+	+
Enterobacter sp.	0	0	0	0	0	0	0	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	+	0	0	0	0	0	0	0	0	+	+	0	+
E. coli	0	0	0	0	0	0	0	±	±	+	+	+	+	+	+	+	0	±	±	±	±	±	±	0	±	±	0	0	0	0	0	0	0	0	+
E. coli, Klebs ESBL	0	0	0	0	0	0	0	0	0	0	0	±	+	+	++	++	0	±	±	±	±	±	±	0	±	±	0	0	0	0	0	0	+	0	+
E. coli, Klebs KPC	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	0	0
Klebsiella sp.	0	0	0	0	0	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Morganella sp.	0	0	0	0	0	0	0	0	0	0	0	+	+	+	+	+	+	+	+	+	?	?	?	0	+	+	0	+	+	+	+	++	+	+	+
P. mirabilis	0	0	0	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
P. vulgaris	0	0	0	0	0	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	+	+	+	+	+	+	+	+	+	?	+
Providencia sp.	0	0	0	0	0	0	0	0	0	0	0	+	++	++	++	++	+	+	+	+	+	?	?	0	+	+	0	+	+	+	+	+	+	?	+
Salmonella sp.	0	0	0	0	0	0	0	±	±	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	?	?	?	+	+	+	+	+	+	?	?
Serratia sp.	0	0	0	0	0	0	0	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	+	0	+	0	0	+	+	+	+	+	+	?	+
Shigella sp.	0	0	0	0	0	0	0	0	0	+	+	+	+	+	+	+	+	++	+	++	+	+	+	0	?	?	?	+	+	+	+	+	+	?	?
Y. enterocolitica	0	0	0	0	0	0	0	0	0	±	±	+	+	?	+	+	+	++	+	++	+	?	+	0	±	±	±	++	+	++	±	++	?	?	?
Aerobic gram-neg bacilli - Miscellaneous																																		
Bartonella sp.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B. pertussis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	?	?	?	?	?	?	0	0	0	0	0	0	0	0	0	0	0	0
B. burgdorferi	+	0	0	0	0	0	0	++	++	+	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	+	0	++	0	0	0	0	0
Brucella sp.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	?	?	?	?	?	0	0	0	0	0	0	0	0	0	0	0	0
Capnocytophagia	±	±	0	0	0	0	0	±	±	++	+	++	+	?	++	++	0	±	±	±	?	?	?	0	0	0	0	+	?	+	+	+	+	0	0
C. burnetii	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	+	+	+	+	+	0	0	0	0	0	0	0	0	0	0	0	0
Ehrlichia, Anaplas	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	?	?	?	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Eikenella sp	±	±	0	0	0	0	0	±	±	+	+	+	+	+	+	+	?	+	+	+	?	?	?	0	?	+	0	+	?	+	?	?	?	?	?
F. tularensis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	++	?	?	?	?	?	0	0	0	0	0	0	0	0	0	0	0	0
H. ducreyi	0	0	0	0	0	0	0	0	0	0	0	0	?	?	?	?	?	++	?	+	?	?	?	0	0	0	0	0	0	++	0	?	0	0	0
H. influenzae	0	0	0	0	0	0	0	±	±	++	++	+	+	+	+	+	+	+	+	++	++	+	+	0	+	+	+	++	+	++	+	+	+	+	+
Kingella sp.	+	+	0	0	0	0	0	+	+	+	+	+	+	+	+	+	?	+	+	++	?	?	?	+	+	+	+	+	+	++	+	+	+	+	+
K. granulomatis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	++	?	?	?	?	?	0	0	+	0	0	0	+	0	0	0	0	0
Legionella sp.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	++	++	++	++	+	+	0	0	0	0	0	0	0	0	0	0	0	0
Leptospira sp.	++	0	0	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	?	?	?	?	++	?	++	?	+	+	?	?
M. catarrhalis	0	0	0	0	0	0	0	0	0	++	+	+	+	+	+	+	+	+	+	+	+	+	+	0	+	±	+	+	+	+	+	+	+	+	+
N. gonorrhoeae	0	0	0	0	0	0	0	0	0	0	0	0	+	+	+	+	+	±	±	±	0	+	0	±	±	±	0	±	±	++	?	+	?	?	?

TABLE 4A (3)

	Penicillins												Carbapenems					Fluoroquinolone						Parenteral Cephalosporins											
	Penicillin G	Penicillin VK	Nafcillin	Oxacillin	Cloxacillin	Flucloxacillin	Dicloxacillin	Ampicillin	Amoxicillin	Amox-Clav	Amp-Sulb	Pip-Tazo	Doripenem	Ertapenem	Imipenem	Meropenem	Aztreonam	Ciprofloxacin	Ofloxacin	Levofloxacin	Moxifloxacin	Gemifloxacin	Gatifloxacin	Cefazolin	Cefotetan	Cefoxitin	Cefuroxime	Cefotaxime	Ceftizoxime	Ceftriaxone	Ceftazidime	Cefepime	Ceftaz-Avibac	Ceftaroline	Ceftol-Tazo
Aerobic gram-neg bacilli - Miscellaneous *(continued)*																																		
N. meningitidis	+	0	0	0	0	0	0	++	++	0	0	+	+	+	+	+	+	?	?	?	?	?	?	0	0	0	+	+	+	++	+	+	+	?	?
P. multocida	++	++	0	0	0	0	0	++	++	++	++	+	+	+	+	+	+	+	+	+	+	+	+	0	?	?	+	+	+	+	?	+	?	+	+
R. rickettsii	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	±	±	±	±	?	?	0	0	0	0	0	0	0	0	0	0	0	0
T. pallidum	++	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	0	0	0	0	0
U. urealyticum	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	+	+	+	?	?	0	0	0	0	0	0	0	0	0	0	0	0
V. cholera	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	?	?	?	?	?	0	0	0	0	0	0	0	0	0	0	0	0
V. parahemolyticus	0	0	0	0	0	0	0	0	0	0	0	0	?	?	?	?	?	+	+	+	?	?	?	0	0	0	0	+	+	+	+	+	+	?	?
V. vulnificus	0	0	0	0	0	0	0	0	0	0	0	0	?	?	?	?	?	+	+	+	?	?	?	0	0	0	0	+	+	+	+	+	+	?	?
Y. pestis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	?	?	?	?	?	0	0	0	0	0	0	0	0	0	0	0	0
Aerobic gram-neg bacilli - Selected non-fermentative GNB (NF-GNB)																																		
Acinetobacter sp.	0	0	0	0	0	0	0	0	0	0	±	±	+	0	++	++	0	+	+	+	+	?	?	0	0	0	0	0	0	±	±	±	?	?	±
B. cepacia	0	0	0	0	0	0	0	0	0	0	0	0	±	0	0	±	0	0	0	0	0	0	0	0	0	0	0	0	0	0	±	±	+	0	+
P. aeruginosa	0	0	0	0	0	0	0	0	0	0	0	+	+	0	+	+	+	+	0	+	0	0	0	0	0	0	0	0	0	0	+	+	+	0	+
S. maltophilia	0	0	0	0	0	0	0	0	0	0	0	±	0	0	0	0	0	0	0	±	±	?	?	0	0	0	0	0	0	0	±	0	±	0	0
Aerobic cell wall-deficient bacteria																																		
C. trachomatis	0	0	0	0	0	0	0	+	+	0	0	0	0	0	0	0	0	0	++	++	+	+	+	0	0	0	0	0	0	0	0	0	0	0	0
Chlamydophila sp.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	+	+	+	+	+	0	0	0	0	0	0	0	0	0	0	0	0
M. genitalium	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	±	++	?	+	0	0	0	0	0	0	0	0	0	0	0	0
M. pneumoniae	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	+	++	++	+	+	0	0	0	0	0	0	0	0	0	0	0	0
Anaerobic gram-negative bacteria																																		
B. fragilis	0	0	0	0	0	0	0	0	0	++	+	++	+	++	++	++	0	0	0	0	±	0	0	0	±	±	0	0	+	0	0	0	0	0	+
F. necrophorum	±	±	0	0	0	0	0	±	±	+	+	+	+	+	+	+	0	0	0	0	?	?	?	0	+	+	?	+	?	+	?	?	?	?	?
P. melaninogenica	±	±	0	0	0	0	0	±	±	+	+	+	+	+	+	+	0	0	0	±	+	?	?	0	+	+	?	?	?	?	?	?	?	?	+
Anaerobic gram-positive bacteria																																		
Actinomyces sp.	++	++	0	0	0	0	0	++	++	+	+	+	+	+	+	+	0	0	0	?	?	?	?	0	?	+	0	+	+	+	?	?	?	?	?
C. difficile	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Clostridium sp.	++	+	0	0	0	0	0	+	+	+	+	+	+	+	+	+	0	0	0	0	0	0	0	0	+	+	?	+	+	+	?	?	?	?	?
P. acnes	++	+	?	?	?	?	?	+	+	+	+	+	+	+	+	+	0	±	±	±	±	?	?	+	+	+	+	+	+	++	+	+	+	+	+
Peptostreptococci	++	++	0	0	0	0	0	++	++	+	+	+	+	+	+	+	0	0	0	+	+	?	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE 4A (4)

	Oral Cephalosporins										Aminoglyco					Macrolides				Tetracycline			Glyco/Lipo					Ox-lid		Other							
	Cefadroxil	Cephalexin	Cefaclor	Cefprozil	Cefurox-Axe	Cefixime	Ceftibuten	Cefpodoxime	Ceftriaxone	Cefditoren	Gentamicin	Tobramycin	Amikacin	Chloramphen	Clindamycin	Erythromycin	Azithromycin	Clarithromycin	Telithromycin	Doxycycline	Minocycline	Tigecycline	Daptomycin	Vancomycin	Telcoplanin	Telavancin	Oritavancin	Dalbavancin	Linezolid	Tedizolid	Fusidic Acid	Rif (comb)	TMP-SMX	Nitrofurantoin	Fosfomycin	Metronidazole	Quinu-Dalfo	Polymyxin B	Colistin
Aerobic gram-pos cocci																																						
E. faecalis	0	0	0	0	0	0	0	0	0	0	±	0	0	±	0	0	0	0	0	±	±	+	+	++	++	+	+	+	+	+	±	±	0	+	+	0	0	0	0
E. faecium	0	0	0	0	0	0	0	0	0	0	±	0	0	±	0	0	0	0	0	±	±	+	+	±	±	±	+	±	++	+	±	±	0	+	+	0	+	0	0
VRE faecalis	0	0	0	0	0	0	0	0	0	0	±	0	0	±	0	0	0	0	0	±	±	±	+	0	0	±	+	0	++	+	0	±	0	+	+	0	0	0	0
VRE faecium	0	0	0	0	0	0	0	0	0	0	±	0	NA	±	0	0	0	0	0	±	±	±	+	0	0	±	+	0	++	+	0	±	0	+	+	0	+	0	0
S. aureus MSSA	+	+	+	+	+	0	0	+	+	+	±	?	?	+	+	±	±	±	+	+	+	+	+	+	+	+	+	+	+	+	++	±	+	0	+	0	+	0	0
S. aureus HA-MRSA	0	0	0	0	0	0	0	0	0	0	±	?	?	+	±	0	0	0	±	+	+	+	++	++	++	+	+	+	++	+	++	±	+	0	+	0	+	0	0
S. aureus CA-MRSA	0	0	0	0	0	0	0	0	0	0	±	?	?	+	+	0	0	0	±	+	+	+	++	++	++	+	+	+	+	+	++	±	+	0	+	0	+	0	0
Staph coag-neg (S)	±	±	±	+	+	0	0	+	+	+	±	?	?	+	+	±	±	±	+	+	+	+	+	+	+	+	+	+	+	+	++	±	+	0	+	0	+	0	0
Staph coag-neg (R)	0	0	0	0	0	0	0	0	0	0	±	?	?	+	±	0	0	0	±	±	±	+	++	++	++	+	+	±	++	+	++	±	+	0	+	0	+	0	0
S. lugdunensis	+	+	+	+	+	?	?	+	+	+	±	?	?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	++	±	+	0	+	0	+	0	0
S. saprophyticus	++	++	++	+	+	?	?	+	+	+	0	0	0	+	+	±	±	±	?	+	+	+	+	+	+	+	?	?	0	0	+	0	+	+	±	0	0	0	0
Strep. anginosus gp	+	+	+	+	+	+	+	+	+	+	±	?	?	+	+	±	±	±	+	±	±	+	+	+	+	+	+	+	+	+	?	0	0	0	0	0	+	0	0
Strep. gp A,B,C,F,G	+	+	+	+	+	+	+	+	+	+	±	0	0	+	+	±	±	±	+	?	?	+	+	+	+	+	+	+	+	+	?	0	±	0	0	0	+	0	0
Strep. pneumoniae	+	+	+	+	+	+	+	+	+	+	0	0	0	+	+	±	±	±	+	±	±	+	±	+	+	+	?	?	+	+	?	0	±	0	0	0	+	0	0
Viridans Strep.	+	+	+	0	+	+	0	+	+	+	±	0	0	+	±	±	±	±	+	±	±	+	+	++	++	+	+	+	+	+	?	0	?	0	0	0	+	0	0
Aerobic gram-pos bacilli																																						
Arcanobacter. sp	+	+	+	+	+	+	+	+	+	?	?	?	?	?	++	++	++	++	+	++	+	+	+	++	+	+	?	?	+	?	0	0	0	0	0	0	+	0	0
C. diphtheriae	?	?	?	?	?	?	?	?	?	?	0	0	0	0	+	++	+	+	?	?	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
C. jeikeium	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	?	?	±	+	++	+	+	0	0	+	?	0	0	0	0	0	0	0	?	0
L. monocytogenes	0	0	0	0	0	0	0	0	0	0	±	?	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	?	0	0	+	0	0	0	0	0	0
Nocardia sp.	0	0	0	0	0	0	0	0	0	0	0	0	++	0	0	0	?	?	?	?	±	?	0	0	0	0	0	0	+	?	0	0	++	0	0	0	0	0	0
Aerobic gram-neg bacilli - Enterobacteriaceae																																						
Aeromonas sp.	?	0	?	?	?	?	?	?	?	?	+	+	+	+	0	0	0	0	0	+	+	+	0	0	0	0	0	0	0	0	0	0	+	0	0	0	0	+	+
C. jejuni	0	0	0	0	0	0	0	0	0	0	+	+	+	?	?	++	++	+	0	±	±	?	0	0	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0
Citrobacter sp.	0	0	0	0	0	+	+	+	+	?	+	+	+	?	0	0	0	0	0	0	0	+	0	0	0	0	0	0	0	0	0	0	±	±	±	0	0	+	+
Enterobacter sp.	0	0	0	0	0	0	0	0	0	0	+	+	+	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0	0	0	0	0	+	±	+	0	0	+	+
E. coli	±	±	±	+	+	+	+	+	+	?	+	+	+	+	0	0	±	0	0	±	±	+	0	0	0	0	0	0	0	0	0	0	±	+	+	0	0	+	+
E. coli, Klebs ESBL	0	0	0	0	0	0	0	0	0	0	±	±	±	±	0	0	0	0	0	0	0	+	0	0	0	0	0	0	0	0	0	0	±	±	+	0	0	+	+
E. coli, Klebs KPC	0	0	0	0	0	0	0	0	0	0	±	±	±	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0	0	0	0	0	±	±	±	0	0	+	+
Klebsiella sp.	±	±	±	+	+	+	+	+	+	?	+	+	+	+	0	0	0	0	0	0	±	+	0	0	0	0	0	0	0	0	0	0	±	+	+	0	0	+	+
Morganella sp.	0	0	0	0	0	0	0	0	0	0	+	+	+	?	0	0	0	0	0	0	0	?	0	0	0	0	0	0	0	0	0	0	±	0	?	0	0	0	0
P. mirabilis	0	0	+	+	+	+	+	+	+	?	+	+	+	?	0	0	0	0	0	0	±	+	0	0	0	0	0	0	0	0	0	0	±	0	?	0	0	0	0
P. vulgaris	0	0	0	0	0	+	+	+	?	?	+	+	+	±	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	±	0	±	0	0	0	0
Providencia sp.	0	0	0	0	0	+	+	+	?	?	±	±	+	?	0	0	0	0	0	0	0	?	0	0	0	0	0	0	0	0	0	0	±	0	?	0	0	0	0
Salmonella sp.	0	0	0	0	0	+	+	+	+	?	+	+	+	+	0	0	+	0	0	±	±	+	0	0	0	0	0	0	0	0	0	0	±	0	0	0	0	0	0
Serratia sp.	0	0	0	0	0	+	0	0	0	0	+	+	+	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0	0	0	0	0	+	0	+	0	0	0	0

TABLE 4A (5)

	Oral Cephalosporins										Aminoglyco					Macrolides				Tetracycline			Glyco/Lipo						Ox-lid		Other							
	Cefadroxil	Cephalexin	Cefaclor	Cefprozil	Cefurox-Axe	Cefixime	Ceftibuten	Cefpodoxime	Cefdinir	Cefditoren	Gentamicin	Tobramycin	Amikacin	Chloramphen	Clindamycin	Erythromycin	Azithromycin	Clarithromycin	Telithromycin	Doxycycline	Minocycline	Tigecycline	Daptomycin	Vancomycin	Teicoplanin	Telavancin	Oritavancin	Dalbavancin	Linezolid	Tedizolid	Fusidic Acid	Rif (comb)	TMP-SMX	Nitrofurantoin	Fosfomycin	Metronidazole	Quinu-Dalfo	Polymyxin B	Colistin
Aerobic gram-neg bacilli - Enterobacteriaceae *(continued)*																																						
Shigella sp.	0	0	0	0	0	+	+	+	+	?	+	+	+	+	0	0	+	0	0	±	±	+	0	0	0	0	0	0	0	0	0	0	±	0	0	0	0	0	0
Y. enterocolitica	0	0	0	0	0	+	+	?	?	?	+	+	+	0	0	0	0	0	0	+	?	?	0	0	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0
Aerobic gram-neg bacilli - Miscellaneous																																						
Bartonella sp.	0	0	0	0	0	0	0	0	0	0	++	0	0	0	0	+	++	++	?	++	+	?	0	0	0	0	0	0	0	0	0	±	0	0	0	0	0	0	0
B. pertussis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	++	++	?	?	?	0	0	0	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0
B. burgdorferi	0	0	0	0	++	0	0	0	0	0	0	0	0	0	0	+	+	+	?	++	+	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Brucella sp.	0	0	0	0	0	0	0	0	0	0	+	?	?	+	0	0	0	0	0	+	+	?	0	0	0	0	0	0	0	0	0	0	±	+	0	0	0	0	0	0
Capnocytophagia	0	0	0	0	0	0	0	0	0	0	±	±	±	+	++	?	?	?	?	+	+	?	0	0	0	0	0	0	0	0	0	0	0	±	0	0	0	0	0	0
C. burnetii	0	0	0	0	0	0	0	0	0	0	0	0	0	+	0	+	+	+	?	++	+	?	0	0	0	0	0	0	0	0	0	0	±	+	0	0	0	0	0	0
Ehrlichia, Anaplas	0	0	0	0	0	0	0	0	0	0	0	0	0	±	0	0	0	0	0	++	+	?	0	0	0	0	0	0	0	0	0	0	±	0	0	0	0	0	0	0
Eikenella sp	0	0	0	?	0	?	?	?	?	?	±	0	0	+	0	0	0	0	0	+	+	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F. tularensis	0	0	0	0	0	0	0	0	0	0	++	+	?	+	?	0	?	?	?	++	+	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
H. ducreyi	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	++	++	?	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
H. influenzae	0	0	±	+	+	+	+	+	+	+	0	0	0	+	0	0	+	+	+	+	+	+	0	0	0	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0
Kingella sp.	0	0	0	+	0	+	+	+	+	+	+	0	0	+	0	0	?	?	?	+	+	+	0	0	0	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0
K. granulomatis	0	0	0	0	0	0	0	0	0	0	+	?	?	+	0	++	++	+	0	++	+	?	0	0	0	0	0	0	0	0	0	0	0	++	0	0	0	0	0	0
Legionella sp.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	++	++	++	+	+	+	+	0	0	0	0	0	0	0	0	0	0	±	+	0	0	0	0	0	0
Leptospira sp.	?	?	?	?	?	?	?	?	?	?	0	0	0	+	0	+	++	+	?	++	+	?	0	0	0	0	0	0	0	0	0	0	0	?	0	0	0	0	0	0
M. catarrhalis	0	0	±	+	+	+	+	+	+	+	0	0	0	0	0	+	+	+	+	+	+	?	0	0	0	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0	0
N. gonorrhoeae	0	0	0	0	0	+	0	+	0	0	0	0	0	0	0	0	+	0	0	±	±	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
N. meningitidis	0	0	0	0	0	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
P. multocida	?	0	0	?	+	+	?	+	+	?	±	±	±	?	0	0	+	0	0	+	+	+	0	0	0	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0	0
R. rickettsii	0	0	0	0	0	0	0	0	0	0	0	0	0	+	0	0	0	±	0	++	+	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
T. pallidum	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	0	0	+	?	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
U. urealyticum	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	++	++	+	?	++	+	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
V. cholera	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	+	?	?	+	?	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
V. parahemolyticus	0	0	0	0	0	0	0	0	0	0	?	?	?	+	?	?	+	0	0	+	0	?	0	0	0	0	0	0	0	0	0	0	0	?	0	0	0	0	0	0	0
V. vulnificus	0	0	0	0	0	0	0	0	0	0	?	?	?	+	0	0	?	0	0	+	+	?	0	0	0	0	0	0	0	0	0	0	0	?	0	0	0	0	0	0	0
Y. pestis	0	0	0	0	0	0	0	0	0	0	+	?	?	+	0	0	0	0	0	+	+	?	0	0	0	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0	0

TABLE 4A (6)

	Oral Cephalosporins										Aminoglyco			Macrolides				Tetracycline			Glyco/Lipo						Ox-Iid		Other							
	Cefadroxil	Cephalexin	Cefaclor	Cefprozil	Cefurox-Axe	Cefixime	Ceftibuten	Cefpodoxime	Cefdinir	Cefditoren	Gentamicin	Tobramycin	Amikacin	Chloramphen	Clindamycin	Erythromycin	Azithromycin	Clarithromycin	Telithromycin	Doxycycline	Minocycline	Tigecycline	Daptomycin	Vancomycin	Teicoplanin	Telavancin	Oritavancin	Dalbavancin	Linezolid	Tedizolid	Fusidic Acid	Rif (comb)	TMP-SMX	Nitrofurantoin	Fosfomycin	Metronidazole	Quinu-Dalfo	Polymyxin B	Colistin
Aerobic gram-neg bacilli - Selected non-fermentative GNB (NF-GNB)																																						
Acinetobacter sp.	0	0	0	0	0	0	0	0	0	0	0	0	±	0	0	0	0	0	0	0	±	+	0	0	0	0	0	0	0	0	0	0	±	0	0	0	0	+	+
B. cepacia	0	0	0	0	0	0	±	0	0	0	0	0	0	±	0	0	0	0	0	0	±	0	0	0	0	0	0	0	0	0	0	0	±	0	0	0	0	0	0
P. aeruginosa	0	0	0	0	0	0	0	0	0	0	+	+	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	±	0	0	+	+
S. maltophilia	0	0	0	0	0	0	0	0	0	0	0	0	0	+	0	0	0	0	0	+	+	+	0	0	0	0	0	0	0	0	0	0	++	0	0	0	+	+
Aerobic cell wall-deficient bacteria																																						
C. trachomatis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	++	+	?	++	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Chlamydophila sp.	0	0	0	0	0	0	0	0	0	0	0	0	0	+	0	+	+	+	+	++	+	+	0	0	0	0	0	0	0	0	0	±	0	0	0	0	0	0	0
M. genitalium	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	?	++	?	?	±	±	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M. pneumoniae	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	±	±	±	±	++	++	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Anaerobic gram-negative bacteria																																						
B. fragilis	0	0	0	0	0	0	0	0	0	0	0	0	0	+	±	0	0	0	0	±	±	+	0	0	0	0	0	0	0	0	0	0	0	0	0	++	0	0	0
F. necrophorum	?	?	?	?	?	?	?	?	?	?	0	0	0	+	+	0	0	0	0	+	±	+	0	0	0	0	0	0	0	0	0	0	0	0	0	++	0	0	0
P. melaninogenica	?	?	?	?	?	?	?	?	?	?	0	0	0	+	+	±	±	±	0	+	+	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	++	0	0	0
Anaerobic gram-positive bacteria																																						
Actinomyces sp.	?	?	?	?	?	?	?	?	?	?	0	0	0	+	++	++	+	+	?	+	+	?	0	?	0	?	0	0	?	0	0	0	0	0	0	+	+	0	0
C. difficile	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	++	0	0	0	0	0	0	0	0	0	++	0	0	0	0	0
Clostridium sp.	?	?	?	?	?	?	?	?	?	?	0	0	0	+	+	+	+	+	?	+	+	+	±	+	+	+	+	+	0	0	0	0	0	0	+	+	+	0	0
P. acnes	+	0	+	+	+	0	+	+	?	?	+	?	?	+	±	±	±	±	?	+	+	+	+	+	+	+	+	+	0	0	0	±	0	0	0	0	0	0	0
Peptostreptococci	+	+	+	+	+	+	+	+	?	?	0	0	0	+	+	±	±	±	?	+	+	+	+	+	+	+	+	+	?	0	0	0	0	0	±	?	?	0	0

TABLE 4B – ANTIFUNGAL ACTIVITY SPECTRA

	Antifungal Drugs								
	Fluconazole	Itraconazole	Voriconazole	Posaconazole	Isavuconazole	Anidulafungin	Caspofungin	Micafungin	Amphotericin B
Fungi									
Aspergillus fumigatus	0	±	++	+	++	±	±	±	+
Aspergillus terreus	0	±	++	+	++	±	±	±	0
Aspergillus flavus	0	±	++	+	++	±	±	±	+
Candida albicans	++	+	+	+	+	++	++	++	+
Candida dubliniensis	++	+	+	+	+	++	++	++	++
Candida glabrata	±	±	±	±	±	++	++	++	++
Candida guilliermondii	++	++	++	++	+	++	++	++	++
Candida krusei	0	0	+	+	+	++	++	++	++
Candida lusitaniae	++	+	+	+	+	++	++	++	±
Candida parapsilosis	++	+	+	+	+	+	+	+	++
Candida tropicalis	++	+	+	+	+	++	++	++	++
Cryptococcus sp.	++	+	+	+	+	0	0	0	++
Dematiaceous molds	0	++	++	+	+	±	±	±	+
Fusarium sp.	0	±	±	±	±	0	0	0	±
Mucormycosis	0	0	0	+	+	0	0	0	++
Scedo apiospermum	0	0	+	±	±	0	0	0	0
Scedo prolificans	0	0	0	0	0	0	0	0	0
Trichosporon spp.	±	+	+	+	?	0	0	0	+
Dimorphic Fungi									
Blastomyces	±	++	+	+	?	0	0	0	++
Coccidioides	++	++	+	+	?	0	0	0	++
Histoplasma	±	++	+	+	?	0	0	0	++
Sporothrix	±	++	+	+	?	0	0	0	++

TABLE 4C – ANTIVIRAL ACTIVITY SPECTRA

	Viruses											
	Adenovirus	BK Virus	Cytomegalovirus	Hepatitis B	Hepatitis C	Herpes simplex	HPV	Influenza A	Influenza B	JC Virus / PML	RSV	Varicella-zoster
Hepatitis B												
Adefovir	NA	NA	NA	++	NA	NA	NA	NA	NA	NA	NA	NA
Emtricitabine	NA	NA	NA	±	NA	NA	NA	NA	NA	NA	NA	NA
Entecavir	NA	NA	NA	++	NA	NA	NA	NA	NA	NA	NA	NA
Lamivudine	NA	NA	NA	±	NA	NA	NA	NA	NA	NA	NA	NA
Telbivudine	NA	NA	NA	±	NA	NA	NA	NA	NA	NA	NA	NA
Tenofovir	NA	NA	NA	++	NA	±	NA	NA	NA	NA	NA	NA
Hepatitis C												
Daclatasvir	NA	NA	NA	NA	++	NA	NA	NA	NA	NA	NA	NA
Dasabuvir	NA	NA	NA	NA	++	NA	NA	NA	NA	NA	NA	NA
Interferon alfa, peg	NA	NA	NA	++	+	NA	NA	NA	NA	NA	NA	NA
Ledipasvir	NA	NA	NA	NA	++	NA	NA	NA	NA	NA	NA	NA
Ombitasvir	NA	NA	NA	NA	++	NA	NA	NA	NA	NA	NA	NA
Paritaprevir	NA	NA	NA	NA	++	NA	NA	NA	NA	NA	NA	NA
Ribavirin	±	NA	NA	0	+	NA	NA	NA	NA	NA	±	NA
Simeprevir	NA	NA	NA	NA	+	NA	NA	NA	NA	NA	NA	NA
Sofosbuvir	NA	NA	NA	NA	++	NA	NA	NA	NA	NA	NA	NA

TABLE 4C (2)

	Viruses											
	Adenovirus	BK Virus	Cytomegalovirus	Hepatitis B	Hepatitis C	Herpes simplex	HPV	Influenza A	Influenza B	JC Virus / PML	RSV	Varicella-zoster
Influenza												
Amantadine	NA	NA	NA	NA	NA	NA	NA	±	±	NA	NA	NA
Oseltamivir	NA	NA	NA	NA	NA	NA	NA	++	+	NA	NA	NA
Peramivir	NA	NA	NA	NA	NA	NA	NA	+	+	NA	NA	NA
Rimantadine	NA	NA	NA	NA	NA	NA	NA	±	±	NA	NA	NA
Zanamivir	NA	NA	NA	NA	NA	NA	NA	++	+	NA	NA	NA
Herpes, CMV, VZV, misc.												
Acyclovir	NA	NA	0	NA	NA	++	NA	NA	NA	NA	NA	+
Cidofovir	+	+	++	NA	NA	+	NA	NA	NA	+	NA	+
Famciclovir	NA	NA	0	NA	NA	++	NA	NA	NA	NA	NA	+
Foscarnet	NA	NA	++	NA	NA	+	NA	NA	NA	NA	NA	+
Ganciclovir	±	NA	++	NA	NA	+	NA	NA	NA	NA	NA	+
Valacyclovir	NA	NA	0	NA	NA	++	NA	NA	NA	NA	NA	++
Valganciclovir	±	NA	++	NA	NA	+	NA	NA	NA	NA	NA	+
Topical Agents												
Imiquimod	NA	NA	NA	NA	NA	NA	++	NA	NA	NA	NA	NA
Penciclovir	NA	NA	0	NA	NA	+	NA	NA	NA	NA	NA	0
Podofilox	NA	NA	NA	NA	NA	NA	++	NA	NA	NA	NA	NA
Sinecatechins	NA	NA	NA	NA	NA	NA	+	NA	NA	NA	NA	NA
Trifluridine	NA	NA	NA	NA	NA	+	NA	NA	NA	NA	NA	NA

TABLE 5A – TREATMENT OPTIONS FOR SYSTEMIC INFECTION DUE TO MULTI-DRUG RESISTANT GRAM-POSITIVE BACTERIA

ORGANISM	RESISTANT TO	PRIMARY TREATMENT OPTIONS	ALTERNATIVE TREATMENT OPTIONS	COMMENTS
Enterococcus faecium; Enterococcus faecalis (Consultation suggested)	Vancomycin (VRE), Ampicillin, Penicillin G, Gentamicin (high level resistance)	**E. faecium**: **Dapto** 8-12 mg/kg IV q24h + (**AMP** 2 gm IV q4h OR **Ceftaroline** *600* mg IV q8h). Less desirable alternatives: [**Linezolid** *600* mg po/IV q12h OR **Quinu-dalfo** 7.5 mg/kg IV (central line)] + **AMP** 2 gm IV q4h	**E. faecalis**: Resistance to AMP or Pen rare. If no resistance: **AMP** 2 gm IV q4h + **Ceftriaxone** 2 gm IV q12h. If Pen-resistant due to beta-lactamase: **Dapto** 8-12 mg/kg IV q12h + **AM-SB** 3 gm IV q6h.	Addition of a beta lactam to Dapto reverses Dapto resistance & impedes development of resistance. E. faecalis rarely resistance to penicillins. Enterococcal endocarditis ref: *Curr Infect Dis Rep 16:431, 2014.*
Staphylococcus aureus *(See also Table 6 for more details)*	Vancomycin (VISA or VRSA) and all beta lactams (except Ceftaroline)	**Daptomycin** 6-12 mg/kg IV q24h or **(Daptomycin** 6-12 mg/kg IV q24h + **Ceftaroline** *600* mg IV q8h *(AAC 56:5296, 2012).*	**Telavancin** *10* mg/kg IV q24h or **Linezolid** *600* mg IV/po q12h	Confirm dapto susceptibility as VISA strains may be non-susceptible. If prior vanco therapy (or persistent infection on vanco) there is significant chance of developing resistance to dapto *(JAC 66:1696, 2011).* Addition of an anti-staphylococcal beta-lactam (nafcillin or oxacillin) may restore susceptibility against Dapto-resistant MRSA *(AAC 54:3161, 2010).* Combination of Dapto + oxacillin has been successful in clearing refractory MRSA bacteremia *(CID 53:158, 2011)*; Dapto + ceftaroline may also be effective.
Streptococcus pneumoniae	Penicillin G (MIC ≥ 4 µg/mL)	If no meningitis: **Ceftriaxone** 2 gm IV once daily OR **Ceftaroline** 600 mg IV q12h OR **Linezolid** 600 mg IV/po q12h	Meningitis: **Vancomycin** 15 mg/kg IV q8h OR **Meropenem** 2 gm IV q8h	Ceftriaxone 2 gm IV q12h should also work for meningitis.

TABLE 5B: TREATMENT OPTIONS FOR SYSTEMIC INFECTION DUE TO SELECTED MULTI-DRUG RESISTANT GRAM-NEGATIVE BACILLI

The suggested treatment options in this Table are usually not FDA-approved. Suggestions are variably based on in vitro data, animal studies, and/or limited clinical experience.

ORGANISM	RESISTANT TO	PRIMARY TREATMENT OPTIONS	ALTERNATIVE TREATMENT OPTIONS	COMMENTS
Acinetobacter baumannii	All Penicillins, All Cephalosporins, Aztreonam, Carbapenems, Aminoglycosides and Fluoroquinolones	Combination therapy: **Polymyxin E (Colistin) + (Imipenem or Meropenem)** *See Table 10A, page 112,* for guidance on Colistin dosing.	**Minocycline** *(IDCP 20:184, 2012)* (in vitro synergy between minocycline and imipenem)	Refs: *Int J Antimicrob Agts 37:244, 2011; BMC Inf Dis 11:109, 2011.* Detergent effect of colistin reconstitutes antibiotic activity of carbapenems and other drugs. Do not use colistin as monotherapy. Colistin + Rifampin failed to influence infection-related mortality *(CID 57:349, 2013).*
Extended spectrum beta lactamase (ESBL) producing E. coli, Klebsiella pneumoniae, or other Enterobacteriaceae	All Cephalosporins, TMP-SMX, Fluoroquinolones, Aminoglycosides	**Imipenem** *500* mg IV q6h OR **Meropenem** 1 gm IV q8h OR **Doripenem** 500 mg IV q8h *(CID 39:31, 2004)* (Note: **DORI** is **not** FDA approved for treatment of pneumonia).	Perhaps high dose **Cefepime** 2 gm IV q12h *(See Comment).* **Polymyxin E (Colistin)** + **(MER** or **IMP).** For dosing, see *Table 10A, page 112.*	For UTI: Fosfomycin, nitrofurantoin *(AAC 53:1278, 2009).* Avoid PIP-TZ even if suscept in vitro *(AAC 57:3402, 2013).* Ceftolozane-tazobactam *(see Lancet 385:1949, 2015 and CID 60:1462, 2015)* and ceftazidime-avibactam *(see Med Lett Drugs Ther. 57:79, 2015)* recently approved for treatment of complicated UTI and intraabdominal infections caused by ESBL+ enterics.
Carbapenemase producing aerobic gram-negative bacilli or P. aeruginosa	All Penicillins, Cephalosporins, Aztreonam, Carbapenems, Aminoglycosides, Fluoroquinolones	Combination therapy: **Polymyxin E (Colistin)** + (**MER** or **IMP**). Ceftazidime-avibactam *(Med Lett Drugs Ther. 57:79, 2015)* active against some carbapenemase producing Gram-negatives (not those producing a metallo-beta-lactamase).	Pneumonia: Inhaled **Colistin**[NAI] 50-75 mg in 3-4 mL saline via nebulizer + **Colistin** + (**MER** or **IMP**)	*See Table 10A, page 112,* for guidance on **Colistin** dosing. For inhalation dosing, see *Table 10F.* Anecdotal reports of successful dual carbapenem rx (MER + ERTA) for KPCs *(JAC:69:1718, 2014).* **Ceftazidime-avibactam** active in vitro against some carbapenemase-producing (but not metallo-beta-lactamase producers) organisms.
Stenotrophomonas maltophilia	All beta-lactams, Aminoglycosides, Fluoroquinolones	**TMP-SMX** 15 mg/kg/day IV divided q6h/q8h/q12h (based on TMP component)	**FO** if suscept in vitro	Ref: *Sem Resp & CCM 36:99, 2015.*

TABLE 6 – SUGGESTED MANAGEMENT OF SUSPECTED OR CULTURE-POSITIVE COMMUNITY-ASSOCIATED METHICILLIN-RESISTANT S. AUREUS INFECTIONS

(See footnote[1] for doses)

IDSA Guidelines: *CID 52 (Feb 1):1, 2011.* With the magnitude of the clinical problem and a number of new drugs, it is likely new data will require frequent revisions of the regimens suggested. *(See page 2 for abbreviations).* NOTE: Distinction between community and hospital strains of MRSA blurring.

CLINICAL ILLNESS	ABSCESS, NO IMMUNOSUPPRESSION, OUT-PATIENT CARE		PNEUMONIA	BACTEREMIA OR POSSIBLE ENDOCARDITIS OR BACTEREMIC SHOCK	TREATMENT FAILURE *(See footnote[2])*
Management *Drug doses in footnote.*	TMP/SMX 1 DS (2 DS if BMI > 40) po bid OR Clinda 300 mg (450 mg for BMI > 40) po tid *(NEJM 372:1093, 2015).* For larger abscesses, multiple lesions or systemic inflammatory response: **I&D** + (**Oritavancin** 1500 mg x1 or **Dalbavancin** 1000 mg x1 than 500 mg x1 a wk later) an option for outpatient management of sicker patients with more extensive infection who might otherwise be admitted *(see NEJM 370:2180, 2014, NEJM 370:2169, 2014).*		**Vanco** IV or **linezolid** IV	**Vanco** 15-20 mg/kg IV q8-12h. Confirm adequate vanco troughs of 15-20 µg/mL Switch to alternative regimen if **vanco** MIC > 2 µg/mL. If patient has slow response to vancomycin and isolate has MIC = 2, consider alternative therapy. **Dapto** 6 mg/kg IV q24h (FDA-approved dose but some authorities recommend 8-12 mg/kg for MRSA bacteremia)	**Dapto** 8-12 mg/kg IV q24h; confirm in vitro susceptibility as prior vanco therapy may select for daptomycin non-susceptibility (MIC >1 µg/mL) & some VISA strains are daptomycin non-susceptible. Use combination therapy for bacteremia or endocarditis: dapto + beta-lactam combination therapy [dapto 8-12 mg/kg IV q24h + (Nafcillin 2 gm IV q4h OR Oxacillin 2 gm IV q4h OR Ceftaroline 600 mg IV q8h) appears effective against MRSA strains as salvage therapy even if non-susceptible to dapto *(Int J Antimicrob Agents, 42:450, 2013, AAC 54:3161, 2010, AAC 56:6192, 2013).* **Ceftaroline** 600 mg IV q8h *(J Antimicrob Chemother 67:1267, 2012, J Infect Chemother 19:42, 2013, Int J Antimicrob Agents 42:450, 2013, AAC 58:2541, 2014.* **Linezolid** 600 mg IV/PO q12h (Linezolid is bacteriostatic and should not be used as a single agent in suspected endovascular infection). **Telavancin** 10 mg/kg q24h IV *(CID 52:31, 2011; AAC 58:2030, 2014).*
Comments	**Fusidic acid** 500 mg tid (not available in the US) **+ rifampin** also an option; do not use rifampin alone as resistance rapidly emerges.	Patients not responding after 2-3 days should be evaluated for complicated infection and switched to **vancomycin**.	Prospective study of **Linezolid** vs **Vanco** showed slightly higher cure rate with Linezolid, no difference in mortality *(CID 54:621, 2012).*	TMP-SMX NOT recommended in bacteremic pts; inferior to Vanco *(BMJ 350:2219, 2015)*	

[1] **Clindamycin:** 300 mg po tid. **Daptomycin:** 6 mg/kg IV q24h is the standard, FDA-approved dose for bacteremia and endocarditis but 8-12 mg/kg q24h is recommended by some and for treatment failures. **Doxycycline or minocycline:** 100 mg po bid. **Linezolid:** 600 mg po/IV bid. **Ouĩnupristin-dalfopristin (O-D):** 7.5 mg per /kg IV q8h via central line. **Rifampin:** Long serum half-life justifies dosing 600 mg po q24h; however, frequency of nausea less with 300 mg po bid. **TMP-SMX-DS:** Standard dose 8–10 mg per kg per day. For 70 kg person = 700 mg TMP component per day. **TMP-SMX** contains 160 mg TMP and 800 mg SMX. The dose for treatment of CA-MRSA skin and soft tissue infections (SSTI) is 1 DS tablet twice daily. **Vancomycin:** 1 gm IV q12h; up to 45-60 mg/kg/day in divided doses may be required to achieve target trough concentrations of 15-20 mcg/mL recommended for serious infections.

[2] The median duration of bacteremia in endocarditis is 7-9 days in patients treated with vancomycin *(AnIM 115:674, 1991).* Longer duration of bacteremia, greater likelihood of endocarditis *(JID 190:1140, 2004).* Definition of failure unclear. Clinical response should be factored in. **Unsatisfactory clinical response especially if blood cultures remain positive >4 days.**

TABLE 7 – ANTIBIOTIC HYPERSENSITIVITY REACTIONS & DRUG DESENSITIZATION METHODS

Penicillin. *Oral route (Pen VK) preferred.* 1/3 pts develop transient reaction, usually mild. **Perform in ICU setting. Discontinue β-blockers. Have IV line, epinephrine, ECG, spirometer available.** Desensitization works as long as pt is receiving Pen; allergy returns after discontinuance. History of Steven-Johnson, exfoliative dermatitis, erythroderma are contraindications. Skin testing for evaluation of Pen allergy: Testing with major determinant (benzyl Pen polylysine) and minor determinants has negative predictive value (97-99%). Risk of systemic reaction to skin testing <1% *(Ann Allergy Asth Immunol 106:1, 2011).* General refs: *CID 58:1140, 2014.*

- **Method:** Prepare dilutions using **Pen-VK** oral soln, 250 mg/5mL. Administer each dose @ 15 min intervals in 30 mL water/flavored bev. After Step 14 observe pt for 30 min, then give full therapeutic dose by route of choice. Ref: *Allergy, Prin & Prac, Mosby, 1993, pg. 1726.*

Step	Dilution (mg/mL)	mL Administered	Dose/Step		Cumulative Dose Given	
			mg	units	mg	units
1	0.5	0.1	0.05	80	0.05	80
2	0.5	0.2	0.1	160	0.15	240
3	0.5	0.4	0.2	320	0.35	560
4	0.5	0.8	0.4	640	0.75	1,200
5	0.5	1.6	0.8	1,280	1.55	2,480
6	0.5	3.2	1.6	2,560	3.15	5,040
7	0.5	6.4	3.2	5,120	6.35	10,160
8	5	1.2	6	9,600	12.35	19,760
9	5	2.4	12	19,200	24.35	38,960
10	5	4.8	24	38,400	48.35	77,360
11	50	1	50	80,000	98.35	157,360
12	50	2	100	160,000	198.35	317,360
13	50	4	200	320,000	398.35	637,360
14	50	8	400	640,000	798.35	1,277,360

TMP-SMX. Perform in hospital/clinic. Refs: *CID 20:849, 1995; AIDS 5:311, 1991.*

- **Method:** Use **TMP-SMX** oral susp, (40 mg TMP/200 mg SMX)/5 mL. Take with 6 oz water after each dose. Corticosteroids, antihistaminics NOT used.

Hour	Dose (TMP/SMX) (mg)
0	0.004/0.02
1	0.04/0.2
2	0.4/2
3	4/20
4	40/200
5	160/800

Penicillin. *Parenteral (Pen G) route.* Follow procedures/notes under Oral (Pen-VK) route. Ref: *Allergy, Prin & Prac, Mosby, 1993, pg. 1726.*

- **Method:** Administer **Pen G** IM, IV or sc as follows:

Step	Dilution (units/mL)	mL Administered	Dose/Step (units)	Cumulative Dose Given (units)
1	100	0.2	20	20
2		0.4	40	60
3		0.8	80	140
4	1,000	0.2	200	340
5		0.4	400	740
6		0.8	800	1,540
7	10,000	0.2	2,000	3,540
8		0.4	4,000	7,540
9		0.8	8,000	15,540
10	100,000	0.2	20,000	35,540
11		0.4	40,000	75,540
12		0.8	80,000	155,540
13	1,000,000	0.2	200,000	355,540
14		0.4	400,000	755,540
15		0.8	800,000	1,555,540

Ceftriaxone. Ref: *Allergol Immunopathol (Madr) 37:105, 2009.*

- **Method:** Infuse **Ceftriaxone** IV @ 20 min intervals as follows:

Day	Dose (mg)
1	0.001, then 0.01, then 0.1, then 1
2	1, then 5, then 10, then 50
3	100, then 250, then 500
4	1000

Desensitization Methods for Other Drugs (References)

- **Imipenem-Cilastatin.** *Ann Pharmacother 37:513, 2003.*
- **Meropenem.** *Ann Pharmacother 37:1424, 2003.*
- **Metronidazole.** *Allergy Rhinol 5:1, 2014*
- **Daptomycin.** *Ann All Asthma Immun 100:87, 2008.*
- **Ceftazidime.** *Curr Opin All Clin Immunol 6(6): 476, 2006.*
- **Vancomycin.** *Intern Med 45:317, 2006.*
- General review, including desensitization protocols for Amp, CFP, CIP, Clarithro, Clinda, Dapto, Linezold, Tobra *(CID 58:1140, 2014).*

TABLE 7 (2)

Ceftaroline. 12-step IV desensitization protocol. Ref: Open Forum Infect Dis 2:1, 2015.

- Method: Cumulative drug infused: 600 mg. Total time required for all 12 steps: 318 minutes.

Step	Conc (mg/mL)	Vol infused (mL)	Infusion duration (min)	Drug infused this step (mg)	Cumulative drug infused (mg)
1	0.0002	5	15	0.001	0.001
2	0.0002	15	15	0.003	0.004
3	0.002	5	15	0.01	0.014
4	0.002	15	15	0.03	0.04
5	0.02	5	15	0.1	0.14
6	0.02	15	15	0.3	0.4
7	0.2	5	15	1	1.4
8	0.2	15	15	3	4.4
9	2	5	15	10	14.4
10	2	15	15	30	44.4
11	2	25	15	50	94.4
12	2	255	153	510	604.4

Valganciclovir. 12-step oral desensitization protocol. Ref: Transplantation 98:e50, 2014.

- Method: Administer doses at 15-minute intervals; entire protocol takes 165 minutes. Cumulative dose administered: 453.6 mg

Step	Drug administered this step (mg)	Cumulative drug administered (mg)
1	0.1	0.1
2	0.2	0.3
3	0.4	0.7
4	0.8	1.5
5	1.6	3.1
6	3.5	6.6
7	7	13.6
8	14	27.6
9	28	55.6
10	58	113.6
11	115	228.6
12	225	453.6

TABLE 8 – PREGNANCY RISK AND SAFETY IN LACTATION

Drug	Risk Category (Old)	Use during Lactation
Antibacterials		
Amikacin	D	Probably safe, monitor infant for GI toxicity
Azithromycin	B	Safe, monitor infant for GI toxicity
Aztreonam	B	Safe, monitor infant for GI toxicity
Cephalosporins	B	Safe, monitor infant for GI toxicity
Chloramphenicol	C	Avoid use
Ciprofloxacin	C	Avoid breastfeeding for 3-4 hrs after a dose, monitor infant for GI toxicity
Clarithromycin	C	Safe, monitor for GI toxicity
Clindamycin	B	Avoid use if possible, otherwise monitor infant for GI toxicity
Colistin (polymyxin E)	C	Probably safe with monitoring, but data limited
Dalbavancin	C	Probably safe with monitoring, but no data available
Daptomycin	B	Probably safe with monitoring, but data limited
Doripenem	B	Probably safe with monitoring, but no data available
Doxycycline	D	Short-term use safe, monitor infant for GI toxicity
Ertapenem	B	Safe
Erythromycin	B	Safe
Fidaxomicin	B	Probably safe
Fosfomycin	B	Probably safe with monitoring
Fusidic acid	-	Safety not established
Gatifloxacin	C	Short-term use safe
Gemifloxacin	C	Short-term use safe
Gentamicin	D	Probably safe
Imipenem	C	Safe, monitor infant for GI toxicity
Isepamicin	D	Safety not established, avoid use
Levofloxacin	C	Avoid breastfeeding for 4-6 hrs after a dose, monitor infant for GI toxicity
Linezolid	C	Probably safe with monitoring, but no data available; avoid if possible
Meropenem	B	Probably safe with monitoring, but no data available
Metronidazole	B	Data and opinions conflict; best to avoid
Minocycline	D	Short-term use safe, monitor infant for GI toxicity
Moxifloxacin	C	Short-term use safe, monitor infant for GI toxicity; avoid if possible
Netilmicin	D	Safety not established
Nitrofurantoin	B	Avoid if infant <8 days of age
Ofloxacin	C	Avoid breastfeeding for 4-6 hrs after a dose, monitor infant for GI toxicity
Oritavancin	C	Probably safe with monitoring, but no data available; avoid if possible
Penicillins	B	Safe, monitor infant for GI toxicity
Polymyxin B	C	Topical administration safe (no data with systemic use)
Quinupristin-Dalfopristin	B	Probably safe with monitoring, but no data available; avoid if possible
Rifaximin	C	Probably safe with monitoring, but no data available; avoid if possible
Streptomycin	D	Probably safe, monitor infant for GI toxicity
Tedizolid	C	Probably safe with monitoring, but no data available; avoid if possible
Telavancin	C	Probably safe with monitoring, but no data available; avoid if possible
Telithromycin	C	Probably safe with monitoring, but no data available; avoid if possible
Tetracycline	D	Short-term use safe, monitor infant for GI toxicity
Tigecycline	D	Safety not established, avoid use
TMP-SMX	C	Risk of kernicterus in premature infants; avoid if infant G6PD-deficient
Tobramycin	D	Probably safe, monitor infant for GI toxicity
Vancomycin	C	Safe with monitoring
Antifungals		
Amphotericin B (all products)	B	Probably safe, but no data available
Anidulafungin	B	Safety not established, avoid use
Caspofungin	C	Probably safe with monitoring, but no data available; avoid if possible
Fluconazole (other regimens)	D	Safe with monitoring
Fluconazole (single dose)	C	Safe with monitoring
Flucytosine	C	Safety not established, avoid use
Griseofulvin	C	Safety not established, avoid use
Isavuconazole	C	Avoid use
Itraconazole	C	Little data available, avoid if possible
Ketoconazole	C	Little data available, avoid if possible
Micafungin	C	Safety not established, avoid use

TABLE 8 (2)

Drug	Risk Category (Old)	Use during Lactation
Antifungals *(continued)*		
Posaconazole	C	Safety not established, avoid use
Terbinafine	B	Little data available, avoid if possible
Voriconazole	D	Safety not established, avoid use
Antimycobacterials		
Amikacin	D	Probably safe, monitor infant for GI toxicity
Bedaquiline	B	Safety not established, avoid use
Capreomycin	C	Probably safe, monitor infant for GI toxicity
Clofazimine	C	May color breast milk pink; probably safe but avoid if possible
Cycloserine	C	Probably safe
Dapsone	C	Safe
Ethambutol	"safe"	Probably safe
Ethionamide	C	Probably safe with monitoring
Isoniazid	C	Safe
Para-aminosalicylic acid	C	Probably safe
Pyrazinamide	C	Probably safe
Rifabutin	B	Probably safe
Rifampin	C	Probably safe
Rifapentine	C	Probably safe
Streptomycin	D	Probably safe
Thalidomide	X	Safety not established
Antiparasitics		
Albendazole	C	Data limited; one-time dose considered safe by WHO
Artemether/Lumefantrine	C	Data limited; probably safe, particularly if infant weighs at least 5 kg
Atovaquone	C	Data limited; probably safe, particularly if infant weighs at least 5 kg
Atovaquone/Proguanil	C	Data limited; probably safe, particularly if infant weighs at least 5 kg
Benznidazole	avoid	Safe with monitoring
Chloroquine	C	Probably safe with monitoring, but data limited; avoid if possible
Dapsone	C	Safe, but avoid if infant G6PD-deficient
Eflornithine	C	Probably safe, monitor infant for toxicity
Ivermectin	C	Probably safe, monitor infant for toxicity
Mebendazole	C	Probably safe, monitor infant for toxicity
Mefloquine	B	Probably safe, monitor infant for toxicity
Miltefosine	D	Safety not established, avoid use
Nitazoxanide	B	Probably safe with monitoring, but data limited; avoid if possible
Pentamidine	C	Safety not established, avoid use
Praziquantel	B	Probably safe, monitor infant for toxicity
Pyrimethamine	C	Safe with monitoring
Quinidine	C	Probably safe, monitor infant for toxicity
Quinine	X	Probably safe, but avoid if infant G6PD-deficient
Sulfadoxine/Pyrimethamine	C	Little data available, avoid use if possible
Tinidazole	C	Safety not established, avoid use
Antivirals		
Acyclovir	B	Safe with monitoring
Adefovir	C	Safety not established, avoid use if possible
Amantadine	C	Avoid use
Cidofovir	C	Avoid use
Daclatasvir	No human data	Safety not established, avoid use if possible
Entecavir	C	Safety not established, avoid use if possible
Famciclovir	B	Safety not established, avoid use
Foscarnet	C	Safety not established, avoid use
Ganciclovir	C	Safety not established, avoid use
Interferons	C	Probably safe, monitor infant for toxicity
Oseltamivir	C	Probably safe, monitor infant for toxicity
Peramivir	C	Safety not established, avoid use if possible
Ribavirin	X	No data, but probably safe with monitoring
Rimantadine	C	Avoid use
Simeprevir	C (X w/ribavirin)	Safety not established, avoid use if possible
Sofosbuvir	B (X w/ribavirin)	Safety not established, avoid use if possible
Telbivudine	B	Safety not established, avoid use if possible

TABLE 8 (3)

Drug	Risk Category (Old)	Use during Lactation
Antivirals *(continued)*		
Valacyclovir	B	Safe with monitoring
Valganciclovir	C	Safety not established, avoid use
Zanamivir	C	Probably safe, but no data
Antivirals (hep C combinations)		
Harvoni	B	Safety not established
Technivie	B	Safety not established
Viekira Pak	B	Safety not established
Antiretrovirals		
Abacavir	C	See general statement about antiretrovirals below
Atazanavir	B	See general statement about antiretrovirals below
Darunavir	C	See general statement about antiretrovirals below
Delavirdine	C	See general statement about antiretrovirals below
Didanosine	B	See general statement about antiretrovirals below
Dolutegravir	B	See general statement about antiretrovirals below
Efavirenz	D	See general statement about antiretrovirals below
Elvitegravir	B	See general statement about antiretrovirals below
Emtricitabine	B	See general statement about antiretrovirals below
Enfuvirtide	B	See general statement about antiretrovirals below
Etravirine	B	See general statement about antiretrovirals below
Fosamprenavir	C	See general statement about antiretrovirals below
Indinavir	C	See general statement about antiretrovirals below
Lamivudine	C	See general statement about antiretrovirals below
Lopinavir/r	C	See general statement about antiretrovirals below
Maraviroc	B	See general statement about antiretrovirals below
Nelfinavir	B	See general statement about antiretrovirals below
Nevirapine	B	See general statement about antiretrovirals below
Raltegravir	C	See general statement about antiretrovirals below
Rilpivirine	B	See general statement about antiretrovirals below
Ritonavir	B	See general statement about antiretrovirals below
Saquinavir	B	See general statement about antiretrovirals below
Stavudine	C	See general statement about antiretrovirals below
Tenofovir	B	See general statement about antiretrovirals below
Tipranavir	C	See general statement about antiretrovirals below
Zalcitabine	C	See general statement about antiretrovirals below
Zidovudine	C	See general statement about antiretrovirals below

GENERAL STATEMENT ABOUT ANTIRETROVIRALS

1) HIV-infected mothers are generally discouraged from breastfeeding their infants

2) In settings where breastfeeding is required, country-specific recommendations should be followed.

TABLE 9A – SELECTED PHARMACOLOGIC FEATURES OF ANTIMICROBIAL AGENTS

For pharmacodynamics, see Table 9B; for Cytochrome P450 interactions, see Table 9C. Table terminology key at bottom of each page. Additional footnotes at end of Table 9A, page 98.

DRUG	REFERENCE DOSE (SINGLE OR MULTIPLE)	PREG RISK	FOOD REC (PO DRUGS)[1]	ORAL ABS (%)	PEAK SERUM CONC[2] (µg/mL)	PROTEIN BINDING (%)	VOLUME OF DISTRIBUTION (Vd)[3]	AVG SERUM T½ (hr)[4]	BILE PEN (%)[5]	CSF/ BLOOD[6] (%)	CSF PENETRATION[7]	AUC[8] (µg*hr/mL)	Tmax (hr)
ANTIBACTERIALS													
Aminoglycosides													
Amik, Gent, Kana, Tobra	See *Table 10D*	D			See *Table 10D*	0-10	0.26 L/kg	2-3	10-60	0-30	No		
Neomycin	po	D	Tab/soln ± food	<3	0	ND	ND	ND	ND	ND	ND	ND	ND
Carbapenems													
Doripenem	500 mg IV	B			23 (SD)	8,1	16.8 L Vss	1	117 (0-611)	ND	ND	36,3	
Ertapenem	1 gm IV	B			154 (SD)	95	0.12 L/kg Vss	4	10	ND	ND	572,1	
Imipenem	500 mg IV	C			40 (SD)	15-25	0.27 L/kg	1	minimal	8,5	Possibly[9]	42,2	
Meropenem	1 gm IV	B			49 (SD)	2	0.29 L/kg	1	3-300	≈ 2	Possibly[9]	72,5	
Cephalosporins (IV)													
Cefazolin	1 gm IV	B			188 (SD)	73-87	0.19 L/kg	1,9	29-300	1-4	No	236	
Cefotetan	1 gm IV	B			158 (SD)	78-91	10.3 L	4,2	2-21			504	
Cefoxitin	1 gm IV	B			110 (SD)	65-79	16.1 L Vss	0,8	280	3	No		
Cefuroxime	1.5 gm IV	B			100 (SD)	33-50	0.19 L/kg Vss	1,5	35-80	17-88	Marginal	150	
Cefotaxime	1 gm IV	B			100 (SD)	30-51	0.28 L/kg	1,5	15-75	10	Yes	70	
Ceftizoxime	1 gm IV	B			60 (SD)	30	0.34 L/kg	1,7	34-82			85	
Ceftriaxone	1 gm IV	B			150 (SD)	85-95	5.8-13.5 L	8	200-500	8-16	Yes	1006	
Cefepime	2 gm IV	B			164 (SD)	20	18 L Vss	2	10-20	10	Yes	284,8	
Ceftazidime	1 gm IV	B			69 (SD)	<10	0.24 L/kg Vss	1,9	13-54	20-40	Yes	127	
Ceftazidime /avibactam	2.5 gm IV q8h	B			Ceftaz 90.4, Avi 14.6 (SS)	Ceftaz <10, Avi 5.7-8.2	Ceftaz 17 L, Avi 22.2 L (Vss)	Ceftaz 2.8, Avi 2.7	ND	ND	ND	Ceftaz 291, Avi 38.2 (8 hr)	
Ceftolozane /tazobactam	1.5 gm IV q8h	B			Ceftolo 74.4, Tazo 18 (SS)	Ceftolo 16-21, Tazo 30	Ceftolo 13.5 L, Tazo 18.2 L (Vss)	Ceftolo 3.1, Tazo 1.0	ND	ND	ND	Ceftolo 182, Tazo 25 (8 hr)	
Ceftaroline	600 mg IV q12h	B			21.3 (SS)	20	20.3 L Vss	2,7		ND	ND	56.3 (12 hr)	
Ceftobiprole[NUS]	500 mg IV	B			33-34.2 (SD)	16	18 L Vss	2.9-3.3				116	

Preg Risk: FDA risk categories: A = no risk in adequate human studies, **B** = animal studies suggest no fetal risk, but no adequate human studies, **C** = adverse fetal effects in animals, but no adequate studies in humans; potential benefit may warrant use despite potential risk, **D** = evidence of human risk, but potential benefit may warrant use despite potential risk **X** = evidence of human risk that clearly exceeds potential benefits; **Food Effect (PO dosing): + food** = take with food, **no food** = take without food, **± food** = take with or without food; **Oral % AB** = % absorbed; **Peak Serum Level: SD** = after single dose, **SS** = steady state after multiple doses; **Volume of Distribution (Vd): V/F** = Vd/oral bioavailability, **Vss** = Vd at steady state, **Vss/F** = Vd at steady state/oral bioavailability; **CSF Penetration:** therapeutic efficacy comment based on dose, usual susceptibility or target organism & penetration into CSF; **AUC** = area under drug concentration curve; **24hr** = AUC 0-24; **Tmax** = time to max plasma concentration.

TABLE 9A (2) *(Footnotes at the end of table)*

DRUG	REFERENCE DOSE (SINGLE OR MULTIPLE)	PREG RISK	FOOD REC (PO DRUGS)[1]	ORAL ABS (%)	PEAK SERUM CONC[2] (µg/mL)	PROTEIN BINDING (%)	VOLUME OF DISTRIBUTION (Vd)[3]	AVG SERUM T½ (hr)[4]	BILE PEN (%)[5]	CSF/ BLOOD[6] (%)	CSF PENETRATION[7]	AUC[8] (µg*hr/mL)	Tmax (hr)
Cephalosporins (po)													
Cefadroxil	500 mg po	B	Cap/tab/susp ± food	90	16 (SD)	20	0.31 L/kg V/F	1,5	22			47,4	ND
Cephalexin	500 mg po	B	Cap/tab/susp ± food	90	18 (SD)	5-15	0.38 L/kg V/F	1	216			29	1
Cefaclor	500 mg po	B	Cap/susp ± food	93	13 (SD)	22-25	0.33 L/kg V/F	0,8	≥ 60			20,5	0.5-1.0
Cefaclor ER	500 mg po	B	Tab + food		8.4 (SD)	22-25		0,8	≥ 60			18,1	2,5
Cefprozil	500 mg po	B	Tab/susp ± food	95	10.5 (SD)	36	0.23 L/kg Vss/F	1,5				25,7	1,5
Cefuroxime axetil	250 mg tab po	B	Susp + food, tab ± food	52	4.1 (SD)	50	0.66 L/kg V/F	1,5				12,9	2,5
Cefdinir	300 mg po	B	Cap/susp ± food	25	1.6 (SD)	60-70	0.35 L/kg V/F	1,7				7,1	2,9
Cefditoren pivoxil	400 mg po	B	Tab + food	16	4 (SD)	88	9.3 L Vss/F	1,6				20	1.5-3.0
Cefixime	400 mg po	B	Tab/susp ± food	50	3-5 (SD)	65	0.93 L/kg V/F	3,1	800			25,8	4
Cefpodoxime proxetil	200 mg po	B	Tab + food, Susp ± food	46	2.3 (SD)	40	0.7 L/kg V/F	2,3	115			14,5	2-3
Ceftibuten	400 mg po	B	Cap/susp no food	80	15 (SD)	65	0.21 L/kg V/F	2,4				73,7	2,6
Monobactams													
Aztreonam	1 gm IV	B			90 (SD)	56	12.6 L Vss	2	115-405	3-52	ND	271	
Penicillins													
Benzathine Penicillin G	1.2 million units IM	B			0.15 (SD)								
Penicillin G	2 million units IV	B			20 (SD)	65	0.35 L/kg	0,5	500	5-10	Yes: Pen-sens S pneumo		
Penicillin V	500 mg po	B	Tab/soln no food	60-73	5-6 (SD)	65		0,5					ND
Amoxicillin	500 mg po	B	Cap/tab/susp ± food	80	5.5-7.5 (SD)	17	0.36 L/kg	1,2	100-3000	13-14	Yes (IV only)	22	1-2
Amoxicillin ER	775 mg po	B	Tab + food		6.6 (SD)	20		1.2-1.5				29,8	3,1
Amox/Clav	875/125 mg po	B	Cap/tab/susp ± food	80/30-98	11.6/2.2 (SD)	18/25	0.36/0.21 (both L/kg)	1.4/1.0	amox 100-3000	ND	ND	26.8/5.1 (0-∞)	ND

Preg Risk: FDA risk categories: A = no risk, **B** = No risk—human studies, **C** = toxicity in animals - inadequate human studies, **D** = human risk, but benefit may outweigh risk, **X** = fetal abnormalities—risk > benefit; **Food Effect (PO dosing): + food** = take with food, **no food** = take without food, **± food** = take with or without food; **Oral % AB** = % absorbed; **Peak Serum Level: SD** = after single dose, **SS** = steady state after multiple doses; **Volume of Distribution (Vd): V/F** = Vd/oral bioavailability, **Vss** = Vd at steady state, **Vss/F** = Vd at steady state/oral bioavailability; **CSF Penetration:** therapeutic efficacy comment based on dose, usual susceptibility or target organism & penetration into CSF; **AUC** = area under drug concentration curve; **24hr** = AUC 0-24; **Tmax** = time to max plasma concentration.

TABLE 9A (3) *(Footnotes at the end of table)*

DRUG	REFERENCE DOSE (SINGLE OR MULTIPLE)	PREG RISK	FOOD REC (PO DRUGS)[1]	ORAL ABS (%)	PEAK SERUM CONC[2] (µg/mL)	PROTEIN BINDING (%)	VOLUME OF DISTRIBUTION (Vd)[3]	AVG SERUM T½ (hr)[4]	BILE PEN (%)[5]	CSF/ BLOOD[6] (%)	CSF PENETRATION[7]	AUC[8] (µg*hr/mL)	Tmax (hr)
Penicillins *(continued)*													
Amox/Clav ER	2 tabs [total 2000/125 mg]	B	Tab + food	ND	17/2.1 (SD)	18/25	0.36/0.2 t (both L/kg)	1.4/1.0	amox 100-3000	ND	ND	71.6/5.3 (0-∞)	1.5/1.03
Ampicillin	2 gm IV	B			100 (SD)	18-22	0.29 L/kg	1.2	100-3000	t3-t4	Yes		
Amp/Sulb	3 gm IV	B			109-150/ 48-88 (SD)	28/38	0.29/0.3 (both L/kg)	1.4/1.7	amp 100-3000	ND	ND	120/71 (0-∞)	
Cloxacillin[NUS]	500 mg po	B	Cap no food	50	7.5-14 (SD)	95	0.1 L/kg	0.5					1-1.5
Dicloxacillin	500 mg po	B	Cap no food	37	10-17 (SD)	98	0.1 L/kg	0.7	5-8	ND	ND	ND	1-1.5
Nafcillin	500 mg IV	B			30 (SD)	90-94	27.1 L Vss	0.5-1	>100	9-20	Yes w/high doses	18.1 (0-∞)	
Oxacillin	500 mg IV	B	Cap no food	50	43 (SD)	90-94	0.4 L/kg	0.5-0.7	25	10-15	Yes		
Pip/Tazo	3.375 gm IV	B			242/24 (SD)	16/48	0.24/0.4 (both L/kg)	1/1	>100	ND	ND	242/25	
Fluoroquinolones[10]													
Ciprofloxacin	750 mg po q12h	C	Tab/susp ± food	70	3.6 (SS)	20-40	2.4 L/kg	4	2800-4500			31.6 (24 hr)	1-2
Ciprofloxacin	400 mg IV q12h	C			4.6 (SS)	20-40	2.4 L/kg	4	2800-4500	26	Inadequate for Strep	25.4 (24 hr)	
Ciprofloxacin	500 mg ER po q24h	C	Tab ± food		1.6 (SS)	20-40	2.4 L/kg	6.6				8 (24 hr)	1-4
Gemifloxacin	320 mg po q24h	C	Tab ± food	71	1.6 (SS)	55-73	2-12 L/kg Vss/F	7				9.9 (24 hr)	0.5-2.0
Levofloxacin	750 mg po/IV q24h	C	Tab ± food, soln no food	99	po 8.6, IV 12.1 (SS)	24-38	244 L Vss	7				po 90.7, IV 108 (24 hr)	po 1.6
Moxifloxacin	400 mg po/IV q24h	C	Tab ± food	89	4.2-4.6 (SS)	30-50	2.2 L/kg	10-14		>50	Yes *(CID 49:1080, 2009)*	po 48, IV 38 (24 hr)	po 1-3
Norfloxacin	400 mg po q12h	C	Tab no food	30-40	1.5 (400 mg SD)	10-15	1.7 L/kg	3-4	700	ND	No	6.4 (400 mg	1
Ofloxacin	400 mg po q12h	C	Tab ± food	98	4.6-6.2 (SS)	32	1-2.5 L/kg	7				82.4 (24 hr)	1-2
Prulifloxacin[NUS]	600 mg po	C	Tab ± food	ND	1.6 (SD)	45	1231 L	10.6-12.1	ND	negligible		7.3	1

Preg Risk: FDA risk categories: A = no risk, **B** = No risk – human studies, **C** = toxicity in animals - inadequate human studies, **D** = human risk, but benefit may outweigh risk, **X** = fetal abnormalities – risk > benefit; **Food Effect (PO dosing): + food** = take with food, **no food** = take without food, **± food** = take with or without food; **Oral % AB** = % absorbed; **Peak Serum Level: SD** = after single dose, **SS** = steady state after multiple doses; **Volume of Distribution (Vd): V/F** = Vd/oral bioavailability, **Vss** = Vd at steady state, **Vss/F** = Vd at steady state/oral bioavailability; **CSF Penetration:** therapeutic efficacy comment based on dose, usual susceptibility or target organism & penetration into CSF; **AUC** = area under drug concentration curve; **24hr** = AUC 0-24; **Tmax** = time to max plasma concentration.

TABLE 9A (4) *(Footnotes at the end of table)*

DRUG	REFERENCE DOSE (SINGLE OR MULTIPLE)	PREG RISK	FOOD REC (PO DRUGS)[1]	ORAL ABS (%)	PEAK SERUM CONC[2] (μg/mL)	PROTEIN BINDING (%)	VOLUME OF DISTRIBUTION (Vd)[3]	AVG SERUM T½ (hr)[4]	BILE PEN (%)[5]	CSF/ BLOOD[6] (%)	CSF PENETRATION[7]	AUC[8] (μg*hr/mL)	Tmax (hr)
GLYCOPEPTIDES, LIPOGLYCOPEPTIDES, LIPOPEPTIDES													
Dalbavancin	1 gm IV	C			280-300 (SD)	93-98	0.11 L/kg	147-258	ND	ND	ND	23,443	
Daptomycin	4-6 mg/kg IV q24h	B			58-99 (SS)	92	0.11 L/kg Vss	8-9		0-8		494-632 (24 hr)	
Oritavancin	1200 mg IV	C			138 (SD)	85	87.6 L	245 (terminal)	ND	ND	ND	2800 (0-∞)	
Teicoplanin	6 mg/kg IV	-	-	-	40-50 (SD)	90-95	0.9-1.6 L/kg Vss	70-100	ND	negligible	No	500-600 (0-∞)	-
Telavancin	10 mg/kg IV q24h	C			108 (SS)	90	0.13 L/kg	8,1	Low			780 (24 hr)	
Vancomycin	1 gm IV q12h	C			20-50 (SS)	10-55	0.7 L/kg	4-6		7-14	Need high doses	500-600 if trough 20 (24 hr)	
MACROLIDES, AZALIDES, LINCOSAMIDES, KETOLIDES													
Azithromycin	500 mg po	B	Tab/susp ± food	37	0.4 (SD)	7-51	31.1 L/kg	68	High			4,3	2,5
Azithromycin	500 mg IV	B			3.6 (SD)	7-51	33.3 L/kg	68	High			9.6 (24 hr, pre SS)	
Azithromycin ER	2 gm po	B	Susp no food	≈ 30	0.8 (SD)	7-51	31.1 L/kg	59	High			20	5
Clarithromycin	500 mg po q12h	C	Tab/susp ± food	50	3-4 (SS)	65-70	4 L/kg	5-7	7000			20 (24 hr)	2.0-2.5
Clarithromycin ER	1 gm ER po q24h	C	Tab + food	≈ 50	2-3 (SS)	65-70							5-8
Clindamycin	150 mg po	B	Cap ± food	90	2.5 (SD)	85-94	1.1 L/kg	2,4	250-300		No	ND	0,75
Clindamycin	900 mg IV q8h	B			14.1 (SS)	85-94	1.1 L/kg	2,4	250-300		No	ND	
Erythromycin base, esters	500 mg po	B	Tab/susp no food, DR caps ± food	18-45	0.1-2 (SD)	70-74	0.6 L/kg	2-4		2-13	No		delay rel: 3
Erythromycin lactobionate	500 mg IV	B			3-4 (SD)	70-74	0.6 L/kg	2-4					
Telithromycin	800 mg po q24h	C	Tab ± food	57	2.3 (SS)	60-70	2.9 L/kg	10	7			12.5 (24 hr)	1
MISCELLANEOUS ANTIBACTERIALS													
Chloramphenicol	1 gm po q6h	C	Cap ± food	High	18 (SS)	25-50	0.8 L/kg	4,1		45-89	Yes	ND	
Fosfomycin	3 gm po	B	Sachet ± food		26 (SD)	<10	136.1 L Vss/F	5,7				150	2
Fusidic acid[NUS]	500 mg po	-	Tab + food	91	30 (SD)	95-99	0.3 L/kg	15	100-200	ND	ND	442 (0-∞)	2-4

Preg Risk: FDA risk categories: A = no risk, **B** = No risk – human studies, **C** = toxicity in animals - inadequate human studies, **D** = human risk, but benefit may outweigh risk, **X** = fetal abnormalities – risk > benefit; **Food Effect (PO dosing): + food** = take with food, **no food** = take without food, **± food** = take with or without food; **Oral % AB** = % absorbed; **Peak Serum Level: SD** = after single dose, **SS** = steady state after multiple doses; **Volume of Distribution (Vd): V/F** = Vd/oral bioavailability, **Vss** = Vd at steady state, **Vss/F** = Vd at steady state/oral bioavailability; **CSF Penetration:** therapeutic efficacy comment based on dose, usual susceptibility or target organism & penetration into CSF; **AUC** = area under drug concentration curve; **24hr** = AUC 0-24; **Tmax** = time to max plasma concentration.

TABLE 9A (5) *(Footnotes at the end of table)*

DRUG	REFERENCE DOSE (SINGLE OR MULTIPLE)	PREG RISK	FOOD REC (PO DRUGS)[1]	ORAL ABS (%)	PEAK SERUM CONC[2] (µg/mL)	PROTEIN BINDING (%)	VOLUME OF DISTRIBUTION (Vd)[3]	AVG SERUM T½ (hr)[4]	BILE PEN (%)[5]	CSF/ BLOOD[6] (%)	CSF PENETRATION[7]	AUC[8] (µg*hr/mL)	Tmax (hr)
MISCELLANEOUS ANTIBACTERIALS *(continued)*													
Metronidazole	500 mg IV/po q6h	B	ER tab no food, tab/cap ± food	100	20-25 (SS)	20	0.6-0.85 L/kg	6-14	100	45-89		560 (24 hr)	ER 6.8, regular 1.6
Quinupristin-dalfopristin	7.5 mg/kg IV q8h	B			Q 3.2/D 8 (SS)	ND	Q 0.45/D 0.24 (L/kg) Vss	Q 0.85/D 0.7	ND	ND	ND	Q 7.2/D 10.6 (24 hr)	
Rifampin	600 mg po	C	Cap no food	70-90	7 (SD)	80	0.65 L/kg Vss	1.5-5	10.000	7-56	Yes	40-60 (24 hr)	1.5-2
Rifaximin	200 mg po tid	C	Tab ± food	<0.4	0.0007-0.002 (SS)	67.5	ND	2-5			No	0,008	1
Trimethoprim	100 mg po	C	Tab ± food	80	1 (SD)	44	100-120 L V/F	8-15					1-4
TMP/SMX	160/800 mg po q12h	C	Tab/susp ± food	85	1-2/40-60 (SS)	44/70	100-120 L/ 12-18 L	11/9	100-200	50/40		ND	1-4
TMP/SMX	160/800 mg IV q8h	C			9/105 (SS)	44/70	100-120 L/ 12-18 L	11/9	40-70			ND	
OXAZOLIDINONES													
Linezolid	600 mg po/IV q12h	C	Tab/susp ± food	100	15-20 (SS)	31	40-50 L Vss	5		60-70	Yes (AAC 50:3971, 2006)	po 276, IV 179 (24 hr)	po 1.3
Tedizolid	200 mg po/IV q24h	C	Tab ± food	91	po 2.2, IV 3.0 (SS)	70-90	67-80 L Vss	12	ND	ND	ND	po 25.6, IV 29.2 (24 hr)	po 3, IV 1.1
POLYMYXINS													
Colistin (polymyxin E)	150 mg IV	C			5-7.5 (SD)	≈ 50	0.34 L/kg	colistimethate 1.5-2, colistin >4	0		No		
Polymyxin B	1.5 mg/kg IV q12h	C			2.8 (avg conc at SS)	60	ND	4.5-6 (old data)	ND	ND	No	66.9 (24 hr)	
TETRACYCLINES, GLYCYLCYCLINES													
Doxycycline	100 mg po	D	Tab/cap/susp + food		1.5-2.1 (SD)	93	53-134 L Vss	18	200-3200	26	No	31,7 (0-∞)	2
Minocycline	200 mg po	D	Cap/tab ± food	ND	2.0-3.5 (SD)	76	80-114 L Vss	16	200-3200	ND	ND	48,3 (0-∞)	2,1
Tetracycline	250 mg po	D	Cap no food	ND	1.5-2.2 (SD)	20-65	1.3 L/kg	6-12	200-3200	Poor	No	30 (0-∞)	2-4
Tigecycline	50 mg IV q12h	D			0.63 (SS)	71-89	7-9 L/kg	42	138	5.9-10.6	No	4.7 (24 hr)	

Preg Risk: FDA risk categories: A = no risk, **B** = No risk – human studies, **C** = toxicity in animals - inadequate human studies, **D** = human risk, but benefit may outweigh risk, **X** = fetal abnormalities – risk > benefit; **Food Effect (PO dosing): + food** = take with food, **no food** = take without food, **± food** = take with or without food; **Oral % AB** = % absorbed; **Peak Serum Level: SD** = after single dose, **SS** = steady state after multiple doses; **Volume of Distribution (Vd): V/F** = Vd/oral bioavailability, **Vss** = Vd at steady state, **Vss/F** = Vd at steady state/oral bioavailability; **CSF Penetration:** therapeutic efficacy comment based on dose, usual susceptibility or target organism & penetration into CSF; **AUC** = area under drug concentration curve; **24hr** = AUC 0-24; **Tmax** = time to max plasma concentration.

TABLE 9A (6) *(Footnotes at the end of table)*

DRUG	REFERENCE DOSE (SINGLE OR MULTIPLE)	PREG RISK	FOOD REC (PO DRUGS)[1]	ORAL ABS (%)	PEAK SERUM CONC[2] (µg/mL)	PROTEIN BINDING (%)	VOLUME OF DISTRIBUTION (Vd)[3]	AVG SERUM T½ (hr)[4]	BILE PEN (%)[5]	CSF/ BLOOD[6] (%)	CSF PENETRATION[7]	AUC[8] (µg*hr/mL)	Tmax (hr)
ANTIFUNGALS													
Polyenes													
Ampho B deoxycholate	0.4-0.7 mg/kg IV q24h	B			0.5-3.5 (SS)		4 L/kg	24		0		17 (24 hr)	
Ampho B lipid complex (ABLC)	5 mg/kg IV q24h	B			1-2.5 (SS)		131 L/kg	173				14 (24 hr)	
Ampho B liposomal	5 mg/kg IV q24h	B			83 (SS)		0.1-0.4 L/kg Vss	6,8				555 (24 hr)	
Antimetabolites													
Flucytosine	2.5 gm po	C	Cap ± food	78-90	30-40 (SD)	ND	0.6 L/kg	3-5		60-100	Yes	ND	2
Azoles													
Fluconazole	400-800 mg po/IV	D	Tab/susp ± food	90	6.7-14 (SD)	10	50 L V/F	20-50		50-94	Yes	140 (8 hr) after 3 mg/kg SD	po: 1-2
Isavuconazole	200 mg po/IV q24h (maint)	C	Cap ± food	98	7.5 (SS)	99	450 L Vss	130	ND	ND	ND	121.4 (24 hr)	2-3
Itraconazole	200 mg oral soln po q24h	C	Cap/tab + food, soln no food	55+	Itra 2.0, OH-Itra 2.0 (SS)	99,8	796 L	35		0		Itra 29.3, OH-Itra 45.2 (24 hr)	Itra 2.5, OH-Itra 5.3
Ketoconazole	200 mg po	C	Tab ± food	variable	3.5 (SD)	99	1.2 L/kg	8	ND	<10	No	12	1-2
Posaconazole oral susp	400 mg po bid	C	Susp + food	ND	0.2-1.0 (200 mg SD)	98-99	226-295 L	20-66	ND	ND	Yes *(JAC 56:745, 2005)*	9.1 (12 hr)	3-5
Posaconazole tab	300 mg tab po q24h	C	Tab + food	54	2.1-2.9 (SS)	98-99	226-295 L	20-66	ND	ND	Yes *(JAC 56:745, 2005)*	37.9 (24 hr)	3-5
Posaconazole injection	300 mg IV q24h	C	-	-	3.3 (SS)	98-99	226-295 L	20-66	ND	ND	Yes *(JAC 56:745, 2005)*	36.1 (24 hr)	1,5
Voriconazole	200 mg po q12h	D	Tab/susp no food	96	3 (SS)	58	4.6 L/kg Vss	variable	ND	22-100	Yes *(CID 37:728, 2003)*	39.8 (24 hr)	1-2
Echinocandins													
Anidulafungin	100 mg IV q24h	B			7.2 (SS)	>99	30-50 L	26,5			No	112 (24 hr)	
Caspofungin	50 mg IV q24h	C			8.7 (SS)	97	9.7 L Vss	13	ND		No	87.3 (24 hr)	
Micafungin	100 mg IV q24h	C			10.1 (SS)	>99	0.39 L/kg	15-17			No	97 (24 hr)	

Preg Risk: FDA risk categories: A = no risk, **B** = No risk – human studies, **C** = toxicity in animals - inadequate human studies, **D** = human risk, but benefit may outweigh risk, **X** = fetal abnormalities – risk > benefit; **Food Effect (PO dosing): + food** = take with food, **no food** = take without food, **± food** = take with or without food; **Oral % AB** = % absorbed; **Peak Serum Level: SD** = after single dose, **SS** = steady state after multiple doses; **Volume of Distribution (Vd): V/F** = Vd/oral bioavailability, **Vss** = Vd at steady state, **Vss/F** = Vd at steady state/oral bioavailability; **CSF Penetration:** therapeutic efficacy comment based on dose, usual susceptibility or target organism & penetration into CSF; **AUC** = area under drug concentration curve; **24hr** = AUC 0-24; **Tmax** = time to max plasma concentration.

TABLE 9A (7) *(Footnotes at the end of table)*

DRUG	REFERENCE DOSE (SINGLE OR MULTIPLE)	PREG RISK	FOOD REC (PO DRUGS)[1]	ORAL ABS (%)	PEAK SERUM CONC[2] (μg/mL)	PROTEIN BINDING (%)	VOLUME OF DISTRIBUTION (Vd)[3]	AVG SERUM T½ (hr)[4]	BILE PEN (%)[5]	CSF/ BLOOD[6] (%)	CSF PENETRATION[7]	AUC[8] (μg*hr/mL)	Tmax (hr)
ANTIMYCOBACTERIALS													
First line, tuberculosis													
Ethambutol	25 mg/kg po	C	Tab + food	80	2-6 (SD)	10-30	6 L/kg Vss/F	4		10-50	No	29,6	2-4
Isoniazid (INH)	300 mg po	C	Tab/syrup no food	100	3-5 (SD)	<10	0.6-1.2 L/kg	0.7-4		up to 90	Yes	20,1	1-2
Pyrazinamide	20-25 mg/kg po	C	Tab ± food	95	30-50 (SD)	5-10		10-16		100	Yes	500	2
Rifabutin	300 mg po	B	Cap + food	20	0.2-0.6 (SD)	85	9.3 L/kg Vss	32-67	300-500	30-70	ND	4.0 (24 hr)	2.5-4.0
Rifampin	600 mg po	C	Cap no food	70-90	7 (SD)	80	0.65 L/kg Vss	1.5-5	10.000	7-56	Yes	40-60 (24 hr)	1.5-2
Rifapentine	600 mg po q72h	C	Tab + food	ND	15 (SS)	98	70 L	13-14	ND	ND	ND	320 (72 hr)	4,8
Streptomycin	15 mg/kg IM	D			25-50 (SD)	0-10	0.26 L/kg	2,5	10-60	0-30	No		
Second line, tuberculosis													
Amikacin	15 mg/kg IM	D			25-50 (SD)	0-10	0.26 L/kg	2.5	10-60	0-30	No		
Bedaquiline	400 mg po qd	B	Tab + food	ND	3.3 (week 2)	>99	≈ 60 x total body water Vss	24-30 (terminal 4-5 mo)	ND	ND	ND	22 (24 hr) after 8 wk	5
Capreomycin	1 gm IM	C			30 (SD)	ND	0.4 L/kg	2-5	ND	<10	No	ND	1-2
Cycloserine	250 mg po	C	Cap no food	70-90	4-8 (SD)	<20	0.47 L/kg	10	ND	54-79	Yes	110	1-2
Ethionamide	500 mg po	C	Tab ± food	90	2.2 (SD)	10-30	80 L	1,9	ND	≈ 100	Yes	10,3	1,5
Kanamycin	15 mg/kg IM	D			25-50 (SD)	0-10	0.26 L/kg	2,5	10-60	0-30	No		
Para-aminosalicylic acid (PAS)	4 g (granules)po	C	Granules + food	ND	9-35 (SD)	50-60	0.9-1.4 L/kg V/F	0.75-1.0	ND	10-50	Marginal	108 (4 gm SD, 0-∞)	8
ANTIPARASITICS													
Antimalarials													
Artemether/ lumefantrine	4 tabs (80 mg/480 mg)	C	Tab + food	ND	Art 0.06-0.08, DHA 0.09-0.1, Lum 7.4-9.8 (SD)	Art 95.4, DHA 47-76, Lum 99.7	ND	Art 1.6-2.2, DHA 1.6-2.2, Lum 101-119				Art 0.15-0.26, DHA 0.29, Lum 158-243	Art 1.5-2, Lum 6-8
Artesunate (AS)	120 mg IV	?	-	-	DHA 2.4 (SD)	AS 62-75, DHA 66-82	AS 0.1-0.3, DHA 0.5-1 L/kg	AS 2-4 min, DHA 0.5-1 hr	ND	ND	ND	DHA 2.1 (SD, 0-∞)	25 min (to DHA)

Preg Risk: FDA risk categories: A = no risk, **B** = No risk – human studies, **C** = toxicity in animals - inadequate human studies, **D** = human risk, but benefit may outweigh risk, **X** = fetal abnormalities – risk > benefit; **Food Effect (PO dosing): + food** = take with food, **no food** = take without food, **± food** = take with or without food; **Oral % AB** = % absorbed; **Peak Serum Level: SD** = after single dose, **SS** = steady state after multiple doses; **Volume of Distribution (Vd): V/F** = Vd/oral bioavailability, **Vss** = Vd at steady state, **Vss/F** = Vd at steady state/oral bioavailability; **CSF Penetration:** therapeutic efficacy comment based on dose, usual susceptibility or target organism & penetration into CSF; **AUC** = area under drug concentration curve; **24hr** = AUC 0-24; **Tmax** = time to max plasma concentration.

TABLE 9A (8) *(Footnotes at the end of table)*

ORUG	REFERENCE DOSE (SINGLE OR MULTIPLE)	PREG RISK	FOOD REC (PO ORUGS)[1]	ORAL ABS (%)	PEAK SERUM CONC[2] (µg/mL)	PROTEIN BINOING (%)	VOLUME OF OISTRIBUTION (Vd)[3]	AVG SERUM T½ (hr)[4]	BILE PEN (%)[5]	CSF/ BLOOO[6] (%)	CSF PENETRATION[7]	AUC[8] (µg*hr/mL)	Tmax (hr)
ANTIPARASITICS, Antimalarials *(continued)*													
Atovaquone	750 po bid	C	Susp + food	47	24 (SS)	99.9	0.6 L/kg Vss	67	ND	<1	No	801 (750 mg x1)	ND
Chloroquine phosphate	300 mg base	C	Tab + food	90	0.06-0.09 (SD)	55	100-1000 L/kg	45-55 days (terminal)	ND	ND	ND	ND	1-6
Mefloquine	1.25 gm po	B	Tab + food		0.5-1.2 (SD)	98	20 L/kg	13-24 days					17
Proguanil[11]	100 mg po	C	Tab + food	ND	ND	75	1600-2600 L V/F	12-21	ND	ND	ND	ND	ND
Quinine sulfate	648 mg po	C	Cap + food	76-88	3.2 (SD)	69.92	2.5 7.1 l /kg V/F	9.7-12.5	ND	2-7	No	28 (12 hr)	2,8
ANTIPARASITICS, Other													
Albendazole	400 mg po	C	Tab + food		0.5-1.6 (sulfoxide)	70	ND	8-12					2-5 (sulfoxide)
Benznidazole	100 mg po	avoid	Tab + food	92	2.2-2.8	44	89.6 L V/F (newer data)	12-15	ND	ND	ND	ND	3-4
Dapsone	100 mg po q24h	C	Tab ± food	70-100	1.1 (SS)	70	1.5 L/kg	10-50				52.6 (24 hr)	2-6
Diethylcarbamazine	6 mg/kg po	avoid	Tab + food	80-85	1.93 (SD)	ND	182 L V/F	9	ND	ND	ND	23.8 (0-∞)	1-2
Ivermectin	12 mg po	C	Tab no food	60	0.05-0.08 (SD)	93	3-3.5 l /kg	20	ND	ND	No	ND	4
Miltefosine	50 mg po tid	D	Cap + food	ND	76 (after 23 days)	95	ND	7-31 days	ND	ND	ND	486	2-8
Nitazoxanide	500 mg po	B	Tab/susp + food	Susp 70% of tab	Tizox 9-11, gluc 7.3-10.5 (SD)	Tizox 99	ND	Tizox 1.3-1.8	ND	ND	ND	Tizox 40, gluc 46.5-63.0	Tizox, gluc: 1-4
Praziquantel	20 mg/kg po	B	Tab + food	80	0.2-2.0 (SD)		8000 l. V/F	0.8-1.5				1,51	1-3
Pyrimethamine	25 mg po	C	Tab ± food	High	0.1-0.3 (SD)	87	3 L/kg	96					2-6
Tinidazole	2 gm po	C	Tab + food	48	48 (SD)	12	50 L	13	ND	ND	ND	902	1.6
ANTIVIRALS (non-HIV)													
Hepatitis B													
Adefovir	10 mg po	C	Tab ± food	59	0.02 (SD)	<4	0.37 L/kg Vss	7,5				0,22	1,75
Entecavir	0.5 mg po q24h	C	Tab/soln no food	100	4.2 ng/mL (SS)	13	>0.6 L/kg V/F	128-149 (terminal)	ND	ND	ND	0.014 (24 hr)	0.5-1.5
Telbivudine	600 mg po q24h	B	Tab/soln ± food		3.7 (SS)	3,3	>0.6 L/kg V/F	40-49				26.1 (24 hr)	2

Preg Risk: FOA risk categories: A = no risk, **B** = No risk – human studies, **C** = toxicity in animals - inadequate human studies, **O** = human risk, but benefit may outweigh risk, **X** = fetal abnormalities – risk > benefit; **Food Effect (PO dosing): + food** = take with food, **no food** = take without food, **± food** = take with or without food; **Oral % AB** = % absorbed; **Peak Serum Level: SO** = after single dose, **SS** = steady state after multiple doses; **Volume of Distribution (Vd): V/F** = Vd/oral bioavailability, **Vss** = Vd at steady state, **Vss/F** = Vd at steady state/oral bioavailability; **CSF Penetration:** therapeutic efficacy comment based on dose, usual susceptibility or target organism & penetration into CSF; **AUC** = area under drug concentration curve; **24hr** = AUC 0-24; **Tmax** = time to max plasma concentration.

TABLE 9A (9) *(Footnotes at the end of table)*

DRUG	REFERENCE DOSE (SINGLE OR MULTIPLE)	PREG RISK	FOOD REC (PO DRUGS)[1]	ORAL ABS (%)	PEAK SERUM CONC[2] (μg/mL)	PROTEIN BINDING (%)	VOLUME OF DISTRIBUTION (Vd)[3]	AVG SERUM T½ (hr)[4]	BILE PEN (%)[5]	CSF/ BLOOD[6] (%)	CSF PENETRATION[7]	AUC[8] (μg*hr/mL)	Tmax (hr)
Hepatitis C													
Daclatasvir	60 mg po q24h		Tab ± food	67	0.18 (Cmin, SS)	99	47 Vss	12-15	ND	ND	ND	11 (24 hr)	2
Dasabuvir	250 mg po q12h	B	Tab + food	ND	0.03-3.1 (10-1200 mg SD)	ND	ND	5-8	ND	ND	ND	ND	3
Ledipasvir + Sofosbuvir	(90 mg + 400 mg) po q24h	B	Tab ± food	ND	Ledip: 0.3 (SS)	Ledip:>99.8	ND	Ledip:47	ND	ND	ND	Ledip: 7.3 (24hr)	Ledip: 4-4.5
Ombitasvir (with Paritaprevir/RTV)	25 mg po q24h	B	Tab + food	ND	0.56 (SS)	ND	ND	28-34	ND	ND	ND	0.53 (24 hr)	4-5
Paritaprevir/RTV (with Ombitasvir)	150 mg (+ RTV 100 mg) po q24h	B	Tab + food	ND	ND	ND	ND	5,8	ND	ND	ND	ND	4,3
Ribavirin	600 mg po	X	Tab/cap/soln + food	64	3.7 (SS)	minimal	2825 L V/F	44 (terminal 298)	ND	ND	ND	228 (12 hr)	2
Simeprevir	150 mg po	C	Cap + food	ND	ND	>99.9	ND	41	ND	ND	ND	57.5 (24 hr)	4-6
Sofosbuvir	400 mg po q24h	B	Tab ± food	ND	Sofos: 0.6 (SS)	Sofos: 61-65	ND	Sofos: 0.5-0.75	ND	ND	ND	Sofos: 0.9 (24 hr)	0.5-2
Herpesvirus													
Acyclovir	400 mg po bid	B	Tab/cap/susp ± food	10-20	1.21 (SS)	9-33	0.7 L/kg	2.5-3.5	ND	ND	ND	7.4 (24 hr)	1.5-2
Cidofovir (w/probenecid)	5 mg/kg IV	C	Probenecid: ± food		19.6 (SD)	<6	0.41 L/kg Vss	2.6 (diphosphate: 17-65)	ND	0	No	40,8	1,1
Famciclovir	500 mg po	B	Tab ± food	77	3-4 (SD)	<20	1.1 L/kg (Penciclovir)	2-3 (Penciclovir)				8.9 (Penciclovir)	0.9 (Penciclovir)
Foscarnet	60 mg/kg IV	C			155 (SD)	4	0.46 L/kg	3 (terminal 18-88)	No			2195 μM*hr	
Ganciclovir	5 mg/kg IV	C			8.3 (SD)	1-2	0.7 L/kg Vss	3,5				24,5	
Valacyclovir	1 gm po	B	Tab + food	55	5.6 (SD)	13-18	0.7 L/kg	3				19.5 (Acyclovir)	
Valganciclovir	900 mg po q24h	C	Tab/soln + food	59	5.6 (SS)	1-2	0.7 L/kg	4				29.1 (Ganciclo)	1-3 (Ganciclo)
Influenza													
Oseltamivir	75 mg po bid	C	Cap/susp ± food	75	carboxylate 0.35 (SS)	3	carboxylate 23-26 L	carboxylate 6-10				carboxylate 5.4 (24 hr)	
Peramivir	600 mg IV	C			46.8 (SD)	<30	12.56 L	20	ND	ND	ND	102.7 (0-∞)	
Rimantadine	100 mg po q12h	C	Tab ± food	75-93	0.4-0.5 (SS)	40	17-19 L/kg	25				3,5	6

Preg Risk: FDA risk categories: A = no risk, **B** = No risk – human studies, **C** = toxicity in animals - inadequate human studies, **D** human risk, but benefit may outweigh risk, **X** = fetal abnormalities – risk > benefit; **Food Effect (PO dosing): + food** = take with food, **no food** = take without food, **± food** = take with or without food; **Oral % AB** = % absorbed; **Peak Serum Level: SD** = after single dose, **SS** = steady state after multiple doses; **Volume of Distribution (Vd): V/F** = Vd/oral bioavailability, **Vss** = Vd at steady state, **Vss/F** = Vd at steady state/oral bioavailability; **CSF Penetration:** therapeutic efficacy comment based on dose, usual susceptibility or target organism & penetration into CSF; **AUC** = area under drug concentration curve; **24hr** = AUC 0-24; **Tmax** = time to max plasma concentration.

TABLE 9A (10) *(Footnotes at the end of table)*

DRUG	REFERENCE DOSE (SINGLE OR MULTIPLE)	PREG RISK	FOOD REC (PO DRUGS)	ORAL ABS (%)	PEAK SERUM CONC (μg/mL)	PROTEIN BINDING (%)	VOLUME OF DISTRIBUTION (Vd)	AVG SERUM T½ (hr)	INTRACEL L T½ (HR)	CPE[12]	CSF/BLOOD (%)	AUC (μg*hr/mL)	Tmax (hr)
ANTIRETROVIRALS													
NRTIs													
Abacavir (ABC)	600 mg po q24h	C	Tab/soln ± food	83	4.3 (SS)	50	0.86 L/kg	1,5	20,6	3	36	12 (24 hr)	1,3
Didanosine enteric coated (ddI)	400 mg EC po q24h (pt ≥60 kg)	B	Cap/soln no food	30-40	ND	< 5	308-363 L	1,6	25-40	2	ND	2,6(24 hr)	2
Emtricitabine (FTC)	200 mg po q24h	B	Cap/soln ± food	cap 93, soln 75	1.8 (SS)	< 4	ND	10	39	3	ND	10 (24 hr)	1-2
Lamivudine (3TC)	300 mg po q24h	C	Tab/soln ± food	86	2.6 (SS)	< 36	1.3 L/kg	5-7	18	2	ND	11 (300 mg x1)	ND
Stavudine (d4T)	40 mg po bid (pt ≥60 kg)	C	Cap/soln ± food	86	0.54 (SS)	< 5	46 L	1.2-1.6	3,5	2	20	2.6 (24 hr)	1
Tenofovir (TDF)	300 mg po q24h	B	Tab ± food	39 w/food	0.3 (300 mg x1)	< 7	1.2-1.3 L/kg Vss	17	>60	1	ND	2.3 (300 mg x1)	1
Zidovudine (ZDV)	300 mg po bid	C	Tab/cap/syrup ± food	60	1-2 (300 mg x1)	< 38	1.6 L/kg	0.5-3	11	4	2	2.1 (300 mg x1)	0.5-1.5
NNRTIs													
Delavirdine (DLV)	400 mg po tid	C	Tab ± food	85	19 (SS)	98	ND	5,8	ND	3	ND	180 μM*hr (24 hr)	1
Efavirenz (EFV)	600 mg po q24h	D	Cap/tab no food	42	4.1 (SS)	99	252 L V/F	40-55	ND	3	ND	184 μM*hr (24 hr)	3-5
Etravirine (ETR)	200 mg po bid	B	Tab + food	ND	0.3 (SS)	99,9	ND	41	ND	2	ND	9 (24 hr)	2.5-4.0
Nevirapine (NVP)	200 mg po bid	B	Tab/susp ± food	>90	2 (200 mg x1)	60	1.21 L/kg Vss	25-30	ND	4	63	110 (24 hr)	4
Rilpivirine (RPV)	25 mg po qd	B	Tab + food	ND	0.1-0.2 (25 mg x1)	99,7	152 L	45-50	ND	ND	ND	2,4 (24 hr)	4-5
PIs													
Atazanavir (ATV)	400 mg po q24h	B	Cap/powder + food	Good	2.3 (SS)	86	88.3 L V/F	7	ND	2	ND	22.3 (24 hr)	2,5
Cobicistat	150 mg po q24h	B	Take with food	ND	0.99 (SS)	97-98	ND	4-Mar	ND	ND	ND	7.6 (24 hr)	3.5
Darunavir (DRV)	600 mg (+ RTV 100 mg) po bid	C	Tab/susp + food	82	3.5 (SS)	95	2 L/kg	15	ND	3	ND	116.8 (24 hr)	2.5-4.0
Fosamprenavir (FPV)	700 mg (+RTV 100 mg) po bid	C	Tab ± food; susp: adult no, peds +	ND	6 (SS)	90	ND	7,7	ND	3	ND	79.2 (24 hr)	2,5
Indinavir (IDV)	800 mg (+ RTV 100 mg) po bid	C	Boosted cap + food	65	20.2 μM (SS)	60	ND	1.2-2.0	ND	4	11	249 μM*hr (24 hr)	0,8 (fasting)
Lopinavir/RTV (LPV/r)	400 mg/100 mg po bid	C	Tab ± food, soln + food	ND	9.6 (SS)	98-99	ND	LPV 5-6	ND	3	ND	LPV 186 (24 hr)	LPV 4

Preg Risk: FDA risk categories: A = no risk, **B** = No risk – human studies, **C** = toxicity in animals - inadequate human studies, **D** = human risk, but benefit may outweigh risk, **X** = fetal abnormalities – risk > benefit; **Food Effect (PO dosing): + food** = take with food, **no food** = take without food, **± food** = take with or without food; **Oral % AB** = % absorbed; **Peak Serum Level: SD** = after single dose, **SS** = steady state after multiple doses; **Volume of Distribution (Vd): V/F** = Vd/oral bioavailability, **Vss** = Vd at steady state, **Vss/F** = Vd at steady state/oral bioavailability; **CSF Penetration:** therapeutic efficacy comment based on dose, usual susceptibility or target organism & penetration into CSF; **AUC** = area under drug concentration curve; **24hr** = AUC 0-24; **Tmax** = time to max plasma concentration.

TABLE 9A (11) *(Footnotes at the end of table)*

DRUG	REFERENCE DOSE (SINGLE OR MULTIPLE)	PREG RISK	FOOD REC (PO DRUGS)	ORAL ABS (%)	PEAK SERUM CONC (μg/mL)	PROTEIN BINDING (%)	VOLUME OF DISTRIBUTION (Vd)	AVG SERUM T½ (hr)	INTRACEL L T½ (HR)	CPE[12]	CSF/BLOOD (%)	AUC (μg*hr/mL)	Tmax (hr)
PIs *(continued)*													
Nelfinavir (NFV)	1250 mg po bid	B	Tab/powder + food	20-80	3-4 (SS)	98	2-7 L/kg V/F	3.5-5	ND	1	0	53 (24 hr)	ND
Ritonavir (RTV)	Boosting dose varies	B	Cap/soln + food	65	11.2 (600 mg bid SS)	98-99	0.41 L/kg V/F	3-5	ND	1	ND	121.7 (600 mg soln SD)	soln 2-4
Saquinavir (SQV)	1 gm (+RTV 100 mg) po bid	B	Tab/cap + food	4 (SQV alone)	0.37 (SS)	97	700 L Vss	1-2	ND	1	ND	29.2 (24 hr)	ND
Tipranavir (TPV)	500 mg (+RTV 200 mg) po bid	C	Cap/soln + food	Low	47-57 (SS)	99,9	7.7-10 L	5.5-6	ND	1	ND	1600 μM*hr (24 hr)	3
INSTIs													
Dolutegravir (DTG)	50 mg po q24h	B	Tab ± food	ND	3.67 (SS)	>99	17.4 L V/F	14	ND	4	ND	53.6 (24 hr)	2-3
Elvitegravir (EVG)	85-150 mg po q24h	B	Tab + food	ND	1.2-1.5 (SS)	98-99	ND	8.7 (w/RTV)	ND	ND	ND	18 (24 hr)	4
Raltegravir (RAL)	400 mg po bid	C	Tab/susp ± food	ND	11.2 μM (SS)	83	287 L Vss/F	9	ND	3	1-53.5	28.7 μM*hr (12 hr)	3
Fusion, Entry Inhibitors													
Enfuvirtide (ENF, T20)	90 mg sc bid	B		84 (sc % ab)	5 (SS)	92	5.5 L Vss	3,8	ND	1	ND	97.4 (24 hr)	4-8
Maraviroc (MVC)	300 mg po bid	B	Tab ± food	33	0.3-0.9 (SS)	76	194 L	14-18	ND	3	ND	3 (24 hr)	0.5-4.0

[1] Refers to adult oral preparations unless otherwise noted; + food = take with food, no food = take without food, ± food = take with or without food
[2] SD = after a single dose, SS = at steady state
[3] V/F = Vd/oral bioavaitability; Vss = Vd at steady state; Vss/F = Vd at steady state/oral bioavailability
[4] Assumes CrCl >80 mL/min
[5] (Peak concentration in bile/peak concentration in serum) x 100. If blank, no data.
[6] CSF concentrations with inflammation.
[7] Judgment based on drug dose and organism susceptibility. CSF concentration ideally ≥10x MIC.
[8] AUC = area under serum concentration vs. time curve; 12 hr = AUC 0-12, 24 hr = AUC 0-24
[9] Concern over seizure potential (see *Table 10B*)
[10] Take all oral FQs 2-4 hours before sucralfate or any multivalent cation (calcium, iron, zinc).
[11] Given with atovaquone as Malarone for malaria prophylaxis
[12] CPE (CNS Penetration Effectiveness) value: 1=low penetration, 2-3=intermediate penetration, 4=highest penetration (Letendre et al, CROI 2010, abs #430)

Preg Risk: FDA risk categories: A = no risk, **B** = No risk – human studies, **C** = toxicity in animals - inadequate human studies, **D** = human risk, but benefit may outweigh risk, **X** = fetal abnormalities – risk > benefit; **Food Effect (PO dosing): + food** = take with food, **no food** = take without food, **± food** = take with or without food; **Oral % AB** = % absorbed; **Peak Serum Level: SD** = after single dose, **SS** = steady state after multiple doses; **Volume of Distribution (Vd): V/F** = Vd/oral bioavailability, **Vss** = Vd at steady state, **Vss/F** = Vd at steady state/oral bioavailability; **CSF Penetration:** therapeutic efficacy comment based on dose, usual susceptibility or target organism & penetration into CSF; **AUC** = area under drug concentration curve; **24hr** = AUC 0-24; **Tmax** = time to max plasma concentration.

TABLE 9B – PHARMACODYNAMICS OF ANTIBACTERIALS*

BACTERIAL KILLING/PERSISTENT EFFECT	DRUGS	THERAPY GOAL	PK/PD MEASUREMENT
Concentration-dependent/Prolonged persistent effect	Aminoglycosides; daptomycin; ketolides; quinolones; metro	High peak serum concentration	24-hr AUC[1]/MIC
Time-dependent/No persistent effect	Penicillins; cephalosporins; carbapenems; monobactams	Long duration of exposure	Time above MIC
Time-dependent/Moderate to long persistent effect	Clindamycin; erythro/azithro/clarithro; linezolid; tetracyclines; vancomycin	Enhanced amount of drug	24-hr AUC[1]/MIC

* Adapted from *Craig, WA: IDC No. Amer 17:479, 2003 & Drusano, G.L.: CID 44:79, 2007*

TABLE 9C– ENZYME -AND TRANSPORTER- MEDIATED INTERACTIONS OF ANTIMICROBIALS

DRUG	ISOZYME/TRANSPORTER THAT DRUG IS A SUBSTRATE OF	INHIBITED BY DRUG	INDUCED BY DRUG	IMPACT ON SERUM DRUG CONCENTRATIONS*
Antibacterials				
Azithromycin	PGP	PGP (weak)		mild ↑
Chloramphenicol		2C19, 3A4		↑
Ciprofloxacin		1A2; 3A4 (minor)		↑
Clarithromycin	3A4	3A4, PGP, OAT		↑
Erythromycin	3A4, PGP	3A4, PGP, OAT		↑
Levofloxacin		OCT		↑
Metronidazole		2C9		↑
Nafcillin			2C9 (?), 3A4	↓
Norfloxacin		1A2 (weak)		mild ↑
Oritavancin		2C9 (weak), 2C19 (weak)	2D6 (weak), 3A4 (weak)	mild ↑ or ↓
Quinupristin-Dalfopristin		3A4		↑
Rifampin	PGP	OAT	1A2, 2B6, 2C8, 2C9, 2C19, 2D6 (weak), 3A4, PGP	↓
Telithromycin		3A4; PGP (?)		↑
TMP/SMX	SMX: 2C9 (major), 3A4	TMP: 2C8; SMX: 2C9		↑
Trimethoprim		2C8		↑
Antifungals				
Fluconazole		2C9, 2C19, 3A4		↑
Isavuconazole	3A4	3A4, PGP, OCT2		↑
Itraconazole	3A4	3A4, PGP		↑
Ketoconazole	3A4	3A4, PGP		↑
Posaconazole	PGP	3A4, PGP		↑
Terbinafine		2D6		↑
Voriconazole	2C9, 2C19, 3A4	2C9, 2C19, 3A4		↑

TABLE 9C (2)

DRUG	Substrate	Inhibits	Induces	Impact
Antimycobacterials (Rifampin listed above)				
Bedaquiline	3A4			
Isoniazid (INH)	2E1	2C19, 3A4		↑
Rifabutin	3A4		3A4	↓
Rifapentine			2C9, 3A4	↓
Thalidomide	2C19			
Antiparasitics				
Artemether/Lumefantrine	3A4 (Art, Lum)	2D6 (Lum)	3A4 (Art)	↑ or ↓
Chloroquine	2C8, 2D6	2D6		↑
Dapsone	3A4			
Halofantrine	3A4	2D6		↑
Mefloquine	3A4, PGP	PGP		↑
Praziquantel	3A4			
Proguanil	2C19 (→cycloguanil)			
Quinine sulfate	main 3A4, also 1A2, 2C9, 2D6	2D6		↑
Tinidazole	3A4			
Antivirals (hepatitis C)				
Daclatasvir	3A4, PGP			-
Dasabuvir	3A4, PGP, OATP1B1	2C8, UGT1A1, OATP1B1, OATP1B3		↑
Ledipasvir	PGP, BCRP	PGP, BCRP		↑
Ombitasvir	3A4, PGP	2C8, UGT1A1		↑
Paritaprevir	2C8, 2D6, 3A4, PGP	UGT1A1, OATP1B1		↑
Simeprevir	3A4, PGP, OAT	1A2 (weak), 3A4, PGP, OAT		↑
Sofosbuvir	PGP, BCRP			
Antivirals (herpesvirus)				
Cidofovir	OAT1, OAT3			

TABLE 9C (3)

DRUG	Substrate	Inhibits	Induces	Impact
Antiretrovirals				
Atazanavir	3A4	1A2, 2C8, 3A4, UGT1A1		↑
Cobicistat (part of Stribild)	2D6, 3A4	2D6, 3A4, PGP, BCRP, OATP1B1, OATP1B3		↑
Darunavir	3A4	3A4		↑
Delavirdine	2D6, 3A4	2C9, 2C19, 3A4		↑
Dolutegravir	3A4, UGT1A1			
Efavirenz	2B6, 3A4	2B6, 2C9, 2C19	2C19, 3A4	↑ or ↓
Elvitegravir (part of Stribild)	CYP3A4, UGT1A1/3	PGP (weak)	2C9 (weak)	mild ↑ or ↓
Etravirine	2C9, 2C19, 3A4	2C9; 2C19 (weak)	3A4	↑ or ↓
Fosamprenavir	3A4	2C19, 3A4		↑
Indinavir	3A4, PGP	3A4, PGP		↑
Lopinavir	3A4	3A4		↑
Maraviroc	3A4, PGP	2D6		↑
Nelfinavir	2C9, 2C19, 3A4, PGP	3A4, PGP	3A4	↑ or ↓
Nevirapine	2B6, 3A4		3A4	↓
Raltegravir	UGT			
Rilpivirine	3A4			
Ritonavir	3A4, PGP	2D6, 3A4, PGP	long term (?): 1A2, 2B6, 2C9, 3A4, PGP	↑ or ↓
Saquinavir	3A4, PGP	3A4, PGP		↑
Tipranavir	3A4, PGP	1A2, 2C9, 2C19, 2D6	3A4; PGP (weak)	↑ or ↓

***Refers to serum concentrations of companion drugs that may be affected by the listed antimicrobial. ↑=increase, ↓=decrease, blank=no drugs should be affected**

TERMINOLOGY:

BCRP = breast cancer resistance protein
CYP450 nomenclature, e.g. 3A4: 3 = family, A = subfamily, 4 = gene
OAT = organic anion transporter
OATP = organic anion transporter polypeptide
OCT = organic cation transporter
PGP = P-glycoprotein
UGT = uridine diphosphate glucuronosyltransferase

REFERENCES:

Hansten PD, Hom JR. The Top 100 Drug Interactions: A Guide to Patient Management. Freeland (WA): H&H Publications, 2014; primary literature; package inserts.

TABLE 10A – ANTIBIOTIC DOSAGE* AND SIDE-EFFECTS

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE*	ADVERSE REACTIONS, COMMENTS *(See Table 10B for Summary)*
NATURAL PENICILLINS		
Benzathine penicillin G (Bicillin L-A)	**600,000–1.2 million units IM q2–4 wks**	**Allergic reactions a major issue.** 10% of all hospital admissions give history of pen allergy; but only 10% have allergic reaction if given penicillin. Why? Possible reasons: inaccurate history, waning immunity with age, aberrant response during viral illness. If given, **Bicillin C-R IM (procaine Pen + benzathine Pen)** could be reaction to procaine.
Penicillin G	**Low: 600,000–1.2 million units IM per day** **High: ≥20 million units IV q24h(=12 gm) div q4h**	**Most serious reaction is immediate IgE-mediated anaphylaxis;** incidence only 0.05% but 5-10% fatal. Other IgE-mediated reactions: urticaria, angioedema, laryngeal edema, bronchospasm, abdominal pain with emesis, or hypotension. All appear within 4 hrs. Can form IgE antibody against either the beta-lactam ring or the R-group side chain. **Morbilliform rash after 72 hrs is not IgE-mediated and not serious.**
Penicillin V (250 & 500 mg caps)	**0.25–0.5 gm po bid, tid, qid before meals & at bedtime.** Pen V preferred over Pen G for oral therapy due to greater acid stability.	**Serious late allergic reactions:** Coombs-positive hemolytic anemia, neutropenia, thrombocytopenia, serum sickness, interstitial nephritis, hepatitis, eosinophilia, drug fever. **Cross-allergy to cephalosporins and carbapenems** varies from 0-11%. One factor is similarity, or lack of similarity, of side chains. **For pen desensitization,** *see Table 7.* For skin testing, suggest referral to allergist. High **CSF** concentrations cause seizures. Reduce dosage with renal impairment, *see Table 17A.* Allergy refs: *AJM 121:572, 2008; NEJM 354:601, 2006; CID 59:1113, 2014; JAC 69:20-43, 2014.*
PENICILLINASE-RESISTANT PENICILLINS		
Dicloxacillin (Dynapen) (250 & 500 mg caps)	**0.125–0.5 gm po q6h before meals**	Blood levels ~2 times greater than cloxacillin so preferred for po therapy. Acute hemorrhagic cystitis reported. Acute abdominal pain with GI bleeding without antibiotic-associated colitis also reported.
Flucloxacillin[NUS] (Floxapen, Lutropin, Staphcil)	**0.25–0.5 gm po q6h** **1–2 gm IV q4h**	Cholestatic hepatitis occurs in 1:15,000 exposures: more frequently in age > 55 yrs, females and therapy > 2 wks duration. Can appear wks after end of therapy and take wks to resolve *(JAC 66:1431, 2011).* **Recommendation: use only in severe infection.**
Nafcillin (Unipen, Nafcil)	**1–2 gm IV/IM q4h.** Due to > 90% protein binding, need 12 gm/day for bacteremia.	Extravasation can result in tissue necrosis. With dosages of 200–300 mg per kg per day hypokalemia may occur. **Reversible neutropenia (over 10% with ≥21-day rx, occasionally WBC <1000 per mm^3).**
Oxacillin (Prostaphlin)	**1–2 gm IV/IM q4h.** Due to > 90% protein binding, need 12 gm/day for bacteremia.	**Hepatic dysfunction with ≥12 gm per day.** LFTs usually ↑ 2–24 days after start of rx, reversible. In children, more rash and liver toxicity with oxacillin as compared to nafcillin *(CID 34:50, 2002).*
AMINOPENICILLINS		
Amoxicillin (Amoxil, Polymox)	**250 mg–1 gm po tid**	IV available in UK & Europe. IV amoxicillin rapidly converted to ampicillin. Rash with infectious mono– *see Ampicillin.* Increased risk of cross-allergenicity with oral cephalosporins with identical side-chains: cefadroxil, cefprozil.
Amoxicillin extended release (Moxatag)	**One 775 mg tab po once daily**	Allergic reactions, C. difficile associated diarrhea, false positive test for urine glucose with clinitest.
Amoxicillin-clavulanate (Augmentin) **AM-CL extra-strength peds suspension (ES-600)** **AM-CL-ER—extended release adult tabs**	*See Comment for adult products* **Peds Extra-Strength susp.: 600/42.9 per 5 mL.** **Dose: 90/6.4 mg/kg div bid.** For adult formulations, *see Comments* IV amox-clav available in Europe	With bid regimen, less clavulanate & less diarrhea. In pts with immediate allergic reaction to AM-CL, ⅓ due to Clav component *(J Allergy Clin Immunol 125:502, 2010).* Positive blood tests for 1,3-beta D-glucan with IV AM-CL *(NEJM 354:2834, 2006).* Hepatotoxicity linked to clavulanic acid; AM-CL causes 13-23% of drug-induced liver injury. Onset delayed. Usually mild; rare liver failure *(JAC 66:1431, 2011).* **Comparison adult Augmentin dosage regimens:** Augmentin 500/125 1 tab po tid Augmentin 875/125 1 tab po bid Augmentin-XR 1000/62.5 2 tabs po bid
Ampicillin (Principen) (250 & 500 mg caps)	**0.25–0.5 gm po q6h.** **50–200 mg/kg IV/day.**	A maculopapular rash occurs (not urticarial), **not true penicillin allergy,** in 65–100% pts with infectious mono, 90% with chronic lymphocytic leukemia, and 15–20% in pts taking allopurinol. EBV-associated rash does not indicate permanent allergy; post-EBV no rash when challenged. Increased risk of true cross-allergenicity with oral cephalosporins with identical side chains: cefaclor, cephalexin, loracarbef.

*NOTE: all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function.

(See page 2 for abbreviations)

TABLE 10A (2)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE*	ADVERSE REACTIONS, COMMENTS *(See Table 10B for Summary)*
AMINOPENICILLINS *(continued)*		
Ampicillin-sulbactam (Unasyn)	**1.5–3 gm IV q6h; for Acinetobacter: 3 gm (Amp 2 gm/Sulb 1 gm) IV q4h**	Supplied in vials: ampicillin 1 gm, sulbactam 0.5 gm or amp 2 gm, sulbactam 1 gm. AM-SB is not active vs pseudomonas. Total daily dose sulbactam ≤4 gm. Increasing resistance of aerobic gram-negative bacilli. Sulbactam doses up to 9-12 gm/day evaluated *(J Infect 56:432, 2008)*. See also *CID 50:133, 2010*.
ANTIPSEUDOMONAL PENICILLINS		
Piperacillin-tazobactam (PIP-TZ) (Zosyn) Prolonged infusion dosing, see *Comment and Table 10E*. Obesity dosing, see *Table 17C*.	**Formulations:** PIP/TZ: **2/0.25 gm (2.25 gm)** PIP/TZ: **3/0.375 gm (3.375 gm)** PIP/TZ: **4/0.5 gm (4.5 gm)** **Standard Dose (no P. aeruginosa): 3.375 gm IV q6h or 4.5 gm IV q8h** **Standard Dose for P. aeruginosa: 3.375 gm IV q4h or 4.5 gm IV q6h**	Based on PK/PD studies, there is emerging evidence in support of **prolonged infusion** of PIP-TZ: Initial "loading" dose of 4.5 gm over 30 min, then ,4 hrs later, start 3.375 gm IV over 4 hrs q 8h (CrCl≥ 20) or 3.375 gm IV over 4 hrs q12h (CrCl<20) *(CID 44:357, 2007; AAC 54:460, 2010)*. • Cystic fibrosis + P. aeruginosa infection: 350-450 mg/kg/day div q4-6h • P. aeruginosa pneumonia: PIP-TZ or CIP or Tobra. If dosed correctly, no need for dual therapy. Misc: Assoc false-pos galactomannan test for aspergillus, thrombocytopenia 2.79 mEq Na^+ per gram of PIP. For obesity dosing adjustment see *Table 17C*, *page 229*. In critically ill pts, may contribute to thrombocytopenia *(PLoS One 8(11):e81477)*.
Temocillin[NUS]	**2 gm IV q12h.**	Semi-synthetic penicillin stable in presence of classical & ESBLs plus AmpC beta-lactamases. Source: *www.eumedica.be*
CARBAPENEMS. Review: *AAC 55:4943, 2011*. **NOTE: Cross allergenicity: In studies of pts with history of Pen-allergy but no confirmatory skin testing, 0-11% had allergic reactions with cephalosporin therapy** *(JAC 54:1155, 2004)*. **In better studies, pts with positive skin tests for Pen allergy were given Carbapenem: no reaction in 99%** *(J Allergy Clin Immunol 124:167, 2009)*. Of 12 pts with IgE-mediated reaction to ceph, 2 suffered rash & 1 an IgE reaction when given a carbapenem *(CID 59:1113, 2014)*. Incidence of carbapenem-resistant GNB highest in Georgia, Maryland & New York *(JAMA 314:1455 & 1479, 2015)*.		
Doripenem (Doribax) Ref: *CID 49:291, 2009. For prolonged infusion dosing, see Table 10E*	Intra-abdominal & complicated UTI: **500 mg IV q8h (1-hr infusion).** For prolonged infusion, see *Table 10E, page 119*. Do not use for pneumonia	Most common adverse reactions (≥5%): Headache, nausea, diarrhea, rash & phlebitis. Seizure reported in post-marketing surveillance. Can lower serum valproic acid levels. Adjust dose if renal impairment. Somewhat more stable in solution than **IMP** or **MER** *(JAC 65:1023, 2010; CID 49:291, 2009)*. FDA safety announcement (01/05/12): Trial of DORI for the treatment of VAP stopped early due to safety concerns. Compared to IMP, patients treated with DORI were observed to have excess mortality and poorer cure rate. **NOTE: DORI is not approved to treat any type of pneumonia; DORI is not approved for doses greater than 500 mg q8h.**
Ertapenem (Invanz)	**1 gm IV/IM q24h.**	**Lidocaine** diluent for IM use; ask about lidocaine allergy. Standard dosage may be inadequate in obesity (BMI ≥40). Reports of DRESS (drug rash eosinophilia systemic symptoms) Syndrome. Visual hallucinations reported *(NZ Med J 122:76, 2009)*. No predictable activity vs. P. aeruginosa.
Imipenem + cilastatin (Primaxin) Ref: *JAC 58:916, 2006*	**0.5 gm IV q6h**; for P. aeruginosa: 1 gm q6–8h *(see Comment)*.	For infection due to P. aeruginosa, increase dosage to 3 or 4 gm per day div. q8h or q6h. Continuous infusion of carbapenems may be more efficacious & safer *(AAC 49:1881, 2005)*. **Seizures:** In meta-analysis, risk of seizure low but greatest with carbapenems among beta-lactams. No diff between IMP and MER (JAC 69:2043, 2014). Cilastatin blocks enzymatic degradation of Imipenem in lumen of renal proximal tubule & also prevents tubular toxicity.
Meropenem (Merrem)	**0.5–1 gm IV q8h. Up to 2 gm IV q8h for meningitis. Prolonged infusion** in critically ill: If CrCl ≥ 50: 2 gm (over 3 hr) q8h If CrCl 30-49: 1 gm (over 3 hr) q8h If CrCl 10-29: 1 gm (over 3 hr) q12h *(Inten Care Med 37:632, 2011)*.	**Seizures:** In meta-analysis, risk of seizure low but greatest with carbapenems among beta-lactams. No diff between IMP and MER *(JAC 69:2043, 2014)*. Comments: Does not require a dehydropeptidase inhibitor (cilastatin). Activity vs aerobic gm-neg. slightly ↑ over IMP, activity vs staph & strep slightly ↓; anaerobes: B. ovatus, B. distasonis more resistant to meropenem.

(See page 2 for abbreviations)

*NOTE: all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function.

TABLE 10A (3)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE*	ADVERSE REACTIONS, COMMENTS *(See Table 10B for Summary)*
MONOBACTAMS		
Aztreonam (Azactam)	**1 gm q8h–2 gm IV q6h.**	Can be used in pts with allergy to penicillins/cephalosporins. Animal data and a letter raise concern about cross-reactivity with ceftazidime as **side-chains of aztreonam and ceftazidime are identical.**
Aztreonam for Inhalation (Cayston)	**75 mg inhaled tid x 28 days.** Use bronchodilator before each inhalation.	Improves respiratory symptoms in CF pts colonized with P. aeruginosa. Alternative to inhaled Tobra. AEs: bronchospasm, cough, wheezing. So far, no emergence of other resistant pathogens. Ref: *Chest 135:1223, 2009.*
CEPHALOSPORINS (1st parenteral, then oral drugs). NOTE: Prospective data demonstrate correlation between use of cephalosporins (esp. 3rd generation) and ↑ risk of C. difficile toxin-induced diarrhea. May also ↑ risk of colonization with vancomycin-resistant enterococci. *See Oral Cephalosporins, page 106*, **for important note on cross-allergenicity.**		
1st Generation, Parenteral		
Cefazolin (Ancef, Kefzol)	**1-1.5 gm IV/IM q8h, occasionally 2 gm IV q8h for serious infections, e.g., MSSA bacteremia (max. 12 gm/day)**	**Do not give into lateral ventricles—seizures!** No activity vs. MRSA.
2nd Generation, Parenteral (Cephamycins): May be active in vitro vs. ESBL-producing aerobic gram-negative bacilli. Do not use as there are no clinical data for efficacy.		
Cefotetan (Cefotan)	**1–3 gm IV/IM q12h. (max. dose not >6 gm q24h).**	Increasing resistance of B. fragilis, Prevotella bivia, Prevotella disiens (most common in pelvic infections); do not use for intra-abdominal infections. Methylthiotetrazole (MTT) side chain can inhibit vitamin K activation. Avoid alcohol-disulfiram reaction.
Cefoxitin (Mefoxin)	**1 gm q8h–2 gm IV/IM q6-8h.**	Increasing resistance of B. fragilis isolates.
Cefuroxime (Kefurox, Ceftin, Zinacef)	**0.75–1.5 gm IV/IM q8h.**	Improved activity against H. influenzae compared with 1st generation cephalosporins. *See Cefuroxime axetil for oral preparation.*
3rd Generation, Parenteral—Use correlates with incidence of C. difficile toxin diarrhea; most are inactivated by ESBLs and amp C cephalosporinase from aerobic gram-negative bacilli.		
Cefoperazone-sulbactam[NUS] (Sulperazon)	**Usual dose (Cefoperazone comp) 1–2 gm IV q12h;** if larger doses, do not exceed 4 gm/day of sulbactam.	In SE Asia & elsewhere, used to treat intra-abdominal, biliary, & gyn. infections. Other uses due to broad spectrum of activity. Possible clotting problem due to side-chain.
Cefotaxime (Claforan)	**1 gm q8–12h to 2 gm IV q4h.**	Maximum daily dose: 12 gm; give as 4 gm IV q8h. Similar to ceftriaxone but, unlike ceftriaxone, but requires multiple daily doses.
Ceftazidime (Fortaz, Tazicef)	**Usual dose: 1–2 gm IV/IM q8–12h.** **Prolonged infusion dosing:** Initial dose: 15 mg/kg over 30 min, then immediately begin: If CrCl > 50: 6 gm (over 24 hr) daily If CrCl 31-50: 4 gm (over 24 hr) daily If CrCl 10-30: 2 gm (over 24 hr) daily *(AAC 49:3550, 2005; Infect 37:418, 2009).*	Often used in healthcare-associated infections, where P. aeruginosa is a consideration. Use may result in ↑ incidence of C. difficile-assoc. diarrhea and/or selection of vancomycin-resistant E. faecium. Risk of cross-allergenicity with aztreonam (same side chain).
Ceftazidime-avibactam(Avycaz)	2.5 gm (2 gm ceftazidime/0.5 gm avibactam) IV q8h for gram-negative complicated UTI & complicated intra-abdominal infection (add metronidazole 500 mg IV q8h)	Infuse over 2 hrs. Active against many isolates with several ESBLs and AmpC beta-lactamases. Cross-reaction in beta-lactam allergic pts. Decreased efficacy w/ CrCl 30-50 mL/min.
Ceftizoxime (Cefizox)	From **1-2 gm IV q8-12h** up to **2 gm IV q4h.**	Maximum daily dose: 12 gm; can give as 4 gm IV q8h
Ceftriaxone (Rocephin)	Commonly used IV dosage in adults: **1-2 gm once daily** Purulent meningitis: **2 gm q12h.** Can give **IM** in 1% lidocaine.	**"Pseudocholelithiasis"** 2° to sludge in gallbladder by ultrasound (50%), symptomatic (9%) *(NEJM 322:1821, 1990).* More likely with ≥2 gm per day with pt on total parenteral nutrition and not eating *(AnIM 115:712, 1991).* Clinical significance still unclear but has led to cholecystectomy *(JID 17:356, 1995)* and gallstone pancreatitis *(Ln 17:662, 1998).* In pilot study: 2 gm once daily by continuous infusion superior to 2 gm bolus once daily *(JAC 59:285, 2007).* For Ceftriaxone Desensitization, *see Table 7, page 83.*

(See page 2 for abbreviations)

*NOTE: all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function.

TABLE 10A (4)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE*	ADVERSE REACTIONS, COMMENTS *(See Table 10B for Summary)*
CEPHALOSPORINS (1st parenteral, then oral drugs) *(continued)*		
Other Generation, Parenteral: All are substrates for ESBLs & amp C cephalosporinase for aerobic gram-negative bacilli. Cefepime penetrates to target faster than other cephalosporins.		
Cefepime (Maxipime) Obesity dosing, *see Table 17C*	**Usual dose: 1–2 gm IV q8-12h.** **Prolonged infusion dosing:** Initial dose: 15 mg/kg over 30 min, then immediately begin: If CrCl > 60: 6 gm (over 24 hr) daily If CrCl 30-60: 4 gm (over 24 hr) daily If CrCl 11-29: 2 gm (over 24 hr) daily	Active vs P. aeruginosa and many strains of Enterobacter, Serratia, C. freundii resistant to ceftazidime, cefotaxime, aztreonam. More active vs MSSA than 3rd generation cephalosporins. Not "porin-dependent". Neutropenia after 14 days rx *(Scand J Infect Dis 42:156, 2010)*. **FDA Safety warning (June 2012)**: risk of non-convulsive status epilepticus, especially in pts with renal insufficiency when doses not adjusted. Seizure activity resolved after drug discontinuation and/or hemodialysis in the majority of pts. Postulated mechanism: binding to GABA receptors *(Scand J Infect Dis 46:272, 2014; Crit Care 17:R264, 2013.*
Cefpirome[NUS] (HR 810)	**1–2 gm IV q12h**	Similar to cefepime; ↑ activity vs enterobacteriaceae, P. aeruginosa, Gm + organisms. Anaerobes: less active than cefoxitin, more active than cefotax or ceftaz.
Ceftaroline fosamil (Teflaro)	**600 mg IV q12h (5-60 min infusion)** Pneumonia/bacteremia 600 mg IV q8h[NAI]. *See Comment*	**Avid binding to PBP 2a; active vs. MRSA.** Inactivated by Amp C & ESBL enzymes. Approved for MRSA skin and skin structure infections and used for MRSA pneumonia and bacteremia, but not approved indications *(J Infect Chemother 19:42, 2013)*. Active in vitro vs. VISA, VRSA. Refs: *CID 52:1156, 2011; Med Lett 53:5, 2011.* Used successfully for bacteremia and bone/joint infections, but NAI *(AAC 58:2541, 2014)*.
Ceftazidime-avibactam (Avycaz)	2.5 gm (2 gm ceftazidime/0.5 gm avibactam) IV over 2 hrs q8h for gram-negative complicated UTI & add metronidazole 500 mg IV q8h for complicated intra-abdominal infection	Active against ESBL- & KPC-producing aerobic gm-neg bacilli. No activity vs. GNB-producing metallo-carbapenemases. Decreased efficacy in pts with w/ CrCl 30-50 mL/min (in clinical trials).
Ceftobiprole[NUS]	**0.5 gm IV q8h for mixed gm- neg & gm-pos infections. 0.5 gm IV q12h for gm-pos infections**	Infuse over 2 hrs for q8h dosing, over 1 hr for q12h dosing. Associated with caramel-like taste disturbance. Ref.: *Clin Microbiol Infections 13(Suppl 2):17 & 25, 2007.* Active vs. MRSA.
Ceftolozane-tazobactam (Zerbaxa)	1.5 gm (1/0.5 gm) IV q8h for gm-neg complicated UTI & complicated intra-abdominal (add Metro 500 mg IV q8h) infection	Infuse over 1 hr. Active vs. P. aeruginosa and many gm-neg bacteria producing beta-lactamases. Cross-reaction in Beta-lactam allergic pts. Decreased efficacy w/ CrCl 30-50 mL/min.

(See page 2 for abbreviations)

*NOTE: all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function.

TABLE 10A (5)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE*	ADVERSE REACTIONS, COMMENTS *(See Table 10B for Summary)*
CEPHALOSPORINS (1st parenteral, then oral drugs) *(continued)*		
Oral Cephalosporins		**Cross-Allergenicity: Patients with a history of IgE-mediated allergic reactions to penicillin (e.g., bronchospasm anaphylaxis, angioneurotic edema, immediate urticaria) should not receive a cephalosporin.** If the history is a "measles-like" rash to penicillin, available data suggest a 5–10% risk of rash in such patients; there is no enhanced risk of anaphylaxis. • In pts with history of Pen "reaction" and no skin testing, 0.2-8.4% react to a cephalosporin *(Aller Asthma Proc 26:135, 2006)*. If positive Pen G skin test, only 2% given a cephalosporin will react. Can predict with cephalosporin skin testing, but not easily available *(An IM 141:16, 2004; AJM 125:572, 2008)*. • IgE antibodies against either ring structure or side chains; 80% pts lose IgE over 10 yrs post-reaction *(J Aller Clin Immunol 103:918, 1999)*. Amox, Cefadroxil, Cefprozil have similar side chains; Amp, Cefaclor, Cephalexin, Cephedrine have similar side chains. • If Pen/Ceph skin testing not available or clinically no time, proceed with cephalosporin if history does not suggest IgE-mediated reaction, prior reaction more than 10 yrs ago or cephalosporin side chain differs from implicated Pen. Any of the cephalosporins can result in **C. difficile toxin**-mediated diarrhea/enterocolitis. The reported frequency of nausea/vomiting and non-C. difficile toxin diarrhea is summarized in *Table 10B*. There are **few drug-specific adverse effects, e.g.:** **Cefaclor:** Serum sickness-like reaction 0.1–0.5%--arthralgia, rash, erythema multiforme but no adenopathy, proteinuria or demonstrable immune complexes. **Cefdinir:** Drug-iron complex causes red stools in roughly 1% of pts. **Cefditoren pivoxil:** Hydrolysis yields pivalate. Pivalate absorbed (70%) & becomes pivaloylcarnitine which is renally excreted; 39–63% **↓ in serum carnitine concentrations.** Carnitine involved in fatty acid (FA) metabolism & FA transport into mitochondria. Effect transient & reversible. Contraindicated in patients with carnitine deficiency or those in whom inborn errors of metabolism might result in clinically significant carnitine deficiency. Also contains caseinate (milk protein); **avoid if milk allergy** (not same as lactose intolerance). Need gastric acid for optimal absorption. **Cefpodoxime:** There are rare reports of acute liver injury, bloody diarrhea, pulmonary infiltrates with eosinophilia. **Cephatexin:** Can cause false-neg. urine dipstick test for leukocytes.
1st Generation, Oral		
Cefadroxil (Duricef) (500 mg caps, 1 gm tabs)	**0.5–1 gm po q12h.**	
Cephalexin (Keflex) (250 & 500 mg tabs)	**0.25–1 gm po q6h (max 4 gm/day).**	
2nd Generation, Oral		
Cefaclor (Ceclor, Raniclor) (250 & 500 mg caps)	**0.25–0.5 gm po q8h.**	
Cefprozil (Cefzil) (250 & 500 mg tabs)	**0.25–0.5 gm po q12h.**	
Cefuroxime axetil po (Ceftin)	**0.125–0.5 gm po q12h.**	
3rd Generation, Oral		
Cefdinir (Omnicef) (300 mg cap)	**300 mg po q12h or 600 mg q24h.**	
Cefditoren pivoxil (Spectracef)	**400 mg po bid.**	
Cefixime (Suprax) (400 mg tab)	**0.4 gm po q12–24h.**	
Cefpodoxime proxetil (Vantin)	**0.1–0.2 gm po q12h.**	
Ceftibuten (Cedax) (400 mg tab)	**0.4 gm po q24h.**	
AMINOGLYCOSIDES AND RELATED ANTIBIOTICS--*See Table 10D, page 118, and* Table 17A, *page 215*		
GLYCOPEPTIDES, LIPOGLYCOPEPTIDES, LIPOPEPTIDES		
Dalbavancin (Dalvance)	**1000 mg IV over 30 min; one week later, 500 mg IV over 30 min.** Avoid use with saline, drug may precipitate out of solution.	**If CrCl<30**: 750 mg IV initial dose, then one week later 375 mg IV. **Hemodialysis:** Dose as for normal renal function Red man syndrome can occur with rapid infusion. Potential cross-reaction in those with hypersensitivity to other glycopeptides. No activity vs. VRE. No drug-drug interactions.
Daptomycin (Cubicin) (Ref on resistance: *CID 50:S10, 2010*). Case series success in treating right- & left-sided endocarditis with higher dose of 8-10 mg/kg/day *(JAC 68:936 & 2921, 2013)*.	**Skin/soft tissue: 4 mg per kg IV over 2 or 30 minutes q24h** **Bacteremia/right-sided endocarditis: 6 mg per kg IV over 2 or 30 minutes q24h; up to 12 mg/kg IV q24h under study** **Morbid obesity:** base dose on total body weight *(AAC 51:2741, 2007)*, for other dosing recommendations, see *Table 17C, page 229*. Dapto + ceftaroline may work as salvage therapy in pts with refractory MRSA bacteremia *(AAC 57:66, 2013; AAC 56:5296, 2012)*.	**Pneumonia:** Dapto should not be used to treat pneumonia unless hematogenous in origin and is FDA approved for right-sided endocarditis with or without septic embolization/hematogenous pneumonia due to S. aureus. **Dapto Resistance:** Can occur de novo, after or during Vanco therapy, or after or during Dapto therapy *(CID 50(Suppl 1):S10, 2010)*. As Dapto MIC increases, MRSA more susceptible to TMP-SMX, nafcillin, oxacillin *(AAC 54:5187, 2010; CID 53:158, 2011)*. **Potential muscle toxicity:** At 4 mg per kg per day, ↑ CPK in 2.8% dapto pts & 1.8% comparator-treated pts. Risk increases if min conc >24.3 mg/L *(CID 50:1568, 2010)*. Suggest weekly CPK; DC dapto if CPK exceeds 10x normal level or if symptoms of myopathy and CPK > 1,000. Package insert: stop statins during dapto rx. Dapto interferes with protime reagents & artificially prolongs the PT. *(Blood Coag & Fibrinolysis 19:32, 2008)*. **NOTE:** Dapto well-tolerated in healthy volunteers at doses up to 12 mg/kg q24h x 14d *(AAC 50:3245, 2006)* and in pts given mean dose of 8 mg/kg/day *(CID 49:177, 2009)*. **Immune thrombocytopenia** reported *(AAC 56:6430, 2012)*. Reversible neutropenia with long-term use reported *(CID 56:1353, 2013)*. **Eosinophilic pneumonia**/chronic steroid-dep pneumonia reported *(CID 50:737, 2010; CID 50:e63, 2010)*.
Oritavancin (Orbactiv) Review: *CID 61:627, 2015*	**1200 mg IV over 3 hr x 1 dose.** Dilute in D5W; do not use saline	Artificially increases PT & INR x 24 hr&aPTT x 48 hr. **Drug-drug interactions with warfarin:** ↑ warfarin serum levels. Acute urticarial has occurred. No dose adjustment for renal or hepatic insuff. Not removed by hemodialysis. In vitro activity vs. VRE *(AAC 56:1639, 2012)*.

(See page 2 for abbreviations)

*NOTE: all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function.

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE*	ADVERSE REACTIONS, COMMENTS *(See Table 10B for Summary)*
GLYCOPEPTIDES, LIPOGLYCOPEPTIDES, LIPOPEPTIDES *(continued)*		
Teicoplanin[NUS] (Targocid)	**For septic arthritis—maintenance dose 12 mg/kg per day; S. aureus endocarditis—trough serum levels >20 mcg/mL required (12 mg/kg q12h times 3 loading dose, then 12 mg/kg q24h)**	Hypersensitivity: fever (at 3 mg/kg 2.2%, at 24 mg per kg 8.2%), skin reactions 2.4%. Marked ↓ platelets (high dose ≥15 mg per kg per day). Red neck syndrome less common than with vancomycin.
Telavancin (Vibativ) Lipoglycopeptide Ref: *CID 60:787, 2015; CID 61(Suppl 2), 2015*	10 mg/kg IV q24h if CrCl >50 mL/min. Infuse each dose over 1 hr.	**Avoid during pregnancy: teratogenic in animals.** Do pregnancy test before therapy. Adverse events: **dysgeusia (taste) 33%;** nausea 27%; vomiting 14%; headache 14%; ↑ creatinine (3.1%); foamy urine (13%); flushing if infused rapidly. In clin trials, **evidence of renal injury** in 3% telavancin vs. 1% vanco. In practice, renal injury reported in 1/3 of 21 complicated pts *(JAC 67:723, 2012)*. Interferes with PT, aPTT & INR for 18 hrs post-infusion.
Vancomycin (Vancocin) Guidelines Ref: *CID 49:325, 2009.* *See Comments for po dose.* Continuous infusion dosing, *see Table 10E*	**Initial doses based on actual wt, including for obese pts.** Subsequent doses adjusted based on measured trough serum levels. **For critically ill pts, give loading dose of 25-30 mg/kg IV then 15-20 mg/kg IV q8-12h.** Target trough level is 15-20 µg/mL. For individual doses over 1 gm, infuse over 1.5-2 hrs. **Dosing for morbid obesity (BMI ≥40 kg/m^2): If CrCl ≥50 mL/min & pt not critically ill:** 30 mg/kg/day divided q8-12h—no dose over 2 gm. Infuse doses of 1 gm or more over 1.5-2 hrs. Check trough levels. **Morbid obesity & critically ill:** Loading dose of 25-30 mg/kg (based on actual wt), then 15-20 mg/kg (actual wt) IV q8-12h. Infuse over 1.5-2 hrs. **Limit maximal single dose to 2 gm.** Oral tabs for C. difficile: 125 mg po q6h Generic drug now available	Vanco treatment failure of MRSA bacteremia associated with Vanco trough concentration <15 µg/mL & MIC > 1 µg/mL *(CID 52:975, 2011)*. IDSA Guideline supports target trough of 15-20 µg/mL *(CID 52:e18, 2011)*. Pertinent issues: • Max Vanco effect vs. MRSA when ratio of AUC/MIC > 400 *(CID 52:975, 2011)*. • MIC values vary with method used, so hard to be sure/compare *(JCM 49:269, 2011)*. • With MRSA Vanco MIC = 1 & Vanco dose >3 gm/day IV, AUC/MIC > 400 in 80% with est. risk of nephrotoxicity of 25%. With MIC = 2 & 4 gm/day IV, AUC/MIC > 400 in only 57% (nephrotoxicity risk 35%) *(CID 52:969, 2011)*. • Higher Vanco doses assoc with nephrotoxicity; causal relation unproven; other factors: renal disease, other nephrotoxic drugs, shock/vasopressors, radiographic contrast *(AAC 52:1330, 2008; AAC 55:3278, 2011; AJM 123:182e1, 2010)*. • If pt clinically failing Vanco (regardless of MIC or AUC/MIC), consider other drugs active vs. MRSA: ceftaroline, daptomycin, linezolid, telavancin. *(see Table 5A for MDR options)*. **PO vanco for C. difficile colitis: 125 mg po q6h.** Commercial po formulation very expensive. Can compound po vanco from IV formulation: 5 g, IV vanco powder + 47.5 mL sterile H_2O, 0.2 gm saccharin, 0.05 gm stevia powder, 40 mL glycerin and then enough cherry syrup to yield 100 mL = 50 mg vanco/mL. Oral dose = 2.5 mL q6h po. **Intrathecal dose:** 5-10 mg/day (infants); 10-20 mg/day (children & adults) to target CSF concentration of 10-20 µg/mL. **Nephrotoxicity:** Risk increases with dose and duration; reversible *(AAC 57:734, 2013)*. **Red Neck Syndrome:** consequence of rapid infusion with non-specific histamine release. **Other adverse effects:** rash, immune thrombocytopenia *(NEJM 356:904, 2007)*, fever, neutropenia, initial report of dose-dependent decrease in platelet count *(JAC 67:727, 2012)*, **IgA bullous dermatitis** *(CID 38:442, 2004)*. **Obesity dosing:** Frequent under dosing *(AJM 121:515, 2008)*. For obesity dosing adjustments, see *Table 17C , page 229*. For CrCl calculation for morbidly obese patient see *Table 10D* or *Am J Health Sys Pharm 66:642, 2009*.

(See page 2 for abbreviations)

*NOTE: all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function.

TABLE 10A (7)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE*	ADVERSE REACTIONS, COMMENTS *(See Table 10B for Summary)*
CHLORAMPHENICOL, CLINDAMYCIN(S), ERYTHROMYCIN GROUP, KETOLIDES, OXAZOLIDINONES, QUINUPRISTIN-DALFOPRISTIN		
Chloramphenicol (Chloromycetin)	**50-100 mg/kg/day po/IV div q6h (max 4 gm/day)**	No oral drug distrib in U.S. Hematologic (↓ RBC ~1/3 pts, aplastic anemia 1:21,600 courses). Gray baby syndrome in premature infants, anaphylactoid reactions, optic atrophy or neuropathy (very rare), digital paresthesias, minor disulfiram-like reactions. Recent review suggests Chloro is probably less effective than current alternatives for serious infection: respiratory tract, enteric, meningitis *(JAC 70:979, 2015)*.
Clindamycin (Cleocin)	**0.15–0.45 gm po q6h. 600–900 mg IV/IM q8h.**	Based on number of exposed pts, these drugs are the most frequent cause of **C. difficile toxin-mediated diarrhea.** In most severe form can cause pseudomembranous colitis/toxic megacolon. Available as caps, IV sol'n, topical (for acne) & intravaginal suppositories & cream. **Used to inhibit synthesis of toxic shock syndrome toxins.**
Lincomycin (Lincocin)	**0.6 gm IV/IM q8h.**	Risk of C. difficile colitis. Rarely used.
Erythromycin Group (Review drug interactions before use)		**Motilin:** activates duodenal/jejunal receptors that initiate peristalsis. Erythro (E) and E esters activate motilin receptors and cause uncoordinated peristalsis with resultant anorexia, nausea or vomiting. Less binding and GI distress with azithromycin/clarithromycin. No peristalsis benefit *(JAC 59:347, 2007)*. Systemic erythro in 1st 2 wks of life associated with **infantile hypertrophic pyloric stenosis** *(J Ped 139:380, 2001)*. **Frequent drug-drug interactions:** see *Table 22, page 235*. Major concern is prolonged QT_c interval on EKG. **Prolonged QTc:** Erythro, clarithro & azithro all increase risk of ventricular tachycardia via increase in QTc interval. Can be congenital or acquired *(NEJM 358:169, 2008)*. Caution if positive family history of sudden cardiac death, electrolyte abnormalities or concomitant drugs that prolong QTc.
Azithromycin (Zithromax) **Azithromycin ER** (Zmax)	**po preps:** Tabs 250 & 600 mg. Peds suspension: 100 & 200 mg per 5 mL. Adult ER suspension: 2 gm. Dose varies with indication, see *Table 1*, Acute otitis media *(page 11)*, acute exac. chronic bronchitis *(page 37)*, Comm.-acq. pneumonia *(pages39–40)*, & sinusitis *(page 50)*. **IV:** 0.5 gm per day.	
Erythromycin Base and esters (Erythrocin) IV name: E. lactobionate	**0.25 gm q6h–0.5 gm po/IV q6h: 15–20 mg/kg up to 4 gm q24h. Infuse over 30+ min.**	**↑ risk QTc >500 msec! Risk amplified by other drugs** [macrolides, antiarrhythmics, & drug-drug interactions *(see FQs page 110 for list)*]. *www.qtdrugs.org* & *www.torsades.org*. Ref: *Am J Med 128:1362, 2015*. Cholestatic hepatitis in approx. 1:1000 adults (not children) given E estolate. **Drug-drug interactions of note:** Erythro or clarithro with statins: high statin levels, rhabdomyolysis *(Ann Int Med 158:869, 2013)*; concomitant clarithro & colchicine (gout) can cause fatal colchicine toxicity (pancytopenia, renal failure) *(CID 41:291, 2005)*. Concomitant clarithro & Ca++ channel blockers increase risk of hypotension, kidney injury *(JAMA 310:2544, 2013)*. Hypoglycemia with concomitant sulfonylureas *(JAMA Int Med 174:1605, 2014)*. **Transient reversible tinnitus or deafness** with ≥4 gm per day of erythro IV in pts with renal or hepatic impairment. Reversible sensorineural hearing loss with Azithro *(J Otolaryngol 36:257, 2007)*. Dosages of oral erythro preparations expressed as base equivalents. Variable amounts of erythro esters required to achieve same free erythro serum level. **Azithromycin** reported to exacerbate symptoms of myasthenia gravis.
Clarithromycin (Biaxin) or clarithro extended release (Biaxin XL)	**0.5 gm po q12h.** **Extended release: Two 0.5 gm tabs po per day.**	
Fidaxomicin (Dificid) (200 mg tab)	**One 200 mg tab po bid x 10 days with or without food**	Approved for C. difficile toxin-mediated diarrhea, including hypervirulent NAP1/B1/027 strains. Minimal GI absorption; high fecal concentrations. Limited activity vs. normal bowel flora. In trial vs. po Vanco, lower relapse rate vs. non-NAP1 strains than Vanco *(NEJM 364:422, 2011)*. Despite absence of CI absorption, 12 pts developed allergic reactions; known macrolide allergy in 3 of 12 (CID 58:537, 2014).
Ketolide: **Telithromycin** (Ketek) *(Med Lett 46:66, 2004; Drug Safety 31:561, 2008)*	**Two 400 mg tabs po q24h.** 300 mg tabs available.	Drug warnings: acute liver failure & serious liver injury post treatment. *(AnIM 144:415, 447, 2006)*. **Uncommon: blurred vision** 2° slow accommodation; may cause exacerbation of **myasthenia gravis (Black Box Warning: Contraindicated in this disorder)**. Liver, eye and myasthenia complications may be due to inhibition of nicotinic acetylcholine receptor at neuromuscular junction *(AAC 54:5399, 2010)*. Potential QT_c prolongation. Several **drug-drug interactions** *(Table 22, page 237) (NEJM 355:2260, 2006)*.

(See page 2 for abbreviations)

*NQTE: all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function.

TABLE 10A (8)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE*	ADVERSE REACTIONS, COMMENTS *(See Table 10B for Summary)*
CHLORAMPHENICOL, CLINDAMYCIN(S), ERYTHROMYCIN GROUP, KETOLIDES, OXAZOLIDINONES, QUINUPRISTIN-DALFOPRISTIN *(continued)*		
Tedizolid phosphate (Sivextro) *Ref: CID 58(Suppl 1):S1557, 2014; CID 61:1315, 2015.*	**200 mg IV/po once daily.** Infuse IV over 1 hr.	**IV dose reconstituted in 250 mL of normal saline;** incompatible with lactated ringers due to absence of solubility in presence of divalent cations. SSI clinical trial result *(LnID 14:696, 2014; JAMA 309:559 & 609, 2013).* Excreted by liver. No adjustment for renal insufficiency. Weak inhibitor of monoamine oxidase, hence risk of serotonin syndrome, but low risk based on in vitro, animal & human study *(AAC 57:3060, 2013).*
Linezolid (Zyvox) (600 mg tab) Review: *JAC 66(Suppl 4):3, 2011*	**PO or IV dose: 600 mg q12h.** Available as 600 mg tabs, oral suspension (100 mg per 5 mL), & IV solution. Special populations Refs: Renal insufficiency *(J Infect Chemother 17:70, 2011)*; Liver transplant *(CID 42:434, 2006)*; Cystic fibrosis *(AAC 48:281, 2004)*; Burns *(J Burn Care Res 31:207, 2010).* Obesity: clinical failure with standard dose in 265 kg patient *(Ann Pharmacother 47:e25, 2013).*	**Reversible myelosuppression:** thrombocytopenia, anemia, & neutropenia reported. Most often after >2 wks of therapy. Increased risk on hemodialysis or peritoneal dialysis *(Int J Antimicrob Ag 36:179, 2010; JAC doi:10.1093/jac/dkv184)* **Lactic acidosis; peripheral neuropathy, optic neuropathy:** After 4 or more wks of therapy. Data consistent with time and dose-dependent inhibition of intramitochondrial protein synthesis *(Pharmacotherapy 27:771, 2007).* Neuropathy, not reversible. **Inhibitor of monoamine oxidase;** risk of severe hypertension if taken with foods rich in tyramine. Avoid concomitant pseudoephedrine, phenylpropanolamine, and caution with SSRIs[1]. **Serotonin syndrome** (fever, agitation, mental status changes, tremors). Risk with concomitant SSRIs: *(CID 42:1578 and 43:180, 2006).* Actual incidence seems low *(AAC 57:5901, 2013).* Other adverse effects: black hairy tongue and acute interstitial nephritis *(IDCP 17:61, 2009).* **Rhabdomyolysis:** case probably related to linezolid in a patient receiving linezolid as a component of multi-drug therapy for XDR tuberculosis *(CID 54:1624, 2012).* **Resistance:** Linezolid resistant S. epidermidis and MRSA due to mutation of the 23S rRNA binding site *(JAC 68:4, 2013).*
Quinupristin + dalfopristin (Synercid) *(CID 36:473, 2003)*	**7.5 mg per kg IV q12h for skin/skin structure infections, infused over 1 hour.** [For previous indication of VRE infection, dose used was 7.5 mg per kg IV q8h.] Give by central line.	Venous irritation (5%); none with central venous line. Asymptomatic ↑ in unconjugated bilirubin. **Arthralgia** 2%–50% *(CID 36:476, 2003).* **Note:** E. faecium susceptible; E. faecalis resistant. **Drug-drug interactions:** Cyclosporine, nifedipine, midazolam, many more—*see Table 22.*
TETRACYCLINES		
Doxycycline (Vibramycin, Doryx, Monodox, Adoxa, Periostat) (20, 50, 75, 100 mg tab)	**0.1 gm po/IV q12h**	Similar to other tetracyclines. ↑ nausea on empty stomach. Erosive esophagitis, esp. if taken at bedtime; **take with lots of water.** Phototoxicity & photo-onycholysis occur but less than with tetracycline. Deposition in teeth less. Can be used in patients with renal failure. *Comments:* Effective in treatment and prophylaxis for malaria, leptospirosis, typhus fevers.
Minocycline (Minocin, Dynacin) (50, 75, 100 mg cap; 45, 90, 135 mg ext rel tab; IV prep)	**200 mg po/IV loading dose, then 100 mg po/IV q12h** IV minocycline available.	**Vestibular symptoms** (30–90% in some groups, none in others): vertigo 33%, ataxia 43%, nausea 50%, vomiting 3%, women more frequently than men. Hypersensitivity pneumonitis, reversible, ~34 cases reported *(BMJ 310:1520, 1995).* Can cause slate-grey **pigmentation** of the skin and other tissues with long-term use. *Comments:* More effective than other tetracyclines vs staph and in prophylaxis of meningococcal disease. P. acnes: many resistant to other tetracyclines, not to mino. Induced autoimmunity reported in children treated for acne *(J Ped 153:314, 2008).* Active vs Nocardia asteroides, Mycobacterium marinum and many acinetobacter isolates.
Tetracycline, Oxytetracycline (Sumycin) (250, 500 mg cap) *(CID 36:462, 2003)*	**0.25–0.5 gm po q6h, 0.5–1 gm IV q12h**	GI (oxy 19%, tetra 4), anaphylactoid reaction (rare), deposition in teeth, negative N balance, hepatotoxicity, enamel agenesis, pseudotumor cerebri/encephalopathy. Outdated drug: Fanconi syndrome. *See drug-drug interactions, Table 22.* **Contraindicated in pregnancy, hepatotoxicity in mother, transplacental to fetus.** *Comments:* **Pregnancy:** IV dosage over 2 gm per day may be associated with fatal hepatotoxicity. (Ref: *JAC 66:1431, 2011*).

[1] **SSRI** = selective serotonin reuptake inhibitors, e.g., fluoxetine (Prozac).

(See page 2 for abbreviations)

*NOTE: all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function.

TABLE 10A (9)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE*		ADVERSE REACTIONS, COMMENTS *(See Table 10B for Summary)*
TETRACYCLINES *(continued)*			
Tigecycline (Tygacil) Meta-analysis & editorial: *Ln ID 11:804 & 834, 2011.* Also *CID 54:1699 & 1710, 2012.*	**100 mg IV initially, then 50 mg IV q12h with po food, if possible to decrease risk of nausea.**	**If severe liver dis. (Child Pugh C):** 100 mg IV initially, then 25 mg IV q12h	Derivative of tetracycline. High incidence of nausea (25%) & vomiting (20%) but only 1% of pts discontinued therapy. Pregnancy Category D. Do not use in children under age 18. Like other tetracyclines, may cause photosensitivity, pseudotumor cerebri, pancreatitis, a catabolic state (elevated BUN) and maybe hyperpigmentation *(CID 45:136, 2007)*. Decreases serum fibrinogen *(AAC 59:1650, 2015)*. **Tetracycline, minocycline & tigecycline** associated with acute pancreatitis *(Int J Antimicrob Agents, 34:486, 2009)*. **Black Box Warning:** In meta-analysis of clinical trials, all cause mortality higher in pts treated with tigecycline (2.5%) vs. 1.8% in comparators. Cause of mortality risk difference of 0.6% (95% CI 0.1, 1.2) not established. Tigecycline should be reserved for use in situations when alternative treatments are not suitable *(FDA MedWatch Sep 27, 2013)*. Poor result due to low serum levels *(AAC 56:1065 & 1466, 2012)*; high doses superior to low doses for HAP *(AAC 57:1756, 2013)*.
FLUOROQUINOLONES (FQs): All can cause false-positive urine drug screen for opiates *(Pharmacother 26:435, 2006)*. Toxicity review: *Drugs Aging 27:193, 2010.*			
Ciprofloxacin (Cipro) and **Ciprofloxacin-extended release** (Cipro XR, Proquin XR) (100, 250, 500, 750 mg tab; 500 mg ext rel tab)	Usual Parenteral Dose: **400 mg IV q12h** For P. aeruginosa: **400 mg IV q8h** Uncomplicated Urethritis/cystitis (Oral) Dose: **250 mg po bid or CIP XR 500 mg po once daily** Other Indications (Oral): **500-750 mg po bid**		FQs are a common precipitant of **C. difficile toxin-mediated diarrhea.** **Children:** No FQ approved for use under age 16 based on joint cartilage injury in immature animals. Articular SEs in children est. at 2–3% *(LnID 3:537, 2003)*. The exception is anthrax. Pathogenesis believed to involve FQ chelation of Mg++ and damaging chondrites *(AAC 51:1022, 2007; Int J Antimicrob Agents 33:194, 2009)*. No evidence of cartilage damage with Levo in children *(Pediatrics 134:e146, 2014)*. **CNS toxicity:** Poorly understood. Varies: lightheadedness, confusion, seizures. May be aggravated by NSAIDs. Peripheral neuropathy occurs: rapid onset, potentially permanent injury. **Gemi skin rash:** Macular rash after 8–10 days of rx. Incidence of rash with ≤5 days of therapy only 1.5%. Frequency highest females, < age 40, treated 14 days (22.6%). In men, < age 40, treated 14 days, frequency 7.7%. Mechanism unclear. Indication to DC therapy. Ref: Diag Micro Intect Dis 68:140, 2010. **Hypoglycemia/hyperglycemia (Dysglycemia):** Increased risk, esp. of hypoglycemia in diabetic pts from any of the marketed FQs *(CID 57:971, 2013)*. **Thrombocytopenia** in critically ill *(PLoS One 8(11):e81477)*. **Opiate screen false-positives:** FQs can cause false-positive urine assay for opiates *(Ann Pharmacotherapy 38:1525, 2004)*. **Photosensitivity:** *See Table 10C, page 117.* **QT_c (corrected QT) interval prolongation:** ↑ QT_c (>500 msec or >60 msec from baseline) is considered possible with any FQ. ↑ QT_c can lead to torsades de pointes and ventricular fibrillation. Overall risk is 4.7/10,000 person yrs *(CID 55:1457, 2012)*. Risk low with current marketed drugs. Risk ↑ in women, ↓ K^+, ↓ mg^{++}, bradycardia. (Refs.: *CID 43:1603, 2006*). Major problem is ↑ risk with concomitant drugs.
Gatifloxacin (Tequin)[NUS] *See comments*	**200–400 mg IV/po q24h**. *(See comment)* Ophthalmic solution (Zymar)		
Gemifloxacin (Factive) (320 mg tab)	**320 mg po q24h**.		

(See page 2 for abbreviations)

*NOTE: all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function.

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE*	ADVERSE REACTIONS, COMMENTS *(See Table 10B for Summary)*
FLUOROQUINOLONES (FQs) *(continued)*		
Levofloxacin (Levaquin) (250, 500, 750 mg tab)	**250–750 mg po/IV q24h.** For most indications, 750 mg is preferred dose. PO therapy: avoid concomitant dairy products, multivitamins, iron, antacids due to chelation by multivalent cations & interference with absorption. No dose adjustment for morbid obesity.	**Avoid concomitant drugs with potential to prolong QTc such as** *(see www.qtdrugs.org; www.torsades.org)*: **Antiarrhythmics:** Amiodarone, Disopyramide, Dofetilide, Flecainide, Ibutilide, Procainamide, Quinidine, quinine, Sotalol **Anti-Infectives:** Azoles (not Posa), Clarithro/erythro, FQs (not CIP), Halofantrine, NNRTIs, Protease Inhibitors, Pentamidine, Telavancin, Telithromycin **Anti-Hypertensives:** Bepridil, Isradipine, Nicardipine, Moexipril **CNS Drugs:** Fluoxetine, Haloperidol, Phenothiazines, Pimozide, Quetiapine, Risperidone, Sertraline, Tricyclics, Venlafaxine, Ziprasidone **Misc:** Dolasetron, Droperidol, Fosphenytoin, Indapamide, Methadone, Naratriptan, Salmeterol, Sumatriptan, Tamoxifen, Tizanidine
Moxifloxacin (Avelox)	**400 mg po/IV q24h.** Note: no need to increase dose for morbid obesity *(JAC 66:2330, 2011)*. Qphthalmic solution (Vigamox)	**Tendinopathy:** Over age 60, approx. 2–6% of all Achilles tendon ruptures attributable to use of FQ *(ArIM 163:1801, 2003)*. ↑ risk with concomitant steroid, renal disease or post-transplant (heart, lung, kidney) *(CID 36:1404, 2003)*. **Chelation:** Risk of chelation of oral FQs by multivalent cations **(Ca++, Mg++, Fe++, Zn++)**. Avoid dairy products, multivitamins *Clin Pharmacokinet 40 (Suppl 1) 33:2001)*.
Ofloxacin (Floxin)	**200–400 mg po bid.** Qphthalmic solution (Qcuflox)	**Allergic Reactions:** Rare (1:50,000). IgE-mediated: urticaria, anaphylaxis. 3 pts with Moxi had immediate reactions but tolerated CIP *(Ann Pharmacother 44:740, 2010)*. **Myasthenia gravis:** Any of the FQs may exacerbate muscle weakness in pts. with myasthenia gravis. **Retinal detachment:** Association with FQs in 2 studies *(JAMA 307:1414, 2012; CID 58:197, 2014)*; no association found in 2 other studies *(JAMA 310:2151 & 2184, 2013; JAC 69:2563, 2014)*.
Prulifloxacin Ref: Drugs 64:2221, 2004.	Tablets: 250 and 600 mg. Usual dose: **600 mg po once daily**	Not available in the U.S.
POLYMYXINS (POLYPEPTIDES) Note: Proteus sp., Providencia sp, Serratia sp., B. cepacia are intrinsically resistant to polymyxins. Review: *CID 59:88, 2014*.		
Polymyxin B (Poly-Rx) 1 mg = 10,000 international units **Where available, Polymyxin B preferred over Colistin.** Avoid monotherapy, see *Comment*.	Doses based on actual body weight. ***LOADING DOSE:*** 2.5 mg/kg IV over 2 hrs. ***MAINTENANCE DOSE:*** 12 hrs later 1.5 mg/kg over 1 hr, then repeat q12h. Combination therapy with **carbapenem** suggested to increase efficacy and reduce risk of resistance. No dose reduction for renal insufficiency. **Intrathecal therapy for meningitis:** 5 mg/day into CSF x 3-4 days, then 5 mg every other day x 2 or more weeks.	**Adverse effects: Neurologic:** rare, but serious, is neuromuscular blockade; other, circumoral paresthesias, extremity numbness, blurred vision, drowsy, irritable, ataxia; can manifest as respiratory arrest *(Chest 141:515, 2012)*. **Renal:** reversible acute tubular necrosis. Renal injury in 42% (Polymyxin B) vs. 60% (Colistin) *(CID 57:1300, 2013)*. PK study showed no need to reduce dose for renal insufficiency *(CID 57:524, 2013)*. **Polymyxin B preferred over Colistin** (see Comment under Colistin for rationale). In retrospective study, lower mortality from P. aeruginosa & A. baumannii with Polymyxin B + carbapenem vs. polymyxin monotherapy *(AAC 59:6575, 2015)*.

(See page 2 for abbreviations)

*NQTE: all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function.

TABLE 10A (11)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE*	ADVERSE REACTIONS, COMMENTS *(See Table 10B for Summary)*
POLYMYXINS (POLYPEPTIDES) *(continued)*		
Colistin, Polymyxin E (Colymycin) **All doses are based on mg of Colistin base.** **Calculated doses are higher than the package insert dosing; need to avoid underdosage in the critically ill.** **Do not use as monotherapy (combine with carbapenem)** Dosing formula based on PK study of 105 pts *(AAC 55:3284, 2011)*. Loading dose *(AAC 53:3430, 2009)*. **Recommendations are evolving: see Sanford Guide digital editions for most current information and dosing calculator.**	• ***Severe Systemic Infection:*** ***LOADING DOSE:*** 2.5 (targeted average serum steady state level) x 2 x body weight in kg (lower of ideal or actual weight) IV. This will often result in a loading dose of over 300 mg of colistin base. First maintenance dose is given 12 hrs. later. ***MAINTENANCE DOSE:*** Formula for calculating the daily maintenance dosage: ▪ 2.5 (the desired serum steady state concentration) x [(1.5 x CrCln) +30] = total daily dose. Divide and give q8h or maybe q12h. The maximum suggested daily dose is 340 mg. ▪ **NOTE:** CrCln is the Creatinine Clearance (CrCl) normalized (n) for Body Surface Area (BSA) such that the CrCln = CrCl x BSA in m^2/1.73 m^2. • *Combination therapy is recommended for all pts:* **Colistin** (as above) + (**IMP** or **MER**) • ***Cystic fibrosis:*** 3-8 mg/kg/day q8h (based on IBW) • **Intrathecal or intraventricular for meningitis:** 10 mg/day • ***Inhalation therapy:*** 50-75 mg in 3-4 mL of Saline via nebulizer 2-3x/day	• **GNB Resistance**: Some sp. are intrinsically resistant: Serratia sp, Proteus sp, Providencia sp., B. cepacia. In vitro and in animal models, gram-negative bacilli quickly become resistant. Synergy with Rifampin or Tigecycline unpredictable. The greater the resistance of GNB to Colistin, the greater the susceptibility to beta-lactams (AM-SB, PIP-TZ, extended spectrum Ceph, maybe carbapenems). • **Caveat**: higher doses of colistin (> 5 mg/kg of ideal body weight per day) are associated with increased risk of nephrotoxicity and should be reserved for critically ill patients (Clin Infect Dis 53:879, 2011). • **Bactericidal activity concentration dependent** but no post-antibiotic effect; do not dose once daily. • **Nephrotoxic:** exact risk unclear, but increased by concomitant nephrotoxins (IV contrast), hypotension, maybe Rifampin. Reversible. • **Neurotoxicity.** Frequent: circumoral paresthesia, vertigo, abnormal vision, confusion, ataxia. Rare: neuromuscular blockade with respiratory failure. • **Caution:** Some colistimethate products are expressed in IUs. To convert IUs to mg of colistin base: 1,000,000 IUs colistimethate = 80 mg colistimethate base = 30 mg colistin base. *See CID 58:139, 2014.* • Colistin preferred over Polymyxin B for treatment of UTIs. **Urine concentration of Polymyxin B is very low.** • Note: Polymyxin B is preferred over Colistin, except for UTIs because: 1) ease of dose calculation; 2) rapid achievement of stable serum level; 3) low inter patient variability in PK; 4) no dose adjustment for renal insufficiency *(CID 59:88, 2014)* • Ascorbic acid 1 gm IV q4-6h may lower risk of nephrotoxicity *(CID doi 10.1093, 2015)*
MISCELLANEOUS AGENTS		
Fosfomycin (Monurol) (3 gm packet)	**3 gm with water po times 1 dose.** For emergency use: single patient IND for IV use. From FDA: 1-888-463-6332.	Diarrhea in 9% compared to 6% of pts given nitrofurantoin and 2.3% given TMP-SMX. Available outside U.S., IV & PO, for treatment of multi-drug resistant bacteria. For MDR-GNB: 6-12 gm/day IV divided q6-8h. Ref: *Int J Antimicrob Ag 37:415, 2011.*
Fusidic acid[NUS] (Fucidin, Taksta)	**500 mg po/IV tid (Denmark & Canada) US: loading dose of 1500 mg po bid x 1 day, then 600 mg po bid**	Activity vs. MRSA of importance. Approved outside the U.S.; currently in U.S. clinical trials. Ref for proposed US regimen: *CID 52 (Suppl 7):S520, 2011.*
Methenamine hippurate (Hiprex, Urex)	**1 gm po bid**	Nausea and vomiting, skin rash or dysuria. Overall ~3%. Methenamine requires (pH ≤ 5.5) urine to liberate formaldehyde. Useful in suppressive therapy after infecting organisms cleared; do not use for pyelonephritis. *Comment:* Do not force fluids; may dilute formaldehyde. Of no value in pts with chronic Foley. If urine pH > 5.5, co-administer ascorbic acid (1–2 gm q4h) to acidify the urine; cranberry juice (1200–4000 mL per day) has been used, results ±. Do not use concomitantly with sulfonamides (precipitate), or in presence of renal or severe hepatic dysfunction.
Methenamine mandelate (Mandelamine)	**1 gm po qid**	
Metronidazole (Flagyl) (250, 375, 500 mg tab/cap) Ref.: *Activity vs. B. fragilis* Still drug of choice *(CID 50 (Suppl 1):S16, 2010).*	Anaerobic infections: **usually IV, 7.5 mg per kg (~500 mg) q6h (not to exceed 4 gm q24h).** With long T½, **can use IV at 15 mg per kg q12h.** If life-threatening, use loading dose of **IV 15 mg per kg. Oral dose: 500 mg qid; extended release tabs** available 750 mg	**Common AEs:** nausea (12%), metallic taste, "furry" tongue. **Avoid alcohol during 48 hrs after last dose to avoid disulfiram reaction (N/V, flushing, tachycardia, dyspnea).** Neurologic AEs with high dose/long Rx: peripheral, autonomic and optic neuropathy. Aseptic meningitis, encephalopathy, seizures & reversible cerebellar lesion reported. Risk of hypoglycemia with concomitant sulfonylureas. Also: topical & vaginal gels. Can use IV soln as enema for *C. diff colitis*. Resistant anaerobic organisms: Actinomycetes, Peptostreptococci. Once-daily IV dosing of 1,500 mg: rational based on long serum T1/2; standard in Europe; supportive retrospective studies in adults with intra-abdominal infections *(JAC 19:410, 2007).*

(See page 2 for abbreviations)

*NOTE: all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function.

TABLE 10A (12)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE*	ADVERSE REACTIONS, COMMENTS *(See Table 10B for Summary)*
MISCELLANEOUS AGENTS *(continued)*		
Nitazoxanide	*See Table 13B, page 162*	
Nitrofurantoin macrocrystals (Macrobid, Macrodantin, Furadantin) (25, 50, 100 mg caps) Systematic rev: *JAC70:2456, 2015*	Active UTI: **Furadantin/Macrodantin 50-100 mg po qid x 5-7 days OR Macrobid 100 mg po bid x 5-7 days** Dose for long-term UTI suppression: **50–100 mg at bedtime**	Absorption ↑ with meals. Increased activity in acid urine, much reduced at pH 8 or over. Nausea and vomiting, **peripheral neuropathy,** pancreatitis. **Pulmonary reactions** (with chronic rx): acute ARDS type, **chronic desquamative interstitial pneumonia with fibrosis**. Intrahepatic cholestasis & **hepatitis** similar to chronic active hepatitis. Hemolytic anemia in G6PD deficiency. Drug rash, eosinophilia, systemic symptoms (DRESS) hypersensitivity syndrome reported *(Neth J Med 67:147, 2009)*. Concern that efficacy may be reduced and AEs increased with CrCl under 40 mL/min. Should not be used in infants <1 month of age. Birth defects: increased risk reported *(Arch Ped Adolesc Med 163:978, 2009)*.
Rifampin (Rimactane, Rifadin) (150, 300 mg cap)	**300 mg po/IV bid or 600 mg po/IV qd.** Rapid selection of resistant bacteria if used as monotherapy	Causes orange-brown discoloration of sweat, urine, tears, contact lens. **Many important drug-drug interactions,** see *Table 22*. Immune complex flu-like syndrome: fever, headache, myalgias, arthralgia--especially with intermittent rx. Thrombocytopenia, vasculitis reported *(C Ann Pharmacother 42: 727, 2008)*. Can cause interstitial nephritis. Risk-benefit of adding RIF to standard therapies for S. aureus endocarditis *(AAC 52:2463, 2008)*. See also, *Antimycobacterial Agents, Table 12B, page 148*.
Rifaximin (Xifaxan) (200, 550 mg tab)	Traveler's diarrhea: **200 mg tab po tid** times 3 days. Hepatic encephalopathy: **550 mg tab po bid.** C. diff diarrhea as "chaser": **400 mg po bid**	For traveler's diarrhea and hepatic encephalopathy *(AAC 54:3618, 2010; NEJM 362:1071, 2010)*. In general, adverse events equal to or less than placebo.
Sulfonamides [e.g., sulfisoxazole (Gantrisin), sulfamethoxazole (Gantanol), (Truxazole), sulfadiazine]	Dose varies with indications. See *Nocardia & Toxoplasmosis*	**CNS:** fever, headache, dizziness; **Derm:** mild rash to life threatening Stevens-Johnson syndrome, toxic epidermal necrolysis, photosensitivity; **Hem:** agranulocytosis, aplastic anemia; **Cross-allergenicity:** other sulfa drugs, sulfonylureas, diuretics, crystalluria (esp. sulfadiazine-need ≥ 1500 mL po fluid/day); **Other:** serum sickness, hemolysis if G6PD def, polyarteritis, SLE reported.
Tinidazole (Tindamax)	**Tabs 250, 500 mg.** Dose for giardiasis: 2 gm po times 1 with food.	**Adverse reactions:** metallic taste 3.7%, nausea 3.2%, anorexia/vomiting 1.5%. All higher with multi-day dosing. Avoid alcohol during & for 3 days after last dose; cause disulfiram reaction, flushing, N/V, tachycardia.
Trimethoprim (Trimpex, Proloprim, and others) (100, 200 mg tab)	**100 mg po q12h or 200 mg po q24h.**	**CNS:** drug fever, aseptic meningitis; **Derm:** rash (3-7% at 200 mg/day), phototoxicity, Stevens-Johnson syndrome (rare), toxic epidermal necrolysis (rare); **Renal:** ↑ K+, ↓ Na+, ↑ Cr; **Hem:** neutropenia, thrombocytopenia, methemoglobinemia.
Trimethoprim (TMP)-Sulfamethoxazole (SMX) (Bactrim, Septra, Sulfatrim, Cotrimoxazole) Single-strength (SS) is 80 TMP/400 SMX, double-strength (DS) 160 TMP/800 SMX	**Standard po rx: 1 DS tab bid. P. carinii:** *see Table 11A, page 132.* **IV rx (base on TMP component): standard 8–10 mg per kg IV per day divided q6h, q8h, or q12h. For shigellosis: 2.5 mg per kg IV q6h.**	Adverse reactions in 10%: GI: nausea, vomiting, anorexia. Skin: Rash, urticaria, photosensitivity. More serious (1–10%): TMP, ACE inhibitors & aldactone increase serum K+. Higher incidence of severity when combined. Increased risk of death *(BMJ 349:g6196, 2014)*. **Stevens-Johnson syndrome & toxic epidermal necrolysis.** Skin reactions may represent toxic metabolites of SMX rather than allergy *(Ann Pharmacotherapy 32:381, 1998)*. Daily ascorbic acid 0.5–1.0 gm may promote detoxification *(JAIDS 36:1041, 2004)*. Risk of **hypoglycemia** with concomitant sulfonylureas. **Sweet's Syndrome** can occur. Hyperkalemia: Both TMP & ACE inhibitors can block renal tubular secretions of K+ & lead to dangerous hyperkalemia *(BMJ 349:g6196, 2014)*. TMP one etiology of **aseptic meningitis**. Report of psychosis during treatment of PCP *(JAC 66:1117, 2011)*. TMP-SMX contains sulfites and may trigger asthma in sulfite-sensitive pts. Frequent drug cause of thrombocytopenia. No cross allergenicity with other sulfonamide non-antibiotic drugs *(NEJM 349:1628, 2003)*. **For TMP-SMX desensitization,** *see Table 7, page 83.*

(See page 2 for abbreviations)

*NOTE: all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function.

TABLE 10A (13)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE*	ADVERSE REACTIONS, COMMENTS *(See Table 10B for Summary)*
Topical Antimicrobial Agents Active vs. S. aureus & Strep. pyogenes *(CID 49:1541, 2009)*. **Review of topical antiseptics, antibiotics** *(CID 49:1541, 2009)*.		
Bacitracin (Baciguent)	20% bacitracin zinc ointment, apply 1-5 x/day.	Active vs. staph, strep & clostridium. Contact dermatitis occurs. Available without prescription.
Fusidic acid[NUS] ointment	**2% ointment, apply tid**	Available in Canada and Europe *(Leo Laboratories)*. Active vs. S. aureus & S. pyogenes.
Mupirocin (Bactroban)	**Skin cream or ointment 2%: Apply tid times 10 days. Nasal ointment 2%: apply bid times 5 days.**	Skin cream: itch, burning, stinging 1–1.5%; Nasal: headache 9%, rhinitis 6%, respiratory congestion 5%. Not active vs. enterococci or gm-neg bacteria. Summary of resistance: *JAC 70:2681, 2015*. If large amounts used in azotemic pts, can accumulate polyethylene glycol *(CID 49:1541, 2009)*.
Polymyxin B—Bacitracin (Polysporin)	5000 units/gm; 400 units/gm. Apply 1-4x/day	Polymyxin active vs. some gm-neg bacteria but not Proteus sp., Serratia sp. or gm-pos bacteria. *See Bacitracin comment above*. Available without prescription.
Polymyxin B—Bacitracin—Neomycin (Neosporin, triple antibiotic ointment (TAO))	5000 units/gm; 400 units/gm; 3.5 mg/gm. Apply 1-3x/day.	*See Bacitracin and polymyxin B comments above*. Neomycin active vs. gm-neg bacteria and staphylococci; not active vs. streptococci. Contact dermatitis incidence 1%; risk of nephro- & oto-toxicity if absorbed. TAO spectrum broader than mupirocin and active mupirocin-resistant strains *(DMID 54:63, 2006)*. Available without prescription.
Retapamulin (Altabax)	1% ointment; apply bid. 5, 10 & 15 gm tubes.	Microbiologic success in 90% S. aureus infections and 97% of S. pyogenes infections *(J Am Acad Derm 55:1003, 2006)*. Package insert says **for MSSA only** (not enough MRSA pts in clinical trials). Active vs. some mupirocin-resistant S. aureus strains.
Silver sulfadiazine	1% cream, apply once or twice daily.	A sulfonamide but the active ingredient is released silver ions. Activity vs. gram-pos & gram-neg bacteria (including P. aeruginosa). Often used to prevent infection in pts with 2nd/3rd degree burns. Rarely, may stain into the skin.

(See page 2 for abbreviations)

*NOTE: all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function.

TABLE 10B – SELECTED ANTIBACTERIAL AGENTS—ADVERSE REACTIONS—OVERVIEW

Adverse reactions in individual patients represent all-or-none occurrences, even if rare. After selection of an agent, the physician should read the manufacturer's package insert [statements in the product labeling (package insert) must be approved by the FDA]. **For unique reactions, see the individual drug** (Table 10A) For drug-drug interactions, see Table 22.
Numbers = frequency of occurrence (%); + = occurs, incidence not available; ++ = significant adverse reaction; 0 = not reported; R = rare, defined as <1%.
NOTE: Important reactions in bold print. A blank means no data found. Any antibacterial can precipitate C. difficile colitis.

ADVERSE REACTIONS (AR) For unique ARs, see Individual drug, Table 10A	PENICILLINS, CARBAPENEMS, MONOBACTAMS, AMINOGLYCOSIDES																
		PENICILLINASE-RESISTANT ANTI-STAPH. PENICILLINS			AMINOPENICILLINS				AP PENS	CARBAPENEMS					AMINOGLYCO-SIDES	MISC.	
	Penicillin G, V	Dicloxacillin	Nafcillin	Oxacillin	Amoxicillin	Amox-Clav	Ampicillin	Amp-Sulb	Pip-Taz	Doripenem	Ertapenem	Imipenem	Meropenem	Aztreonam	Amikacin Gentamicin Kanamycin Netilmicin[NUS] Tobramycin	Linezolid	Tedizolid
Rx stopped due to AR						2-4.4			3.2	3.4			t.2	~ 1			0.5
Rash	**3**	**4**	**4**	**4**	**5**	**3**	**5**	**2**	**4**	**1-5**	+	+	+	**2**		**2**	
+ Coombs	3	0	R	R	+	0	+	0	+		**1**	2	+	R			
Neutropenia	R	0	+	R	+	+	+	+	+	R	+	+	+	+		1.1	0.5
Eosinophilia[1]	+	+	22	22	2	+	22	22	+		+	+	+	8			
Thrombocytopenia	R	0	R	R	R	R	R	R	+	+		+	+	+		3	2.3
Nausea/vomiting		+	0	0	2	3	2	+	7	4-12	3	2	4	R		6/4	8/3
Diarrhea		+	0	0	**5**	**9**	**10**	**2**	11	6-11	6	2	5	R		8.3	10
↑ LFTs	R	R	0	+	R	+	R	6	+	+	6	4	4	2		5-10	6
↑ BUN, Cr	R	0	0	0	R	R	R	R	+			+	0	0	**5–25**		
Seizures	R	0	0	+	0	R	R	0	R	*See footnote*[2]				+			
Ototoxicity	0	0	0	0	0	0	0	0	0			R		0	**3–14**		
Vestibular	0	0	0	0	0	0	0	0	0			0		0	**4–6**		

1 Eosinophilia in 25% of pts; of those 30% have clinical event (rash 30%, renal injury 15%, liver injury 6%, DRESS in 0.8% (J Allergy Clin Immunol doi 10.1076/j.jaci.2015.04.005

2 **All β-lactams in high concentration can cause seizures**. In rabbit, IMP 10x more neurofoxic than benzyl penicillin *(JAC 22:687, 1988)*. In clinical trial of IMP for pediatric meningitis, trial stopped due to seizures in 7/25 IMP recipients; hard to interpret as purulent meningitis causes seizures *(PIDJ 10:122, 1991)*. Risk with IMP ↓ with careful attention to dosage *(Epilepsia 42:1590, 2001)*.
Postulated mechanism: Drug binding to $GA8A_A$ receptor. IMP binds with greater affinity than MER.
Package insert, percent seizures: ERTA 0.5, IMP 0.4, MER 0.7. However, in 3 clinical trials of MER for bacterial meningitis, no drug-related seizures *(Scand J Inf Dis 31:3, 1999; Drug Safety 22:191, 2000)*.
In meta-analysis, seizure risk low but greatest with carbapenems vs. other beta-lactams. No difference in incidence between IMP & MER (JAC 69:2043, 2014).

TABLE 10B (2)

ADVERSE REACTIONS (AR) For unique ARs, see individual drug, Table 10A	CEPHALOSPORINS/CEPHAMYCINS																						
	Cefazolin	Cefotetan	Cefoxitin	Cefuroxime	Cefotaxime	Ceftazidime	Ceftaz-avi	Ceftizoxime	Ceftriaxone	Cefepime	Ceftaroline	Ceftobiprole[NUS]	Ceftolo-tazo	Cefaclor/ Cef.ER/ Loracarbef[NUS]	Cefadroxil	Cefdinir	Cefixime	Cefpodoxime	Cefprozil	Ceftibuten	Cefditoren pivoxil	Cefuroxime axetil	Cephalexin
Rx stopped due to AR		.								1.5	2.7	4	2			3		2.7	2	2	2	2.2	
Rash	+		2	R	2	2	<5	2	2	2	3	2.7	1	1	+	R	1	1	1	R	R	R	1
+ Coombs	3	+	2	R	6	4	2			14	9.8		<1	R							R	R	+
Neutropenia	+		2	R	+	1		+	2	1		+		+	+	R	R	R	R		R		3
Eosinophilia		+	3	7	1	8	<5	4	6	1		+				R	R	3	2	5	R	1	9
Thrombocytopenia	+					+	<5	+		+		+		2			R	R	+	R			
↑ PT/PTT		++	+		+	+		+	+	+													
Nausea/vomiting		1		R	R	R	2		R	1	4/2	+	3/1	2			7	4	4	2	6/1	3	
Diarrhea		4		R	1	1	4		3	1	5	9.1/4.8	2	1–4		15	16	7	3	3	1.4	4	
↑ LFTs	+	1	3	4	1	6	3	4	3	+	2	<2	1.7	3	+	1	R	4	2	R	R	2	+
Hepatic failure	0	0	0	0	0	0		0	0	0													
↑ BUN, Cr	+		3			R	1.5		1	+		R	1.5	+		R	+	4	R	R	R		+
Headache	0					1	10		R	2		4.5	6	3		2		1	R	R	2	R	+

ADVERSE REACTIONS (AR) For unique ARs, see individual drug, Table 10A	MACROLIDES			FLUOROQUINOLONES						OTHER AGENTS													
	Azithromycin, Reg. & ER	Clarithromycin, Reg. & ER	Erythromycin	Ciprofloxacin/ Cipro XR	Gatifloxacin[NUS]	Gemifloxacin	Levofloxacin	Moxifloxacin	Ofloxacin	Chloramphenicol	Clindamycin	Polymyxin B & E (Colistin)	Dalbavancin	Oritavancin	Daptomycin	Metronidazole	Quinupristin-dalfopristin	Rifampin	Telavancin	Tetracycline /Doxy/Mino	Tigecycline	TMP-SMX	Vancomycin
Rx stopped due to AR	1	3		3.5	2.9	2.2	4.3	3.8	4				3	3.8	2.8						5		
Rash	R		+	3	R	1–22[3]	2	R	2	+	+	+	2.7	<1.5	4	+	R		4	+	2.4	+	3
Nausea/vomiting	3	3	**25**	**5**	**8/<3**	**2.7**	**7/2**	**7/2**	**7**		+	+	6/3	9.9/4.6	6.3	**12**		+	27/14	+	30/20	+	+
Diarrhea	5	3–6	**8**	2	4	3.6	5	5	4	+	**7**		4.4	3.7	5	+		+	7	+	13	3	
↑ LFTs	R	R	+	2	R	1.5	0.1–1		2		+		0.8	2.8			2	+		+	4		0
↑ BUN, Cr	+	4		1					R		0	++			R			+	3	+	2	+	5
Dizziness, light headedness				R	3	0.8	**3**	**2**	**3**					2.7							3.5		
Headache	R	2		1	4	1.2	6	2		+	+	++	4.7	7.1	5	+				+		+	

[3] **Highest frequency:** females <40 years of age after 14 days of rx; with 5 days or less of Gemi, incidence of rash <1.5%.

TABLE 10C – ANTIMICROBIAL AGENTS ASSOCIATED WITH PHOTOSENSITIVITY

The following drugs (listed alphabetically) are known to cause photosensitivity in some individuals. Note that photosensitivity lasts for several days after the last dose of the drug, at least for tetracyclines. There is no intent to indicate relative frequency or severity of reactions. *Ref: Drug Saf 34:821, 2011.*

DRUG OR CLASS	COMMENT
Azole antifungals	Voriconazole, Itraconazole, Ketoconazole, but not Fluconazole
Bithionol	Old reports
Cefotaxime	Manifested as photodistributed telangiectasia
Ceftazidime	Increased susceptibility to sunburn observed
Dapsone	Confirmed by rechallenge
Doxycycline	Increased susceptibility to sunburn
Efavirenz	Three reports
Flucytosine	Two reports
Fluoroquinolones	Worst offenders have halogen atom at position 8
Griseofulvin	Not thought to be a potent photosensitizer
Isoniazid	Confirmed by rechallenge
Pyrimethamine	One report
Pyrazinamide	Confirmed by rechallenge
Quinine	May cross-react with quinidine
Saquinavir	One report
Tetracyclines	Least common with Minocycline; common with Doxycycline
Trimethoprim	Alone and in combination with Sulfamethoxazole

TABLE 10D – AMINOGLYCOSIDE ONCE-DAILY AND MULTIPLE DAILY DOSING REGIMENS

(See Table 17A, page 215, if estimated creatinine clearance <90 mL per min.)

- General Note: dosages are given as **once daily dose (OD)** and **multiple daily doses (MDD).**
- For **calculation of dosing weight in non-obese patients** use **Ideal Body Weight (IBW):**

  Female: 45.5 kg + 2.3 kg per inch over 60 inch height = dosing weight in kg;

  Male: 50 kg + 2.3 kg per inch over 60 inch height = dosing weight in kg.
- **Adjustment for calculation of dosing weight in obese patients** (actual body weight (ABW) is ≥ 30% above IBW): IBW + 0.4 (ABW minus IBW) = adjusted weight (*Pharmacotherapy 27:1081, 2007; CID 25:112, 1997*).
- If CrCl >90 mL/min, use doses in this table. If CrCl <90, *use doses in Table 17A, page 215.*
- **For non-obese patients, calculate estimated creatinine clearance (CrCl) as follows:**

$$\frac{(140 \text{ minus age})(\text{IBW in kg})}{72 \times \text{serum creatinine}} = \begin{array}{l}\text{CrCl in mL/min for men.}\\ \text{Multiply answer by 0.85}\\ \text{for women (estimated)}\end{array}$$

- **For morbidly obese patients, calculate estimated creatinine clearance (CrCl) as follows** *(AJM 84:1053, 1988):*

$$\frac{(137 \text{ minus age}) \times [(0.285 \times \text{wt in kg}) + (12.1 \times \text{ht in meters}^2)]}{51 \times \text{serum creatinine}} = \text{CrCl (obese male)}$$

$$\frac{(146 \text{ minus age}) \times [(0.287 \times \text{wt in kg}) + (9.74 \times \text{ht in meters}^2)]}{60 \times \text{serum creatinine}} = \text{CrCl (obese female)}$$

DRUG	MDD AND OD IV REGIMENS/ TARGETED PEAK (P) AND TROUGH (T) SERUM LEVELS	COMMENTS For more data on once-daily dosing, *see AAC 55:2528, 2011 and Table 17A, page 215*
Gentamicin (Garamycin), **Tobramycin** (Nebcin)	MDD: 2 mg per kg load, then 1.7 mg per kg q8h P 4–10 mcg/mL, T 1–2 mcg per mL	**All aminoglycosides have potential to cause tubular necrosis and renal failure, deafness due to cochlear toxicity, vertigo due to damage to vestibular organs, and rarely neuromuscular blockade.** Risk minimal with oral or topical application due to small % absorption unless tissues altered by disease. Risk of nephrotoxicity ↑ with concomitant administration of cyclosporine, vancomycin, ampho B, radiocontrast. Risk of nephrotoxicity ↓ by once-daily dosing method (especially if baseline renal function normal). In general, same factors influence risk of ototoxicity. **NOTE: There is no known method to eliminate risk of aminoglycoside nephro/ototoxicity. Proper rx attempts to ↓ the % risk.** The clinical trial data of OD aminoglycosides have been reviewed extensively by meta-analysis *(CID 24:816, 1997).* **Serum levels:** Collect peak serum level (PSL) exactly 1 hr after the start of the infusion of the 3rd dose. In critically ill pts, PSL after the 1st dose as volume of distribution and renal function may change rapidly. Other dosing methods and references: For once-daily 7 mg per kg per day of gentamicin Hartford Hospital method (may under dose if <7 mg/kg/day dose), *see AAC 39:650, 1995.* One in 500 patients (Europe) have mitochondrial mutation that predicts cochlear toxicity *(NEJM 360:640 & 642, 2009).* Aspirin supplement (3 gm/day) attenuated risk of cochlear injury from gentamicin *(NEJM 354:1856, 2006).* Vestibular injury usually bilateral & hence no vertigo but imbalance & oscillopsia *(Med J Aust 196:701, 2012).*
	OD: 5.1 (7 if critically ill) mg per kg q24h P 16–24 mcg per mL, T <1 mcg per mL	
Kanamycin (Kantrex), **Amikacin** (Amikin), Streptomycin	MDD: 7.5 mg per kg q12h P 15–30 mcg per mL, T 5–10 mcg per mL	
	OD: 15 mg per kg q24h P 56–64 mcg per mL, T <1 mcg per mL	
Netilmicin[NUS]	MDD: 2 mg per kg q8h P 4–10 mcg per mL, T 1–2 mcg per mL	
	OD: 6.5 mg per kg q24h P 22–30 mcg per mL, T <1 mcg per mL	
Isepamicin[NUS]	Only OD: Severe infections 15 mg per kg q24h, less severe 8 mg per kg q24h	
Spectinomycin (Trobicin)[NUS]	2 gm IM times 1–gonococcal infections	
Neomycin—oral	Prophylaxis GI surgery: 1 gm po times 3 with erythro, *see Table 15B, page 200* For hepatic coma: 4–12 gm per day po	
Tobramycin—inhaled (Tobi): *See Cystic fibrosis, Table 1, page 43 & Table 10F, page 120.* Adverse effects few: transient voice alteration (13%) and transient tinnitus (3%).		
Paromomycin—oral: *See Entamoeba and Cryptosporidia, Table 13A, page 151.*		

TABLE 10E: PROLONGED OR CONTINUOUS INFUSION DOSING OF SELECTED BETA LACTAMS

Based on current and rapidly changing data, it appears that prolonged or continuous infusion of beta-lactams is at least as successful as intermittent dosing. Hence, this approach can be part of stewardship programs as supported by recent publications.

Antibiotic stability is a concern. Factors influencing stability include drug concentration, IV infusion diluent *(e.g. NS vs. D5W)*, type of infusion device, and storage temperature *(Ref: P&T 36:723, 2011)*. Portable pumps worn close to the body expose antibiotics to temperatures closer to body temperature (37°C) than to room temperature (around 25°C). Carbapenems are particularly unstable and may require wrapping of infusion pumps in cold packs or frequent changes of infusion bags or cartridges.

A meta-analysis of observational studies found reduced mortality among patients treated with extended or continuous infusion of carbapenems or piperacillin-tazobactam (pooled data) as compared to standard intermittent regimens. The results were similar for extended and continuous regimens when considered separately. There was a mortality benefit with piperacillin-tazobactam but not carbapenems *(CID 56:272, 2013)*. The lower mortality could, at least in part, be due to closer professional supervision engendered by a study environment. On the other hand, a small prospective randomized controlled study of continuous vs. intermittent Pip-Tazo, and meropenem found a higher clinical cure rate and a trend toward lower mortality in the continuous infusion patients *(CID 56:236, 2013)*.

DRUG/METHOD	MINIMUM STABILITY	RECOMMENDED DOSE	COMMENTS
Cefepime (Continuous)	@ 37°C: 8 hours @ 25°C: 24 hours @ 4°C: ≥24 hours	Initial dose: 15 mg/kg over 30 min, then immediately begin: • If CrCl > 60: 6 gm (over 24 hr) daily • If CrCl 30-60: 4 gm (over 24 hr) daily • If CrCl 11-29: 2 gm (over 24 hr) daily	CrCl adjustments extrapolated from prescribing information, not clinical data. Refs: *JAC 57:1017, 2006; Am. J. Health Syst. Pharm. 68:319, 2011.*
Ceftazidime (Continuous)	@ 37°C: 8 hours @ 25°C: 24 hours @ 4°C: ≥24 hours	Initial dose: 15 mg/kg over 30 min, then immediately begin: • If CrCl > 50: 6 gm (over 24 hr) daily • If CrCl 31-50: 4 gm (over 24 hr) daily • If CrCl 10-30: 2 gm (over 24 hr) daily	CrCl adjustments extrapolated from prescribing information, not clinical data. Refs: *Br J Clin Pharmacol 50:184, 2000; IJAA 17:497, 2001; AAC 49:3550, 2005; Infect 37: 418, 2009; JAC 68:900, 2013.*
Doripenem (Prolonged)	@ 37°C: 8 hours (in NS) @ 25°C: 24 hours (in NS) @ 4°C: 24 hours (in NS)	• If CrCl ≥ 50: 500 mg (over 4 hr) q8h • If CrCl 30-49: 250 mg (over 4 hr) q8h • If CrCl 10-29: 250 mg (over 4 hr) q12h	Based on a single study *(Crit Care Med 36:1089, 2008)*.
Meropenem (Prolonged)	@ 37°C: <4 hours @ 25°C: 4 hours @ 4°C: 24 hours	• If CrCl ≥ 50: 2 gm (over 3 hr) q8h • If CrCl 30-49: 1 gm (over 3 hr) q8h • If CrCl 10-29: 1 gm (over 3 hr) q12h	Initial 1 gm dose reasonable but not used by most investigators. Ref: *Intens Care Med 37:632, 2011.*
PIP-TZ (Prolonged)	@ 37°C: 24 hours @ 25°C: 24 hours @ 4°C: no data	Initial dose: 4.5 gm over 30 min, then 4 hrs later start: • If CrCl ≥ 20: 3.375 gm (over 4 hr) q8h • If CrCl < 20: 3.375 gm (over 4 hr) q12h	Reasonable to begin first infusion 4 hrs after initial dose. Refs: *CID 44:357, 2007; AAC 54:460, 2010. See CID 56:236, 245 & 272, 2013.* In obese patients (> 120 kg), may need higher doses: 6.75 gm or even 9 gm (over 4 hrs) q8h to achieve adequate serum levels of tazobactam *(Int J Antimicrob Agts 41:52, 2013)*.
Temocillin	@ 37°C: 24 hours @ 25°C: 24 hours These apply to Temocillin 4 gm/48 mL dilution *(JAC 61:382, 2008)*	Initial dose: 2 gm over 30 min, then immediately begin: • If CrCl >50: 6 gm (over 24 hr) daily • If CrCl 31-50: 3 gm (over 24 hr) daily • If CrCl 10-30: 1.5 gm (over 24 hr) daily • If CrCl <10: 750 mg (over 24 hr) daily CVVH: 750 mg (over 24 hr) daily	Offers higher probability of reaching desired PK/PD target than conventional q8h dosing. This study not designed to assess clinical efficacy *(JAC 70:891, 2015)*.
Vancomycin (Continuous)	@ 37°C: 48 hours @ 25°C: 48 hours @ 4°C: 58 days (at conc 10 µg/mL)	Loading dose of 15-20 mg/kg over 30-60 minutes, then 30 mg/kg by continuous infusion over 24 hrs. No data on pts with renal impairment.	Adjust dose to target plateau concentration of 20-25 µg/mL. Higher plateau concentrations (30-40 µg/mL) achieved with more aggressive dosing increase the risk of nephrotoxicity *(Ref: Clin Micro Inf 19:E98, 2013)*. Continuous infusion may reduce risk of Vanco nephrotoxicity *(CCM 42:2527 & 2635, 2014)*.

TABLE 10F: INHALATION ANTIBIOTICS

Introductory remarks: There is interest in inhaled antimicrobials for several patient populations, such as those with bronchiectasis due to cystic fibrosis or as a result of other conditions. Interest is heightened by growing incidence of infection due to multi-drug resistant Gram-negative bacilli. Isolates of *P. aeruginosa, A. baumannii,* or *Klebsiella* species susceptible only to colistin are of special concern.

There are a variety of ways to generate aerosols for inhalation: inhalation of dry powder, jet nebulizers, ultrasonic nebulizers, and most recently, vibrating mesh nebulizers. The vibrating mesh inhalers generate fine particle aerosols with enhanced delivery of drug to small airways *(Cochrane Database of Systematic Reviews 4:CD007639, 2013).* Review: *Curr Opin Infect Dis 26:538, 2013.*

Inhaled DRUG	DELIVERY SYSTEM	DOSE	COMMENT
Amikacin + Ceftazidime	Vibrating plate nebulizer	AMK: 25 mg/kg once daily x 3 days Ceftaz: 15 mg/kg q3h x 8 days	Radiographic and clinical cure of *P. aeruginosa* ventilator-associated pneumonia (VAP) similar to IV AMK/Ceftaz, including strains with intermediate resistance *(AJRCCM 184:106. 2011).*
Aztreonam (Cayston)	Altera vibrating mesh nebulizer	75 mg tid x 28 days (every other month)	Improves pulmonary function, reduces bacterial load, reduces frequency of exacerbations, and improves symptoms in cystic fibrosis (CF) pts *(Exp Opin Pharmacother 14:2115, 2013).* Cost per treatment cycle about $6070.
Colistin	Various *(see comment)*	Various *(see comment)*	Much variability and confusion in dosing. Nebulized colistimethate (CMS) 1-2 million U (33-66 mg colistin base) effective for CF *(Exp Opin Drug Deliv 9:333, 2012).* Summary of available studies *(Expert Rev Antiinfect Ther 13:1237, 2015).* Adjunctive role for VAP still unclear *(CID 43:S89, 2006; CID 51:1238, 2010).* "High-dose" nebulized CMS (400 mg q8h) via **vibrating-mesh nebulizer effective for VAP due to multidrug-resistant P. aeruginosa and A. baumannii** *(Anesth 117:1335, 2012).* Efficacy of adding inhaled colistin to IV colistin for VAP due to GNB susceptible only to colistin was studied. Colistin: 1 million IU q8h (as CMS) nebulized with either jet or ultrasonic nebulizer. Higher cure rate with combined inhaled plus IV colistin as compared to IV colistin alone *(Chest 144: 1768, 2013).*
Fosfomycin + Tobramycin (FTI) 4:1 wt/wt	eFlow vibrating mesh nebulizer	FTI 160/40 or 80/20 bid x 28 days	Both doses maintained improvements in FEV_1 following a 28-day inhaled aztreonam run-in (vs. placebo) in CF patients with *P. aeruginosa*; FTI 80/20 better tolerated than 160/40 *(AJRCCM 185:171, 2012).*
Levofloxacin	eFlow vibrating mesh nebulizer	240 mg bid x 28 days	Reduced sputum density of *P. aeruginosa*, need for other antibiotics, and improved pulmonary function compared to placebo in CF pts (AJRCCM 183:1510, 2011).
Liposomal Amikacin	PARI LC STAR jet nebulizer	500 mg qd x 28 days (every other month)	Company reports Phase 3 study in CF pts with *P. aeruginosa* has met primary endpoint of non-inferiority compared to TOBI for FEV_1 improvement. Insmed website: *http://investor.insmed.com/releasedetail.cfm?ReleaseID=774638.* Accessed November 30, 2013.
Tobramycin (TOBI, Bethkis)	PARI LC PLUS jet nebulizer	300 mg bid x 28 days (every other month)	Cost: about $6700 for one treatment cycle *(Med Lett 56:51, 2014)*
Tobramycin (TOBI Podhaler)	28 mg dry powder caps	4 caps (112 mg) bid x 28 days (every other month)	Improvement in FEV_1 similar to Tobra inhaled solution in CF patients with chronic *P. aeruginosa* but more airway irritation with the powder. Cost of one month treatment cycle about $6700 *(Med Lett 56:51, 2014).*

TABLE 11A – TREATMENT OF FUNGAL INFECTIONS—ANTIMICROBIAL AGENTS OF CHOICE*

For Antifungal Activity Spectra, *see Table 4B, page 79*

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Aspergillosis (A. fumigatus most common, also A. flavus and others) *(See NEJM 360:1870, 2009; Chest 146:1358, 2014).*			
Allergic bronchopulmonary aspergillosis (ABPA) Clinical manifestations: wheezing, pulmonary infiltrates, bronchiectasis & fibrosis. Airway colonization assoc. with ↑ blood eosinophils, ↑ serum IgE, ↑ specific serum antibodies.	Acute asthma attacks associated with ABPA: **Corticosteroids**	Rx of ABPA: **Itraconazole** oral sol'n 200 mg po bid **l**imes 16 wks or longer	Itra decreases number of exacerbations requiring corticosteroids with improved immunological markers, improved lung function & exercise tolerance *(IDSA Guidelines updated CID 46:327, 2008).*
Allergic fungal sinusitis: relapsing chronic sinusitis; nasal polyps without bony invasion; asthma, eczema or allergic rhinitis; ↑ IgE levels and isolation of Aspergillus sp. or other dematiaceous sp. (Alternaria, Cladosporium, etc.)	**Rx controversial:** systemic corticosteroids + surgical debridement (relapse common).	For failures try **Itra** 200 mg po bid times 12 mos or flucon nasal spray.	Controversial area.
Aspergilloma (fungus ball)	No therapy or surgical resection. Efficacy of antimicrobial agents not proven.		Aspergillus may complicate pulmonary sequestration.
Invasive, pulmonary (IPA) or extrapulmonary: Post-transplantation and post-chemotherapy in neutropenic pts (PMN <500 per mm^3) but may also present with neutrophil recovery. Common pneumonia in transplant recipients. Usually a late (≥100 days) complication in allogeneic bone marrow & liver transplantation: High mortality *(CID 44:531, 2007).* **Typical x-ray/CT lung lesions** (halo sign, cavitation, or macronodules) *(CID 44:373, 2007).* An immunologic test that detects circulating **galactomannan antigen** is available for dx of invasive aspergillosis *(Lancet ID 4:349, 2005).* Serum galactomannan relatively insensitive; antifungal rx may decrease sensitivity *(CID 40:1762, 2005).* Improved sensitivity when performed on BAL fluid. *(Am J Respir Crit Care Med 177:27, 2008).* **False-pos. tests occur with serum from pts receiving PIP-TZ, Amox-Clav** & other beta lactams, infection with other fungi & some blood product conditioning fluid *(CID 55:e22, 2012).* **Better diagnostic strategy:** combination of serum galactomannan & aspergillus PCR (not routinely available) *(LnID 13:519, 2013).* **Beta D-Glucan:** in fungal cell wall. Can detect with immunoassay. Many false positives + low sensitivity *(JCM 51:3478, 2013).*	**Primary therapy** *(See CID 46:327, 2008):* **Voriconazole 6 mg/kg IV q12h on day 1; then either (4 mg/kg IV q12h) or (200 mg po q12h for body weight ≥40 kg, but 100 mg po q12h for body weight <40 kg) (use actual wt). Goal trough (day 4): 1.0–5.5 mg/L associated with improved response rates and reduced adverse effects *(Clin Infect Dis 55:1080, 2012).*** **Alternative therapies:** **Isavuconazole** 200 mg IV/po q8h x 1 day then 200 mg IV/po daily; OR **Liposomal ampho B** (L-AmB) 3-5 mg/kg/day IV; OR **Ampho B lipid complex** (ABLC) 5 mg/kg/d IV; OR **Caspofungin** 70 mg/day then 50 mg/day thereafter; OR **Micafungin**[NAI] 100 mg bid *(JAC 64:840, 2009– based on PK/PD study);* OR **Posaconazole**[NAI] 200 mg qid, then 400 mg bid after stabilization of disease;		**Voriconazole** more effective than ampho B. Vori, both a substrate and an inhibitor of CYP2C19, CYP2C9, and CYP3A4, has potential for deleterious drug interactions (e.g., with protease inhibitors). Review concomitant medications. Measure serum level with prolonged therapy or for patients with possible drug-drug interactions. In patients with CrCl < 50 mL/min, po may be preferred due to concerns for nephrotoxicity of IV vehicle in renal dysfunction. *(Clin Infect Dis 54:913, 2012)* **Isavuconazole:** Isavuconazole (prodrug isavuconazonium sulfate): A randomized control trial of Isavuconazole vs. Voriconazole for invasive aspergillosis demonstrated that Isavuconazole is non-inferior to voriconazole for the treatment of invasive aspergillosis (Package insert, clinical trial not published) **Ampho B: not recommended except as a lipid formulation,** either L-AMB or ABLC. 10 mg/kg and 3 mg/kg doses of L-AMB are equally efficacious with greater toxicity of higher dose *(CID 2007; 44:1289–97).* One comparative trial found greater toxicity with ABLC than with L-AMB: 34.6% vs 9.4% adverse events and 21.2% vs 2.8% nephrotoxicity *(Cancer 112:1282, 2008).* Vori preferred as primary therapy. **Posaconazole:** 42% response rate in open-label trial of patients refractory/intolerant to conventional therapy *(Clin Infect Dis 44:2, 2007).* Concern for cross-resistance with azole-non-responders. Measurement of serum concentrations advisable. **Caspofungin:** ~50% response rate in IPA. Licensed for salvage therapy. **Micafungin:** Favorable responses to micafungin as a single agent in 6/12 patients in primary therapy group and 9/22 in the salvage therapy group *(J Infect 53: 337, 2006).* **Combination therapy:** A RCT of Voriconazole plus Anidulafungin vs. Voriconazole alone showed a trend towards reduced mortality in all patients with invasive aspergillosis in the combination therapy arm *(Ann Intern Med 162:81, 2015).* Subgroup of patients with invasive aspergillosis whose diagnosis was established by radiographic findings and GM positivity had lower mortality with combination therapy. Combination therapy should be strongly considered although further data is needed to determine which patients would benefit the most. Some experts would recommend addition of echinocandin to amphotericin-based regimen or other azoles as well.

See page 2 for abbreviations. All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 11A (2)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Aspergillosis *(continued)*			
Blastomycosis *(CID 46: 1801, 2008)* (Blastomyces dermatitidis) Cutaneous, pulmonary or extrapulmonary.	**LAB,** 3-5 mg/kg per day; OR **Ampho B**, 0.7-1 mg/kg per day, for 1-2 weeks, **then Itra** oral sol'n 200 mg tid for 3 days followed by Itra 200 mg bid for 6 -12 months	**Itra** oral sol'n 200 mg tid for 3 days then once or twice per day for 6-12 months for mild to moderate disease; OR **Flu** 400-800 mg per day for those intolerant to Itra	Serum levels of **Itra** should be determined after 2 weeks to ensure adequate drug exposure. Flu less effective than Itra; role of Vori or Posa unclear but active in vitro. Can look for Blastomyces in antigen in urine as aid to diagnosis.
Blastomycosis: CNS disease *(CID 50:797, 2010)*	**LAB** 5 mg/kg per day for 4–6 weeks, followed by **Flu** 800 mg per day	**Itra** oral sol'n 200 mg bid or tid; OR **Vorl** 200-400 mg q12h	Flu and Vori have excellent CNS penetration, to counterbalance their slightly reduced activity compared to Itra. Treat for at least 12 months and until CSF has normalized. Monitor serum Itra levels to assure adequate drug concentrations. More favorable outcome with Voriconazole *(CID 50:797, 2010)*.
Candidiasis: Candida is a common cause of nosocomial bloodstream infection. *C. albicans* & non-albicans species show ↓ susceptibility to antifungal agents (esp. fluconazole). In immunocompromised pts where antifungal prophylaxis (esp. fluconazole) is widely used. Oral, esophageal, or vaginal candidiasis is a major manifestation of advanced HIV & represents common AIDS-defining diagnosis. *See CID 48:503, 2009 for updated IDSA Guidelines.*			
Candidiasis: Bloodstream Infection			
Bloodstream: non-neutropenic patient Remove all intravascular catheters if possible; replace catheters at a new site (not over a wire). Higher mortality associated with delay in therapy *(CID 43:25, 2006)*.	**Capsofungin** 70 mg IV loading dose, then 50 mg IV daily; OR **Micafungin** 100 mg IV daily; OR **Anidulafungin** 200 mg IV loading dose then 100 mg IV daily. Note: Reduce **Caspo** dose for renal impairment	**Fluconazole** 800 mg (12 mg/kg) loading dose, then 400 mg daily IV OR **Lipid-based ampho B** 3-5 mg/kg IV daily; OR **Ampho B** 0.7 mg/kg IV daily; OR **Voriconazole** 400 mg (6 mg/kg) IV twice daily for 2 doses then 200 mg q12h.	**Echinocandin** is recommended for empiric therapy, particularly for patients with recent azole exposure or with moderately severe or severe illness, hemodynamic instability. An echinocandin should be used for treatment of *Candida glabrata* unless susceptibility to fluconazole or voriconazole has been confirmed. Echinocandin preferred empiric therapy in centers with high prevalence of non-albicans candida species. Echinocandin vs. polyenes or azole associated with better survival *(Clin Infect Dis 54:1110, 2012)*. A double-blind randomized trial of anidulafungin (n=127) and fluconazole (n=118) showed an 88% microbiologic response rate (119/135 candida species) with anidulafungin vs a 76% (99/130 candida species) with fluconazole (p 0.02) *(NEJM 356: 2472, 2007)*. **Fluconazole** is not recommended for empiric therapy but could be considered recommended for patients with mild-to-moderate illness, hemodynamically stable, with no recent azole exposure. Fluconazole not recommended for treatment of documented *C. krusei*: use an echinocandin or voriconazole or posaconazole (note: echinocandins have better in vitro activity than either Vori or Posa against *C. glabrata*). Fluconazole recommended for treatment of *Candida parapsilosis* because of reduced susceptibility of this species to echinocandins. Transition from echinocandin to fluconazole for stable patients with *Candida albicans* or other azole-susceptible species. **Voriconazole** with little advantage over fluconazole (more drug-drug interactions) except for oral step-down therapy of *Candida krusei* or voriconazole-susceptible *Candida glabrata*. Recommended **duration of therapy** is 14 days after last positive blood culture. Duration of systemic therapy should be extended to 4-6 weeks for eye involvement.
	Funduscopic examination within first week of therapy to exclude ophthalmic involvement. Ocular disease present in 15% of patients with candidemia, but endophthalmitis is uncommon (2%) *(CID 53:262, 2011)*. Intraocular injections of ampho B required for endophthalmitis as echinocandins have poor penetration into the eye. For **septic thrombophlebitis,** catheter removal and incision and drainage and resection of the vein, as needed, are recommended; duration of therapy at least 2 weeks after last positive blood culture.		

TABLE 11A (3)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Candidiasis: Bloodstream infection *(continued)*			
Bloodstream: neutropenic patient Remove all intravascular catheters if possible; replace catheters at a new site (not over a wire).	**Capsofungin** 70 mg IV loading dose, then 50 mg IV daily, 35 mg for moderate hepatic insufficiency; OR **Micafungin** 100 mg IV daily; OR **Anidulafungin** 200 mg IV loading dose then 100 mg IV daily; OR **Lipid-based ampho B** 3-5 mg/kg IV daily.	**Fluconazole** 800 mg (12 mg/kg) loading dose, then 400 mg daily IV or PO; OR **Voriconazole** 400 mg (6 mg/kg) IV twice daily for 2 doses then 200 mg (3 mg/kg) IV q12h.	**Duration of therapy** in absence of metastatic complications is for 2 weeks after last positive blood culture, resolution of signs, and resolution of neutropenia. Perform funduscopic examination after recovery of white count as signs of ophthalmic involvement may not be seen during neutropenia. *See comments above for recommendations concerning choice of specific agents.*
Candidiasis: Bone and joint infections			
Osteomyelitis	**Fluconazole** 400 mg (6 mg/kg) daily IV or PO; OR **Lipid-based ampho B** 3–5 mg/kg daily for several weeks, then oral fluconazole.	**Caspo**, **Mica** or **Anidula** or **ampho** B 0.5–1 mg/kg IV daily for several weeks then oral **fluconazole.**	Treat for a total of 6-12 months. **Surgical debridement** often necessary; **remove hardware** whenever possible.
Septic arthritis	**Fluconazole** 400 mg (6 mg/kg) daily IV or PO; OR **Lipid-based ampho B** 3–5 mg/kg IV daily for several weeks, then oral fluconazole.	**Caspo**, **Mica** or **Anidula** or **ampho** B 0.5–1 mg/kg IV daily for several weeks then oral **fluconazole.**	**Surgical debridement** in all cases; removal of prosthetic joints whenever possible. Treat for at least 6 weeks and indefinitely if retained hardware.
Candidiasis: Cardiovascular infections			
Endocarditis *(See Eur J Clin Microbiol Infect Dis 27:519, 2008)*	**Caspofungin** 50–150 mg/day IV; OR **Micafungin** 100–150 mg/day IV; OR **Anidulafungin** 100–200 mg/day IV; OR **Lipid-based ampho B** 3–5 mg/kg IV daily + **5-FC** 25 mg/kg po qid.	**Ampho B** 0.6–1 mg/kg IV daily + **5-FC** 25 mg/kg po qid	Consider use of higher doses of echinocandins for endocarditis or other endovascular infections. Can switch to **fluconazole 400-800 mg orally in stable patients** with negative blood cultures and fluconazole susceptible organism. *See Med 90:237, 2011.* Valve replacement strongly recommended, particularly if prosthetic valve endocarditis. Duration of therapy not well defined, but treat for at least 6 weeks after valve replacement and longer in those with complications (e.g., perivalvular or myocardial abscess, extensive disease, delayed resolution of candidemia). Long-term (life-long?) suppression with fluconazole 400-800 mg daily for native valve endocarditis and no valve replacement; life-long suppression for prosthetic valve endocarditis if no valve replacement.
Myocarditis	**Lipid-based ampho B** 3–5 mg/kg IV daily; OR **Fluconazole** 400–800 mg (6–12 mg/kg) daily IV or PO; OR **Caspo**, **Mica** or **Anidula** *(see endocarditis).*		Can switch to **fluconazole 400-800 mg orally in stable patients** with negative blood cultures and fluconazole susceptible organism. Recommended duration of therapy is for several months.

See page 2 for abbreviations. All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 11A (4)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Candidiasis: Cardiovascular infections *(continued)*			
Pericarditis	**Lipid-based ampho B** 3–5 mg/kg daily; OR **Fluconazole** 400–800 mg (6–12 mg/kg) daily IV or po; OR **An echinocandin** IV *(see endocarditis)*		**Pericardial window or pericardiectomy** also is recommended. Can switch to **fluconazole 400-800 mg orally in stable patients** with negative blood cultures and fluconazole susceptible organism. Recommended duration of therapy is for several months.
Candidiasis: Mucosal, esophageal, and oropharyngeal			
Candida esophagitis Primarily encountered in HIV-positive patients Dysphagia or odynophagia predictive of esophageal candidiasis.	**Fluconazole** 200-400 (3-6 mg/kg) mg IV/po daily; OR **echinocandin** (**caspofungin** 50 mg IV daily; OR **micafungin** 150 mg IV daily; OR **anidulafungin** 200 mg IV loading dose then 100 mg IV daily); OR **Ampho B** 0.5 mg/kg IV daily.	An azole (**itraconazole** solution 200 mg daily; or **posaconazole** suspension 400 mg bid for 3 days then 400 mg daily or **voriconazole** IV/po 200 mg q12h.	**Duration of therapy** 14-21 days. IV echinocandin or ampho B for patients unable to tolerate oral therapy. For fluconazole refractory disease, Itra (80% will respond), Posa, Vori, an echinocandin, or ampho B. Echinocandins associated with higher relapse rate than fluconazole. ART recommended. Suppressive therapy with fluconazole 200 mg po 3x/wk until CD4 > 200/mm^3.
Oropharyngeal candidiasis			
Non-AIDS patient	**Clotrimazole troches** 10 mg 5 times daily; OR **Nystatin suspension** or pastilles po qid; OR **Fluconazole** 100-200 mg daily.	**Itraconazole** solution 200 mg daily; OR **posaconazole** suspension 400 mg bid for 3 days then 400 mg daily; or **voriconazole** 200 mg q12h; OR an echinocandin (**capsofungin** 70 mg loading dose then 50 mg IV daily; or **micafungin** 100 mg IV daily; or **anidulafungin** 200 mg IV loading dose then 100 mg IV daily); OR **Ampho B** 0.3 mg/kg daily.	**Duration of therapy** 7-14 days. Clotrimazole or nystatin recommended for mild disease; fluconazole preferred for moderate-to-severe disease. Alternative agents reserved for refractory disease.
AIDS patient	**Fluconazole** 100-200 mg po daily for 7-14 days.	Same as for non-AIDS patient for 7-14 days.	ART in HIV-positive patients. Suppressive therapy until CD4 > 200/mm^3, but if required fluconazole 100 mg po thrice weekly. Oral Itra, Posa, or Vori for 28 days for fluconazole-refractory disease. IV echinocardin also an option. Dysphagia or odynophagia predictive of esophageal candidiasis.

TABLE 11A (5)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Candidiasis: Mucosal, esophageal, and oropharyngeal *(continued)*			
Vulvovaginitis			
Non-AIDS Patient	**Topical azole therapy: Butoconazole 2% cream** (5 gm) q24h at bedtime x 3 days or 2% cream SR 5 gm x 1; OR **Clotrimazole 100 mg vaginal tabs** (2 at bedtime x 3 days) or 1% cream (5 gm) at bedtime times 7 days (14 days may ↑ cure rate) or 100 mg vaginal tab x 7 days or 500 mg vaginal tab x 1; OR **Miconazole 200 mg vaginal suppos** (1 at bedtime x 3 days) or 100 mg vaginal suppos. q24h x 7 days or 2% cream (5 gm) at bedtime x 7 days; OR **Terconazole 80 mg vaginal tab** (1 at bedtime x 3 days) or 0.4% cream (5 gm) at bedtime x 7 days or 0.8% cream 5 gm intravaginal q24h x 3 days; or tioconazole 6.5% vag. ointment x 1 dose. **Oral therapy:** **Fluconazole** 150 mg po x 1; OR **Itraconazole** 200 mg po bid x 1 day.		**Recurrent vulvovaginal candidiasis: fluconazole** 150 mg weekly for 6 months.
AIDS Patient	Topical **azoles** (clotrimazole, buto, mico, tico, or tercon) x3–7d; OR Topical **nystatin** 100,000 units/day as vaginal tablet x14d; OR Oral **Flu** 150 mg x1 dose.		For recurrent disease 10-14 days of topical azole or oral Flu 150 mg, then **Flu** 150 mg po weekly for 6 mos.
Candidiasis: Other infections			
CNS Infection	**Lipid-based ampho B** 3–5 mg/kg IV daily ± 5-FC 25 mg/kg po qid.	**Fluconazole** 400–800 mg (6–12 mg/kg) IV or po.	Removal of **intraventricular devices** recommended. Flu 400-800 mg as step-down therapy in the stable patient and in patient intolerant of ampho B. Experience too limited to recommend echinocandins at this time. **Treatment duration** for several weeks until resolution of CSF, radiographic, and clinical abnormalities.
Cutaneous *(including paronychia, Table 1, page 27)*	Apply topical ampho B, clotrimazole, econazole, miconazole, or nystatin 3-4 x daily for 7–14 days or ketoconazole 400 mg po once daily x 14 days. Ciclopirox olamine 1% cream/lotion; apply topically bid x 7–14 days.		
Endophthalmitis /Chorioretinitis • Occurs in 10% of candidemia, thus ophthalmological consult for all pts • Diagnosis: typical white exudates on retinal exam and/or positive vitrectomy culture • Chorioretinitis accounts for 85% of ocular disease while endophthalmitis occurs in only 15% *(Clin Infect Dis 53:262, 2011).*	Chorioretinitis or Endophthalmitis: Lipid-based **Amphotericin B** 3-5 mg/kg daily + **Flucytosine** 25 mg/kg qid OR **Voriconazole** 6 mg/kg po/IV q12 x 2 doses and then 4 mg/kg po/IV q12. Consider intravitreal **Amphotericin B** 5-10 mcg in 0.1 mL or intravitreal **Voriconazole** 100 mcg in 0.1 mL for sight threatening disease.	Chorioretinitis or Endophthalmitis: **Fluconazole** 6-12 mg/kg IV daily (poor activity against C. glabrata or C. krusei) and consider intravitreal **Amphotericin B** 5-10 mcg in 0.1 mL for sight-threatening disease. Consider vitrectomy in advanced disease. *Clin Infect Dis. 52:648, 2011.*	**Duration of therapy**: 4-6 weeks or longer, based on resolution determined by repeated examinations. Vitrectomy may be necessary for those with vitritis or endophthalmitis *(Br J Ophthalmol 92:466, 2008; Pharmacotherapy 27:1711, 2007).*

TABLE 11A (6)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Candidiasis: Other infections *(continued)*			
Neonatal candidiasis	**Ampho B** 1 mg/kg IV daily; OR **Fluconazole** 12 mg/kg IV daily.	**Lipid-based ampho B** 3-5 mg/kg IV daily.	**Lumbar puncture** to rule out CNS disease, **dilated retinal examination,** and **intravascular catheter removal** strongly recommended. Lipid-based ampho B used only if there is no renal involvement. Echinocandins considered 3rd line therapy. **Duration of therapy is at least 3 weeks.**
Peritonitis (Chronic Ambulatory Peritoneal Dialysis) *See Table 19, page 231.*	**Fluconazole** 400 mg po q24h x 2–3 wks; or **caspofungin** 70 mg IV on day 1 followed by 50 mg IV q24h for 14 days; or **micafungin** 100 mg IV q24h for 14 days.	**Ampho B,** continuous intraperitoneal dosing at 1.5 mg/L of dialysis fluid times 4–6 wks.	Remove cath immediately or if no clinical improvement in 4–7 days.
Candidiasis: Urinary tract infections			
Cystitis **Asymptomatic** *See CID 52:s427, 2011; CID 52:s452, 2011.*	**If possible, remove catheter or stent.** **No therapy indicated except in patients at high risk for dissemination or undergoing a urologic procedure.**		**High risk patients** (neonates and neutropenic patients) should be managed as outlined for treatment of bloodstream infection. For patients undergoing urologic procedures, Flu 200 mg (3 mg/kg) IV/po daily or ampho B 0.5 mg/kg IV daily (for flu-resistant organisms) for several days pre- and post-procedure.
Symptomatic	**Fluconazole** 200 mg (3 mg/kg) IV/po daily for 14 days.	**Ampho B** 0.5 mg/kg IV daily (for fluconazole resistant organisms) for 7-10 days.	Concentration of echinocandins is low; case reports of efficacy versus azole resistant organisms *(Can J Infect Dis Med Microbiol 18:149, 2007; CID 44:e46, 2007).* Persistent candiduria in immunocompromised pt warrants ultrasound or CT of kidneys to rule out fungus ball.
Pyelonephritis	**Fluconazole** 200–400 mg (3–6 mg/kg) once daily orally.	**Ampho B** 0.5 mg/kg daily IV ± 5-FC 25 mg/kg po qid.	**Treat for 2 weeks.** For suspected disseminated disease treat as if bloodstream infection is present.
Chromoblastomycosis *(Clin Exp Dermatol, 34:849, 2009).* (Cladophialophora, Phialophora, or Fonsecaea); Cutaneous (usually feet, legs): raised scaly lesions, most common in tropical areas	If lesions small & few, **surgical excision or cryosurgery with liquid nitrogen.** If lesions chronic, extensive, burrowing: **itraconazole.**	**Itraconazole:** 200-400 mg oral sol'n q24h or 400 mg pulse therapy once daily for 1 week of each month for 6-12 months (or until response)[NAI].	**Terbinafine**[NAI] 500-1000 mg once daily alone or in combination with **itraconazole** 200-400 oral sol'n mg; or **posaconazole** (800 mg/d) po may be effective. Anecdotal report of efficacy of topical imiquimod 5%: 5x/wk *(CID 58:1734, 2014).*

TABLE 11A (7)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Coccidioidomycosis (Coccidioides immitis) *(IDSA Guidelines 2005; CID 41:1217, 2005; see also Mayo Clin Proc 83:343, 2008)*			
Primary pulmonary (San Joaquin or Valley Fever): **For pts at low risk of persistence/complication**	**Antifungal rx not generally recommended.** Treat if fever, wt loss and/or fatigue that does not resolve within 4-8 wks		Uncomplicated pulmonary in normal host common in endemic areas *(Emerg Infect Dis 12:958, 2006)* Influenza-like illness of 1–2 wks duration.
Primary pulmonary in pts with ↑ risk for complications or dissemination. Rx indicated: • Immunosuppressive disease, post-transplantation, hematological malignancies or therapies (steroids, TNF-α antagonists) • Pregnancy in 3rd trimester. • Diabetes • CF antibody >1:16 • Pulmonary Infiltrates • Dissemination (identification of spherules or culture of organism from ulcer, joint effusion, pus from subcutaneous abscess or bone biopsy, etc.)	**Mild to moderate severity** *(EID 20:983, 2014)*: **Itraconazole** solution 200 mg po or IV bid; OR **Fluconazole** 400 mg po q24h for 3–12 mos **Locally severe or disseminated disease** **Ampho B** 0.6–1 mg/kg per day x 7 days then 0.8 mg/kg every other day or **liposomal ampho B** 3-5 mg/kg/d IV or **ABLC** 5 mg/kg/d IV, until clinical improvement (usually several wks or longer in disseminated disease), followed by **Itra** or **Flu** for at least 1 year. Some use combination of Ampho B & Flu for progressive severe disease; controlled series lacking. **Consultation with specialist recommended:** surgery may be required. Suppression in HIV+ patients until CD4 >250 & infection controlled: Flu 200 mg po q24h or Itra oral sol'n 200 mg po bid *(Mycosis 46:42, 2003)*.		**Ampho B cure rate 50–70%. Responses to azoles are similar. Itra** may have slight advantage esp. in soft tissue infection. Relapse rates after rx 40%; Relapse rate ↑ if ↑ CF titer ≥1:256. Following CF titers after completion of rx important; rising titers warrant retreatment. **Posaconazole** reported successful in 73% of pts with refractory non-meningeal cocci *(Chest 132:952, 2007)*. Not frontline therapy. Treatment of pediatric cocci to include salvage therapy with Vori & Caspo *(CID 56:1573, 1579 & 1587, 2013)*. Can detect delayed hypersensitivity with skin test antigen called Spherusol; helpful if history of Valley Fever.
Meningitis: occurs in 1/3 to 1/2 of pts with disseminated coccidioidomycosis			
Adult *(CID 42:103, 2006)*	**Fluconazole** 400–1,000 mg po q24h indefinitely	**Ampho B** IV as for pulmonary *(above)* + 0.1–0.3 mg daily intrathecal (intraventricular) via reservoir device. **OR Itra** oral sol'n 400–800 mg q24h **OR voriconazole** *(see Comment)*	**80% relapse rate, continue flucon indefinitely, Voriconazole** successful in high doses (6 mg/kg IV q12h) followed by oral suppression (200 mg po q12h)
Child (Cryptococcus neoformans, C. gattii)	**Fluconazole** (po) (Pediatric dose not established, 6 mg per kg q24h used)		
Cryptococcosis *IDSA Guideline:* CID 50:291, 2010.			
Non-meningeal (non-AIDS) Risk 57% in organ transplant & those receiving other forms of immunosuppressive agents *(EID 13:953, 2007)*.	**Fluconazole** 400 mg/day IV or po for 8 wks to 6 mos **For more severe disease:** **Ampho B** 0.5–0.8 mg/kg per day IV till response then change to **fluconazole** 400 mg po q24h for 8–10 wks course	**Itraconazole** 200-400 mg solution q24h for 6-12 mos OR (**Ampho B** 0.3 mg/kg per day IV + **flucytosine** 37.5 mg/kg po qid) times 6 wks (use ideal body wt)	**Flucon alone 90% effective for meningeal and non-meningeal forms.** Fluconazole as effective as ampho B. Addition of **interferon-γ** (IFN-γ-1b 50 mcg per M^2 subcut. 3x per wk x 9 wks) to liposomal ampho B assoc. with response in pt failing antifungal rx *(CID 38: 910, 2004)*. Posaconazole 400-800 mg also effective in a small series of patients *(CID 45:562, 2007; Chest 132:952, 2007)*
Meningitis (non-AIDS)	**Ampho B** 0.5–0.8 mg/kg per day IV + **flucytosine** 37.5 mg/kg (some use 25 mg/kg) po q6h until pt afebrile & cultures neg (~6 wks) *(NEJM 301:126, 1979)*, then stop ampho B/flucyt, start **fluconazole** 200 mg po q24h *(AnIM 113:183, 1990)*; OR **Fluconazole** 400 mg po q24h x 8–10 wks (less severely ill pt). Some recommend Flu for 2 yrs to reduce relapse rate *(CID 28:297, 1999)*. Some recommend Ampho B plus fluconazole as induction Rx. Studies underway.		**If CSF opening pressure >25 cm H_2O, repeat LP to drain fluid to control pressure.** **C. gattii** meningitis reported in the Pacific Northwest *(EID 13:42, 2007)*; severity of disease and prognosis appear to be worse than with C. neoformans; initial therapy with **ampho B + flucytosine** recommended. C. gattii less susceptible to flucon than C. neoformans *(Clin Microbiol Inf 14:727, 2008)*. Outcomes in both AIDS and non-AIDS cryptococcal meningitis improved with Ampho B + 5-FC induction therapy for 14 days in those with neurological abnormalities or high organism burden *(PLoS ONE 3:e2870, 2008)*.

See page 2 for abbreviations. All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 11A (8)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Cryptococcosis *(continued)*			
HIV+/AIDS: Cryptococcemia and/or Meningitis			
Treatment *See Clin Infect Dis 50:291, 2010 (IDSA Guidelines).* ↓ with ARV but still common presenting OI in newly diagnosed AIDS pts. Cryptococcal infection may be manifested by positive blood culture or positive serum cryptococcal antigen (CRAG: >95% sens). CRAG no help in monitoring response to therapy. With ARV, symptoms of acute meningitis may return: immune reconstitution inflammatory syndrome (IRIS). ↑ CSF pressure **(> 250 mm H_2O)** associated with high mortality: lower with CSF removal. If frequent LPs not possible, ventriculoperitoneal shunts an option *(Surg Neurol 63:529 & 531, 2005).*	**Ampho B** 0.7 mg/kg IV q24H + **flucytosine** 25 mg/kg po q6h for at least two weeks or longer until CSF is sterilized. *See Comment.*	**Amphotericin B** IV or **liposomal ampho B** IV+ **fluconazole** 400 mg po or IV daily; **OR Amphotericin B** 0.7 mg/kg **or liposomal ampho B** 4 mg/kg IV q24h alone; **OR Fluconazole** ≥ 800 mg/day (1200 mg preferred) (po or IV) **plus flucytosine** 25 mg/kg po q6h for 4–6 weeks. **Then** **Consolidation therapy: Fluconazole** 400-800 mg po q24h to complete a 10-wks course then suppression *(see below).* Deferring ART for 5 wks after initiation cryptococcal meningitis therapy significantly improved survival as compared to starting ART during the first 2 wks *(NEJM 370:2487, 2014).*	Outcome of treatment: treatment failure associated with dissemination of infection & high serum antigen titer, indicative of high burden of organisms and lack of 5FC use during inductive Rx, abnormal neurological evaluation & underlying hematological malignancy. Mortality rates still high, particularly in those with concomitant pneumonia *(Postgrad Med 121:107, 2009).* Early Dx essential for improved outcome *(PLOS Medicine 4:e47, 2007).* Ampho B + 5FC treatment ↓ crypto CFUs more rapidly than ampho + Flu or ampho + 5FC + Flu. Ampho B 1 mg/kg/d alone much more rapidly fungicidal in vivo than Flu 400 mg/d *(CID 45:76&81, 2007).* Use of lipid-based ampho B associated with lower mortality compared to ampho B deoxycholate in solid organ transplant recipients *(CID 48:1566, 2009).* Monitor 5-FC levels: peak 70-80 mg/L, trough 30-40 mg/L. Higher levels assoc. with bone marrow toxicity. No difference in outcome if given IV or po *(AAC 51:1038, 2007).* Failure of Flu may rarely be due to resistant organism, especially if burden of organism high at initiation of Rx. Although 200 mg qd = 400 mg qd of Flu: median survival 76 & 82 days respectively, authors prefer 400 mg po qd *(BMC Infect Dis 6:118, 2006).* Trend toward improved outcomes with fluconazole 400-800 mg combined with ampho B versus ampho B alone in AIDS patients *(CID 48:1775, 2009).* Role of other azoles uncertain: successful outcomes were observed in 14/29 (48%) subjects with cryptococcal meningitis treated with posaconazole *(JAC 56:745, 2005).* Voriconazole also may be effective. **When to initiate antiretroviral therapy (ART)?** Defer ART to allow for 5 weeks of anti-fungal treatment. When ART was started 1-2 weeks after diagnosis of cryptococcal meningitis mortality was increased when compared to initiation of ART > 5 weeks after diagnosis *(NEJM 370:2487, 2014).*
Suppression (chronic maintenance therapy) Discontinuation of antifungal rx can be considered among pts who remain asymptomatic, with CD4 >100–200/mm^3 for ≥6 months. Some perform a lumbar puncture before discontinuation of maintenance rx. Reappearance of pos. serum CRAG may predict relapse	**Fluconazole** 200 mg/day po [If CD4 count rises to >100/mm^3 with effective antiretroviral rx, some authorities recommend dc suppressive rx. See *www.hivatis.org.* Authors would only dc if CSF culture negative.]	**Itraconazole** 200 mg po q12h if Flu intolerant or failure. No data on Vori for maintenance.	Itraconazole less effective than fluconazole & not recommended because of higher relapse rate (23% vs 4%). Recurrence rate of 0.4 to 3.9 per 100 patient-years with discontinuation of suppressive therapy in 100 patients on ARV with CD4 >100 cells/mm^3.

TABLE 11A (9)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Dermatophytosis			
Onychomycosis (Tinea unguium) (primarily cosmetic) **Laser rx FDA approved:** modestly effective, expensive *(Med Lett 55:15, 2013).(NEJM 360:2108, 2009)* *Ref: Am J Clin Derm 15:17, 2014; BMJ 348:g1800, 2014; Clinics Derm 31:544, 2013*	**Fingernail Rx Options:** **Terbinafine**[1] 250 mg po q24h [children <20 kg: 67.5 mg/day, 20–40 kg: 125 mg/day, >40 kg: 250 mg/day] x 6 wks (79% effective) OR **Itraconazole**[2] 200 mg po q24h x 3 mos.[NAI] OR **Itraconazole** 200 mg po bid x 1 wk/mo x 2 mos OR **Fluconazole** 150–300 mg po q wk x 3–6 mos.[NAI]		**Toenail Rx Options:** **Terbinafine**[1] 250 mg po q24h [children <20 kg: 67.5 mg/day, 20–40 kg: 125 mg/day, >40 kg: 250 mg/day] x 12 wks (76% effective) OR **Itraconazole** 200 mg po q24h x 3 mos (59% effective) OR **Efinaconazole** 10% solution applied to nail once daily for 48 wks OR **Itraconazole** 200 mg bid x 1 wk/mo. x 3–4 mos (63% effective)[NAI] OR **Fluconazole** 150–300 mg po q wk x 6–12 mos (48% effective)[NAI] OR topical **Tavaborole** (Kerydin) or topical **efinaconazole** (Jublia)
Tinea capitis ("ringworm") (Trichophyton tonsurans, Microsporum canis, N. America; other sp. elsewhere) *(PIDJ 18:191, 1999)*	**Terbinafine**[1] 250 mg po q 24h x 2-4 wks (adults); 5 mg/kg/day x 4 wks (children).	**Itraconazole**[2] 5 mg/kg per day x 4 wks[NFDA]. **Fluconazole** 6 mg/kg q wk x 8-12 wks.[NAI] Cap at 150 mg po q wk for adults **Griseofulvin:** adults 500 mg po q24h x 6-8 wks, children 10–20 mg/kg per day until hair regrows.	Durations of therapy are for T. tonsurans; treat for approx. twice as long for M. canis. All agents with similar cure rates (60-100%) in clinical studies. Addition of topical ketoconazole or selenium sulfate shampoo reduces transmissibility *(Int J Dermatol 39:261, 2000)*
Tinea corporis, cruris, or pedis (Trichophyton rubrum, T. mentagrophytes, Epidermophyton floccosum) "Athlete's foot, jock itch", and ringworm	**Topical rx:** Generally applied 2x/day. Available as creams, ointments, sprays, by prescription & "over the counter". Apply 2x/day for 2–3 wks. Recommend: Lotrimin Ultra or Lamisil AT; contain butenafine & terbinafine—both are fungicidal	**Terbinafine** 250 mg po q24h x 2 wks[NAI] OR **ketoconazole** 200 mg po q24h x 4 wks OR **fluconazole** 150 mg po 1x/wk for 2–4 wks[NAI] **Griseofulvin:** adults 500 mg po q24h times 4–6 wks, children 10–20 mg/kg per day. Duration: 2-4 wks for corporis, 4-8 wks for pedis.	**Keto** po often effective in severe recalcitrant infection. Follow for hepatotoxicity; many drug-drug interactions.
Tinea versicolor (Malassezia furfur or Pityrosporum orbiculare) Rule out erythrasma—see *Table 1, page 54*	**Ketoconazole** (400 mg po single dose)[NAI] or (200 mg q24h x 7 days) or (2% cream 1x q24h x 2 wks)	**Fluconazole** 400 mg po single dose or **Itraconazole** 400 mg po q24h x 3–7 days	**Keto** (po) times 1 dose was 97% effective in 1 study. Another alternative: **Selenium sulfide** (Selsun), 2.5% lotion, apply as lather, leave on 10 min then wash off, 1/day x 7 day or 3–5/wk times 2–4 wks
Fusariosis Third most common cause of invasive mold infections, after *Aspergillus* and *Mucorales* and related molds, in patients with hematologic malignancies *(Mycoses 52:197, 2009)*. Pneumonia, skin infections, bone and joint infections, and disseminated disease occur in severely immunocompromised patients. In contrast to other molds, blood cultures are frequently positive. *Fusarium solani*, *F. oxysporum*, *F. verticillioides* and *F. moniliforme* account for approx. 90% of isolates *(Clin Micro Rev 20: 695, 2007)* Frequently fatal, outcome depends on decreasing the level of immunosuppression.			
	Lipid-based ampho B 5-10 mg/kg/d IV; OR **Ampho B** 1-1.5 mg/kg/d IV.	**Posaconazole** 400 mg po bid with meals (if not taking meals, 200 mg qid); OR **Voriconazole** IV: 6 mg per kg q12h times 1 day, then 4 mg per kg q12h; PO: 400 mg q12h, then 200 mg q12h. *See comments.*	**Surgical debridement** for localized disease. *Fusarium* spp. resistance to most antifungal agents, including echinocandins. *F. solani* and *F. verticillioides* typically are resistant to azoles. *F. oxysporum* and *F. moniliforme* may be susceptible to voriconazole and posaconazole. Role of combination therapy not well defined but case reports of response *(Mycoses 50: 227, 2007)*. Given variability in susceptibilities can consider combination therapy with Vori and ampho B awaiting speciation. Outcome dependent on reduction or discontinuation of immuno-suppression. Duration of therapy depends on response; long-term suppressive therapy for patients remaining on immunosuppressive therapy.

[1] **Serious but rare cases of hepatic failure** have been reported in pts receiving terbinafine & should not be used in those with chronic or active liver disease *(see Table 11B, page 136)*.
[2] Use of itraconazole has been associated with myocardial dysfunction and with onset of congestive heart failure.

See page 2 for abbreviations. All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 11A (10)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Histoplasmosis (Histoplasma capsulatum): *See IDSA Guideline: CID 45:807, 2007.* Best diagnostic test is urinary, serum, or CSF histoplasma antigen: MiraVista Diagnostics (1-866-647-2847)			
Acute pulmonary histoplasmosis	**Mild to moderate disease, symptoms <4 wks:** No rx; If symptoms last over one month: **Itraconazole** oral soln 200 mg po tid for 3 days then once or twice daily for 6-12 wks. **Moderately severe or severe: Liposomal ampho B,** 3-5 mg/kg/d IV or **ABLC** 5 mg/kg/d IV or ampho B 0.7-1.0 mg/kg/d for 1-2 wks, then Itra 200 mg tid for 3 days, then bid for 12 wks. + **methylprednisolone** 0.5-1 mg/kg/d for 1-2 wks.		Ampho B for patients at low risk of nephrotoxicity. Check for Itra drug-drug interactions.
Chronic cavitary pulmonary histoplasmosis	**Itra** oral soln 200 mg po tid for 3 days then once or twice daily for at least 12 mos (some prefer 18-24 mos).		Document therapeutic itraconazole blood levels at 2 wks. Relapses occur in 9-15% of patients.
Mediastinal lymphadenitis, mediastinal granuloma, pericarditis; and rheumatologic syndromes	**Mild cases:** Antifungal therapy not indicated. Nonsteroidal anti-inflammatory drug for pericarditis or rheumatologic syndromes. If no response to non-steroidals, **Prednisone** 0.5-1.0 mg/kg/d tapered over 1-2 weeks for 1) pericarditis with hemodynamic compromise, 2) lymphadenitis with obstruction or compression syndromes, or 3) severe rheumatologic syndromes. **Itra** 200 oral soln mg po once or twice daily for 6-12 wks for moderately severe to severe cases, or if prednisone is administered.		Check Itra blood levels to document therapeutic concentrations. Check for Itra drug-drug interactions.
Progressive disseminated histoplasmosis	**Mild to moderate disease: Itra** 200 mg po tid for 3 days then bid for at least 12 mos. **Moderately severe to severe disease: Liposomal ampho B,** 3 mg/kg/d or **ABLC** 5 mg/kg/d for 1-2 weeks then **Itra** 200 mg tid for 3 days, then bid for at least 12 mos.		**Ampho B** 0.7-1.0 mg/kg/d may be used for patients at low risk of nephrotoxicity. Confirm therapeutic Itra blood levels. Azoles are teratogenic; Itra should be avoided in pregnancy; use a lipid ampho formulation. Urinary antigen levels useful for monitoring response to therapy and relapse
CNS histoplasmosis	**Liposomal ampho B,** 5 mg/kg/d, for a total of 175 mg/kg over 4-6 wks, then **Itra** 200 mg 2-3x a day for at least 12 mos. Vori likely effective for CNS disease or Itra failures. *(Arch Neurology 65: 666, 2008; J Antimicro Chemo 57:1235, 2006).*		Monitor CNS histo antigen, monitor Itra blood levels. PCR may be better for Dx than histo antigen. Absorption of Itra (check levels) and CNS penetration may be an issue; case reports of success with Fluconazole *(Braz J Infect Dis 12:555, 2008)* and Posaconazole *(Drugs 65:1553, 2005)* following Ampho B therapy.
Prophylaxis (immunocompromised patients)	**Itra** 200 mg po daily. Check for Itra drug-drug interactions.		Consider primary **prophylaxis in HIV-infected** patients with < 150 CD4 cells/mm^3 in high prevalence areas. Secondary prophylaxis (i.e., suppressive therapy) indicated in HIV-infected patients with < 150 CD4 cells/mm^3 and other immunocompromised patients in who immunosuppression cannot be reversed

TABLE 11A (11)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Madura foot *(See Nocardia & Scedosporium)*			
Mucormycosis & other related species - Rhizopus, Rhizomucor, Lichtheimia *(CID 54:1629, 2012).* Rhinocerebral, pulmonary due to angioinvasion with tissue necrosis. Key to successful rx: early dx with symptoms suggestive of sinusitis (or lateral facial pain or numbness): think mucor with palatal ulcers, &/or black eschars, onset unilateral blindness in immunocompromised or diabetic pt. Rapidly fatal without rx. Dx by culture of tissue or stain: wide ribbon-like, non-septated with variation in diameter & right angle branching. Diabetics are predisposed to mucormycosis due to microangiopathy & ketoacidosis. Iron overload also predisposes: iron stimulates fungal growth.	**Liposomal ampho B** 5-10 mg/kg/day; OR **Ampho B** 1-1.5 mg/kg/day.	**Posaconazole** 400 mg po bid with meals (if not taking meals, 200 mg po qid)[NAI] OR **Isavuconazole** 200 mg po/iv q8 x 1 day and then 200 mg daily	**Ampho B** (ABLC) monotherapy relatively ineffective with 20% success rate vs 69% for other polyenes *(CID 47:364, 2008).* Complete or partial response rates of 60-80% in **posaconazole** salvage protocols *(JAC 61, Suppl 1, i35, 2008).* **Isavuconazole:** Approved for treatment of invasive mucor infection based on historical controls (Package insert, clinical trial not published) **Combination therapy:** Adjunctive echinocandin to liposomal Amphotericin B is promising given safety profile, synergy in murine models, and observational clinical data *(Clin Infect Dis 54(S1):S73, 2012).* Adjunctive Deferasirox therapy to liposomal Amphotericin B failed to demonstrate benefit *(J Antimicrob Chemother. 67:715, 2012).* Resistant to **voriconazole:** prolonged use of voriconazole prophylaxis predisposes to mucormycosis infections. Total duration of therapy based on response: continue therapy until 1) resolution of clinical signs and symptoms of infection, 2) resolution or stabilization of radiographic abnormalities; and 3) resolution of underlying immunosuppression. Posaconazole for secondary prophylaxis for those on immunosuppressive therapy *(CID 48:1743, 2009).*
Paracoccidioidomycosis (South American blastomycosis) P. brasiliensis *(Dermatol Clin 26:257, 2008; Expert Rev Anti Infect Ther 6:251, 2008).* Important cause of death from fungal infection in HIV-infected patients in Brazil *(Mem Inst Oswaldo Cruz 104:513, 2009).*	Mild-moderate disease: **Itra** 200 mg po daily for 6-9 months for mild and for 12-18 months for moderate disease. Severe disease: **Ampho B** 0.7-1 mg/kg IV daily to a cumulative total of 30 mg/kg followed by **Itra** 200 mg po daily for at least 12 months	**Ketoconazole** 200-400 mg daily for 6-18 months; OR **Ampho B** total dose > 30 mg/kg OR **TMP/SMX** 800/160 mg bid-tid for 30 days, then 400/80 mg/day indefinitely (up to 3-5 years)	Improvement in >90% pts on Itra or Keto.[NAI] **Ampho B** reserved for severe cases and for those intolerant to other agents. TMP-SMX suppression life-long in HIV+. Check for Itra or Keto drug-drug interactions.
Lobomycosis (keloidal blastomycosis)/ P. loboi	**Surgical excision**, **clofazimine** or **itraconazole**.		
Penicilliosis (Penicillium marneffei): Common disseminated fungal infection in AIDS pts in SE Asia (esp. Thailand & Vietnam).	**Ampho B** 0.5–1 mg/kg per day times 2 wks followed by **itraconazole** 400 mg/day for 10 wks followed by 200 mg/day po **indefinitely for HIV-infected pts.**	For less sick patients **Itra** oral soln 200 mg po bid x 3 days, then 200 mg po bid x 12 wks, then 200 mg po q24h. (IV if unable to take po) (Oral soln better absorbed)	3rd most common OI in AIDS pts in SE Asia following TBc and cryptococcal meningitis. Prolonged fever, lymphadenopathy, hepatomegaly. Skin nodules are umbilicated (mimic cryptococcal infection or molluscum contagiosum). Preliminary data suggests Vori effective: *CID 43:1060, 2006.*
Phaeohyphomycosis, Black molds, Dematiaceous fungi *(See Clin Microbiol Rev 27:527, 2014.)* Opportunistic infection in immunocompromised hosts (e.g., HIV/AIDS, transplants). Most often presents with skin and soft tissue infection or mycetoma but can cause disease in bone and joint, brain abscess, endocarditis, and disseminated disease. Most clinically relevant species are within the genera of Exophiala, Cladophialophora, Coniosporium, Cyphellophora, Fonsecaea, Phialophora, and Rhinocladiella.	**Surgery** + **itraconazole** oral soln 400 mg/day po, duration not defined, probably 6 mo[NAI]	Voriconazole 6 mg/kg po bid x 1 day and then 4 mg/kg po bid or Posaconazole (suspension) 400 mg po bid	Both Vori and Posa have demonstrated efficacy *(Med Mycol 48:769, 2010; Med Mycol 43:91, 2005)* often in addition to surgical therapy. Consider obtaining anti-fungal susceptibility testing.

TABLE 11A (12)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Pneumocystis pneumonia (PCP) caused by **Pneumocystis jirovecI**. *Ref: JAMA 301:2578, 2009.*			
Not acutely ill, able to take po meds. PaO_2 >70 mmHg Diagnosis: sputum PCR. Serum Beta-D Glucan may help; reasonable sensitivity & specificity, but also many false positives *(JCM 51:3478, 2013).*	(**TMP-SMX-DS**, 2 tabs po q8h x21 days) OR (**Dapsone** 100 mg po q24h + **trimethoprim** 5mg/kg po tid x21 days)	[**Clindamycin** 300–450 mg po q6h + **primaquine** 15 mg base po q24h] x21 days OR **Atovaquone** suspension 750 mg po bid with food x21 days	Mutations in gene of the enzyme target (dihydropteroate synthetase) of sulfamethoxazole identified. Unclear whether mutations result in resist to TMP-SMX or dapsone + TMP *(EID 10:1721, 2004)*. Dapsone ref.: *CID 27:191, 1998.* **After 21 days, chronic suppression in AIDS pts *(see below—post-treatment suppression).***
	NOTE: Concomitant use of corticosteroids usually reserved for sicker pts with PaO_2 <70 *(see below)*		
Acutely Ill, po rx not possible. PaO2 <70 mmHg. Still unclear whether antiretroviral therapy (ART) should be started during treatment of PCP (CID 46: 634, 2008).	[**Prednisone**(15–30 min. before **TMP-SMX**): 40 mg po bid times 5 days, then 40 mg q24h times 5 days, then 20 mg po q24h times 11 days] + [**TMP-SMX**(15 mg of TMP component per kg per day) IV div. q6–8h times 21 days]	**Prednisone** as in primary rx PLUS[(Clinda 600 mg IV q8h) + (**primaquine** 30 mg base po q24h)] times 21 days OR **Pentamidine** 4 mg per kg per day IV times 21 days. **Caspofungin** active in animal models: *CID 36:1445, 2003*	**After 21 days, chronic suppression in AIDS pts** (see post-treatment suppression). **PCP can occur in absence of HIV infection & steroids** (CID 25:215 & 219, 1997). Wait 4–8 days before declaring treatment failure& switching to clinda + primaquine or pentamidine (JAIDS 48:63, 2008), or adding caspofungin *(Transplant 84:685, 2007).*
	Can substitute IV prednisolone (reduce dose 25%) for po prednisone		
Primary prophylaxis and post-treatment suppression	(**TMP-SMX-DS or -SS**, 1 tab po q24h or 1 DS 3x/wk) OR (**dapsone** 100mg po q24h). DC when CD4 >200 x/3 mos *(NEJM 344:159, 2001).*	(**Pentamidine** 300mg in 6mL sterile water by aerosol q4wks) OR (**dapsone** 200mg po + **pyrimethamine** 75mg po + **folinic acid** 25mg po —**all once a week**) or **atovaquone** 1500mg po q24h with food.	TMP-SMX-DS regimen provides cross-protection vs Toxo and other bacterial infections. Dapsone + pyrimethamine protects vs Toxo. Atovaquone suspension 1500mg once daily as effective as daily dapsone *(NEJM 339:1889, 1998)* or inhaled pentamidine *(JID 180:369, 1999).*
Scedosporium species (Scedosporium apiospermum [Pseudallescheria boydii] and Scedosporium prolificans) Infection occurs via inhalation or inoculation of skin. Normal hosts often have cutaneous disease. Immunocompromised hosts can have pulmonary colonization -> invasive disease in lung or skin -> disseminated disease.	*Scedosporium apiospermum:* Voriconazole 8 mg/kg PO/IV q12h on day 1, then 4 mg/kg PO/IV q12h. *Scedosporium prolificans:* Surgical debridement and reduction of immunosuppression, consider addition of Voriconazole as above although usually resistant.	Posaconazole 400 mg po bid with meals (may be less active)	Surgical debridement should be considered in most cases. S. apiospermum is resistant Amphotericin B and Scedosporium prolificans is resistant to all antifungal agents. Synergy with Terbinafine and echinocandins have been reported in vitro although clinical data is limited *(AAC 56:2635, 2012).* S. prolificans osteomyelitis responded to miltefosine *(CID 48:1257, 2009)* in a case report. Consider susceptibility testing. Treatment guidelines/review: *Clin Microbiol Infect 3:27, 2014. Clin Microbiol Rev 21:157, 2008.*

TABLE 11A (13)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Sporotrichosis *IDSA Guideline: CID 45:1255, 2007.*			
Cutaneous/Lymphocutaneous	**Itraconazole** oral sol'n po 200 mg/day for 2-4 wks after all lesions resolved, usually 3-6 mos.	If no response, **Itra** 200 mg po bid or **terbinafine** 500 mg po bid or **SSKI** 5 drops (eye drops) tid & increase to 40-50 drops tid	Fluconazole 400-800 mg daily only if no response to primary or alternative suggestions. Pregnancy or nursing: local hyperthermia *(see below).*
Osteoarticular	**Itra** oral sol'n 200 mg po bid x 12 mos.	**Liposomal ampho B** 3-5 mg/kg/d IV or **ABLC** 5 mg/kg/d IV or **ampho B deoxycholate** 0.7-1 mg/kg IV daily; if response, change to **Itra** oral sol'n 200 mg po bid x total 12 mos.	After 2 wks of therapy, document adequate serum levels of itraconazole.
Pulmonary	If severe, **lipid ampho B** 3-5 mg/kg IV or **standard ampho B** 0.7-1 mg/kg IV once daily until response, then **Itra** 200 mg po bid. Total of 12 mos.	Less severe: **Itraconazole** 200 mg po bid x 12 mos.	After 2 weeks of therapy document adequate serum levels of Itra. Surgical resection plus ampho B for localized pulmonary disease.
Meningeal or Disseminated	**Lipid ampho B** 5 mg/kg IV once daily x 4-6 wks, then—if better—**Itra** 200 mg po bid for total of 12 mos.	AIDS/Other immunosuppressed pts: chronic therapy with **Itra** oral sol'n 200 mg po once daily.	After 2 weeks, document adequate serum levels of Itra.
Pregnancy and children	**Pregnancy:** Cutaneous—local hyperthermia. Severe: **lipid ampho B** 3-5 mg/kg IV once daily. **Avoid itraconazole.**	**Children:** Cutaneous: **Itra** 6-10 mg/kg (max of 400 mg) daily. Alternative is **SSKI** 1 drop tid increasing to max of 1 drop/kg or 40-50 drops tid/day, whichever is lowest.	For children with disseminated sporotrichosis: Standard ampho B 0.7 mg/kg IV once daily & after response, Itra 6-10 mg/kg (max 400 mg) once daily.

TABLE 11B – ANTIFUNGAL DRUGS: DOSAGE, ADVERSE EFFECTS, COMMENTS

DRUG NAME, GENERIC (TRADE)/USUAL DOSAGE	ADVERSE EFFECTS/COMMENTS
Non-lipid amphotericin B deoxycholate (Fungizone): 0.5-0.7 mg/kg IV per day as single infusion **Ampho B predictably not active vs. Scedosporium, Candida lusitaniae & Aspergillus terreus**	**Admin:** Ampho B is a colloidal suspension that must be prepared in electrolyte-free D5W at 0.1 mg/mL to avoid precipitation. No need to protect suspensions from light. Infusions cause chills/fever, myalgia, anorexia, nausea, rarely hemodynamic collapse/hypotension. Postulated due to proinflammatory cytokines, doesn't appear to be histamine release *(Pharmacol 23:966, 2003)*. **Infusion duration usu. 4+ hrs.** No difference found in 1 vs 4 hr infus. except chills/fever occurred sooner with 1 hr infus. Febrile reactions ↓ with repeat doses. Rare pulmonary reactions (severe dyspnea & focal infiltrates suggest pulmonary edema) assoc with rapid infus. **Severe rigors respond to meperidine (25–50 mg IV).** Premedication with acetaminophen, diphenhydramine, hydrocortisone (25–50 mg) and heparin (1000 units) had no influence on rigors/fever. If cytokine postulate correct, NSAIDs or high-dose steroids may prove efficacious but their use may risk worsening infection under rx or increased risk of **nephrotoxicity** (i.e., NSAIDs). Clinical side effects ↓ with ↑ age. **Toxicity:** Major concern is nephrotoxicity. Manifest initially by kaliuresis and **hypokalemia**, then fall in serum bicarbonate (may proceed to renal tubular acidosis), ↓ in renal erythropoietin and anemia, and rising BUN/serum creatinine. Hypomagnesemia may occur. Can reduce risk of renal injury by **(a) pre- & post-infusion hydration with 500 mL saline (if clinical status allows salt load), (b)** avoidance of other nephrotoxins, eg, radiocontrast, aminoglycosides, cis-platinum, **(c)** use of lipid prep of ampho B.
Lipid-based ampho B products[1]: **Amphotericin B lipid complex (ABLC)** (Abelcet): 5 mg/kg per day as single infusion	**Admin:** Consists of ampho B complexed with 2 lipid bilayer ribbons. Compared to standard ampho B, larger volume of distribution, rapid blood clearance and high tissue concentrations (liver, spleen, lung). Dosage: **5 mg/kg once daily;** infuse at 2.5 mg/kg per hr; adult and ped. dose the same. Saline pre- and post-dose lessens toxicity. Do NOT use an in-line filter. Do not dilute with saline or mix with other drugs or electrolytes.[2] **Toxicity:** Fever and chills 14–18%; nausea 9%, vomiting 8%; serum creatinine ↑ in 11%; renal failure 5%; anemia 4%; ↓ K 5%; rash 4%. A fatal fat embolism following ABLC infusion *(Exp Mol Path 177:246, 2004)*. Majority of pts intolerant of liposomal ampho B can tolerate ABLC *(CID 56:701, 2013)*.
Liposomal amphotericin B (LAB, AmBisome): 3–5 mg/kg IV per day as single infusion. If intolerant, majority OK with lipid form *(CID 56:701, 2013)*.	**Admin:** Consists of vesicular bilayer liposome with ampho B intercalated within the membrane. Dosage: **3–5 mg/kg per day** IV as single dose infused over a period of approx. 120 min. If tolerated, infusion time reduced to 60 min. *(see footnote[2])*. Saline pre- and post-dose lessens toxicity. **Major toxicity:** Gen less than ampho B. Nephrotoxicity 18.7% vs 33.7% for ampho B, chills 47% vs 75%, nausea 39.7% vs 38.7%, vomiting 31.8% vs 43.9%, rash 24% for both, ↓ Ca 18.4% vs 20.9%, ↓ K 20.4% vs 25.6%, ↓ mg 20.4% vs 25.6%. Acute reactions common with liposomal ampho B, 20– 40%. 86% occur within 5 min of intusion, incl chest pain, dyspnea, hypoxia or severe abdom, flank or leg pain; 14% dev flushing & urticaria near end of 4 hr infusion. All responded to diphenhydramine (1 mg/kg) & interruption of infusion. Reactions may be due to complement activation by liposome *(CID 36:1213, 2003)*.
Caspofungin (Cancidas) 70 mg IV on day 1 followed by 50 mg IV q24h (reduce to 35 mg IV q24h with moderate hepatic insufficiency)	An echinocandin which inhibits synthesis of β-(1,3)-D-glucan. Fungicidal against candida (MIC <2 mcg/mL) including those resistant to other antifungals & active against aspergillus (MIC 0.4–2.7 mcg/mL). Approved indications: empirical rx tor febrile, neutropenic pts; rx of candidemia, candida intraabdominal abscesses, peritonitis, & pleural space infections; esophageal candidiasis; & invasive aspergillosis in pts refractory to or intolerant of other theraples. Serum levels on rec. dosages = peak 12, trough 1.3 (24 hrs) mcg/mL. **Toxicity:** remarkably non-toxic. Most common adverse effect: pruritus at infusion site & headache, fever, chills, vomiting, & diarrhea assoc with infusion. ↑ serum creatinine in 8% on caspo vs 21% short-course ampho B in 422 pts with candidemia *(Ln, Oct. 12, 2005, online)*. Drug metab in liver & dosage ↓ to 35 mg in moderate to severe hepatic failure. Class C for preg (embryotoxic in rats & rabbits). *See Table 22, page 235 for drug-drug interactions, esp. cyclosporine (hepatic toxicity) & tacrolimus (drug level monitoring recommended)*. Reversible thrombocytopenia reported *(Pharmacother 24:1408, 2004)*. **No drug in CSF, urine or vitreous humor of the eye.**
Micafungin (Mycamine) 50 mg IV q24h for prophylaxis post-bone marrow stem cell trans; 100 mg IV q24h candidemia, 150 mg IV q24h candida esophagitis.	Approved for rx of esophageal candidiasis & prophylaxis against candida infections in HSCT[3] recipients. Active against most strains of candida sp. & aspergillus sp. incl those resist to fluconazole such as C. glabrata & C. krusei. No antagonism seen when combo with other antifungal drugs. No dosage adjust for severe renal failure or moderate hepatic impairment. Watch for drug-drug interactions with sirolimus or nifedipine. Micafungin well tolerated & common adverse events incl nausea 2.8%, vomiting 2.4%, & headache 2.4%. Transient ↑ LFTs, BUN, creatinine reported; rare cases of significant hepatitis & renal insufficiency. *See CID 42:1171, 2006.* **No drug in CSF or urine.**

[1] Published data from patients intolerant of or refractory to conventional ampho B deoxycholate. **None of the lipid ampho B preps has shown superior efficacy compared to ampho B in prospective trials (except liposomal ampho B was more effective vs ampho B in rx of disseminated histoplasmosis at 2 wks). Dosage equivalency has not been established** *(CID 36:1500, 2003)*. Nephrotoxicity ↓ with all lipid ampho B preps.

[2] Comparisons between Abelcet & AmBisome suggest higher infusion-assoc. toxicity (rigors) & febrile episodes with Abelcet (70% vs 36%) but higher frequency of mild hepatic toxicity with AmBisome (59% vs 38%, p=0.05). Mild elevations in serum creatinine were observed in 1/3 of both *(BJ Hemat 103:198, 1998; Focus on Fungal Inf #9, 1999; Bone Marrow Tx 20:39, 1997; CID 26:1383, 1998)*.

[3] HSCT = hematopoietic stem cell transplant.

See page 2 for abbreviations. All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 11B (2)

DRUG NAME, GENERIC (TRADE)/USUAL DOSAGE	ADVERSE EFFECTS/COMMENTS
Anidulafungin (Eraxis) For Candidemia; 200 mg IV on day 1 followed by 100 mg/day IV). Esophageal candida: 100 mg IV x 1, then 50 mg IV once/d.	An echinocandin with antifungal activity (cidal) against candida sp. & aspergillus sp. including ampho B- & triazole-resistant strains. FDA approved for treatment of esophageal candidiasis (EC), candidemia, and other complicated Candida infections. Effective in clinical trials of esophageal candidiasis & in 1 trial was superior to fluconazole in rx of invasive candidiasis/candidemia in 245 pts (75.6% vs 60.2%). Like other echinocandins, remarkably non-toxic; most common side-effects: nausea, vomiting, ↓ mg, ↓ K & headache in 11–13% of pts. No dose adjustments for renal or hepatic insufficiency. *See CID 43:215, 2006.* **No drug in CSF or urine.**
Fluconazole (Diflucan) 100 mg tabs 150 mg tabs 200 mg tabs 400 mg IV Oral suspension: 50 mg per 5 mL.	IV=oral dose because of excellent bioavailability. **Pharmacology:** absorbed po, water solubility enables IV. For peak serum levels *(see Table 9A, page 93).* T½ 30hr (range 20–50 hr). 12% protein bound. **CSF levels 50–90% of serum in normals,** ↑ in meningitis. No effect on mammalian steroid metabolism. **Drug-drug interactions common,** *see Table 22.* Side-effects overall 16% [more common in HIV (+) pts (21%)]. Nausea 3.7%, headache 1.9%, skin rash 1.8%, abdominal pain 1.7%, vomiting 1.7%, diarrhea 1.5%, ↑ SGOT 20%. Alopecia (scalp, pubic area) in 12–20% pts on >400 mg po q24h after median of 3 mos (reversible in approx. 6mo). Rare: severe hepatotoxicity *(CID 41:301, 2005)*, exfoliative dermatitis. **Note: Candida krusei and Candida glabrata resistant to Flu.**
Flucytosine (Ancobon, 5-FC) 500 mg cap **Expensive:** $11,000 for 100 capsules (Sep 2015 US price)	AEs: Overall 30%. GI 6% (diarrhea, anorexia, nausea, vomiting), hematologic 22% [leukopenia, thrombocytopenia, when serum level >100 mcg/mL (esp. in azotemic pts)]; hepatotoxicity (asymptomatic ↑ SGOT, reversible); skin rash 7%, aplastic anemia (rare—2 or 3 cases). False ↑ in serum creatinine on EKTACHEM analyzer.
Griseofulvin (Fulvicin, Grifulvin, Grisactin) 500 mg, susp 125 mg/mL.	Photosensitivity, urticaria, GI upset, fatigue, leukopenia (rare). Interferes with warfarin drugs. Increases blood and urine porphyrins, should not be used in patients with porphyria. Minor disulfiram-like reactions. Exacerbation of systemic lupus erythematosus.
Imidazoles, topical For vaginal and/or skin use	Not recommended in 1st trimester of pregnancy. Local reactions: 0.5-1.5%: dyspareunia, mild vaginal or vulvar erythema, burning, pruritus, urticaria, rash. Rarely similar symptoms in sexual partner.
Isavuconazole(Cresemba) PO: 186 mg caps IV: 372 mg vials	An azole antifungal agent for treatment of invasive aspergillosis and invasive mucormycosis in adults. **Contraindications:** Coadministration with strong CYP3A4 inhibitors, e.g., Ketoconazole or high-dose Ritonavir, or strong CYP3A4 inducers, e.g., Rifampin, carbamazepine, St. John's wort, or long-acting barbiturates is contraindicated. Do not use in patients with shortened QT interval. **Loading Dose**: 200 mg of Isavuconazole which equals 1 reconstituted vial of 372 mg of the prodrug Isavuconazonium sulfate, IV or po, q8h x 6 doses (48 hours) and THEN **Maintenance Dose:** 200 mg of Isavuconazole which equals 1 reconstituted vial of 372 mg of the prodrug isavuconazonium sulfate, IV or po once daily. No dosage adjustment for renal impairment. **AEs:** Most common: nausea, vomiting, diarrhea, headache, elevated liver chemistry tests, hypokalemia, constipation, dyspnea, cough, peripheral edema, and back pain. Hepatic: increased ALT, AST
Itraconazole (Sporanox) 100 mg cap 10 mg/mL oral solution IV usual dose 200 mg bid x 4 doses followed by 200 mg q24h for a max of 14 days	**Itraconazole tablet & solution forms not interchangeable, solution preferred.** Many authorities recommend measuring drug serum concentration after 2 wks to ensure satisfactory absorption. To obtain highest plasma concentration, tablet is given with food & acidic drinks (e.g., cola) while solution is taken in fasted state; under these conditions, the peak conc. of capsule is approx. 3 mcg/mL & of solution 5.4 mcg/mL. Peak levels reached faster (2.2 vs 5 hrs) with solution. **Peak plasma concentrations after IV injection (200 mg) compared to oral capsule (200 mg): 2.8 mcg/mL (on day 7 of rx) vs 2 mcg/mL (on day 36 of rx).** Protein-binding for both preparations is over 99%, which explains virtual absence of penetration into CSF **(do not use to treat meningitis).** Adverse effects: dose-related nausea 10%, diarrhea 8%, vomiting 6%, & abdominal discomfort 5.7%. Allergic rash 8.6%, ↑ bilirubin 6%, edema 3.5%, & hepatitis 2.7% reported. ↑ doses may produce hypokalemia 8% & ↑ blood pressure 3.2%. Delirium, peripheral neuropathy & tremor reported *(J Neur Neurosurg Psych 81:327, 2010).* **Reported to produce impairment in cardiac function.** Severe liver failure req transplant in pts receiving pulse rx for onychomycosis: FDA reports 24 cases with 11 deaths out of 50 mill people who received the drug prior to 2001. Other concern, as with fluconazole and ketoconazole, is **drug-drug interactions;** *see Table 22.* Some can be life-threatening.
Ketoconazole (Nizoral) 200 mg tab	**Gastric acid required for absorption**—cimetidine, omeprazole, antacids block absorption. In achlorhydria, dissolve tablet in 4 mL 0.2N HCl, drink with a straw. Coca-Cola ↑ absorption by 65%. CSF levels "none". **Drug-drug interactions important,** *see Table 22.* **Some interactions can be life-threatening.** **Dose- dependent nausea and vomiting.** Liver toxicity of hepatocellular type reported in about 1:10,000 exposed pts—usually after several days to weeks of exposure. At doses of ≥800 mg per day serum testosterone and plasma cortisol levels fall. With high doses, adrenal (Addisonian) crisis reported.

See page 2 for abbreviations. All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 11B (3)

DRUG NAME, GENERIC (TRADE)/USUAL DOSAGE	ADVERSE EFFECTS/COMMENTS
Miconazole (Monistat IV) 200 mg—*not available in U.S.*	IV miconazole indicated in patient critically ill with Scedosporium (Pseudallescheria boydii) infection. Very toxic due to vehicle needed to get drug into solution.
Nystatin (Mycostatin) 30 gm cream 500,000 units oral tab	Topical: virtually no adverse effects. Less effective than imidazoles and triazoles. PO: large doses give occasional GI distress and diarrhea.
Posaconazole *(Noxafil)* Suspension (40 mg/mL): 400 mg po bid with meals (if not taking meals, 200 mg qid). 200 mg po tid (with food) for prophylaxis. Delayed-release tabs (100 mg): 300 mg bid x 1 day and then 300 mg daily for prophylaxis. Intravenous formulation: 300 mg IV bid x 1 day the 300 mg daily (prophylaxis). Takes 7-10 days to achieve steady state. **Takes 7-10 days to achieve steady state. No IV formulation.**	**Suspension is dosed differently than delayed-release tablets (not interchangeable) – check dose carefully.** An oral triazole with activity against a wide range of fungi refractory to other antifungal rx including: aspergillosis, mucormycosis (variability by species), fusariosis, Scedosporium (Pseudallescheria), phaeohyphomycosis, histoplasmosis, refractory candidiasis, refractory coccidioidomycosis, refractory cryptococcosis, & refractory chromoblastomycosis. **Should be taken with high fat meal for maximum absorption.** Approved for prophylaxis of invasive aspergillus and candidiasis. Clinical response in 75% of 176 AIDS pts with azole-refractory oral/esophageal candidiasis. Posaconazole has similar toxicities as other triazoles: nausea 9%, vomiting 6%, abd. pain 5%, headache 5%, diarrhea, ↑ ALT, AST, & rash (3% each). In pts rx for >6 mos., serious side-effects have included adrenal insufficiency, nephrotoxicity, & QTc interval prolongation. Significant drug-drug interactions; inhibits CYP3A4 *(see Table 22)*. Consider monitoring serum concentrations *(AAC 53:24, 2009)*. **100 mg delayed-release tablets:** loading dose of 300 mg (three 100 mg delayed-release tablets) twice daily on the first day, followed by a once-daily maintenance dose of 300 mg (three 100 mg delayed-release tablets) starting on the second day of therapy. Approved for prophylaxis only and not treatment. Tablets allow patients to achieve better levels than the suspension. Treatment dose unknown but prophylactic dose often achieves therapeutic levels. The tablet and solution are not interchangeable. Intravenous formulation approved for prophylaxis at 300 mg IV daily after a loading dose of 300 mg bid x 1 day. Consider therapeutic drug monitoring with a goal trough of > 0.7 for prophylaxis and > 1.0 for treatment. *JAC 69:1162, 2014.*
Terbinafine (Lamisil) 250 mg tab	In pts given terbinafine for onychomycosis, rare cases (8) of idiosyncratic & symptomatic hepatic injury & more rarely liver failure leading to death or liver transplant. The drug is **not recommended** for pts with **chronic or active liver disease;** hepatotoxicity may occur in pts with or without pre-existing disease. Pretreatment serum transaminases (ALT & AST) advised & alternate rx used for those with abnormal levels. Pts started on terbinafine should be warned about symptoms suggesting liver dysfunction (persistent nausea, anorexia, fatigue, vomiting, RUQ pain, jaundice, dark urine or pale stools). If symptoms develop, drug should be discontinued & liver function immediately evaluated. In controlled trials, changes in ocular lens and retina reported—clinical significance unknown. Major drug-drug interaction is 100% ↑ in rate of clearance by rifampin. AEs: usually mild, transient and rarely caused discontinuation of rx. % with AE, terbinafine vs placebo: nausea/diarrhea 2.6–5.6 vs 2.9; rash 5.6 vs 2.2; taste abnormality 2.8 vs 0.7. Inhibits CYP2D6 enzymes *(see Table 22)*. An acute generalized exanthematous pustulosis and subacute cutaneous lupus erythematosus reported.
Voriconazole (Vfend) **IV: Loading dose 6 mg per kg q12h times 1 day, then 4 mg per kg q12h IV** for invasive aspergillus & serious mold infections; **3 mg per kg IV q12h** for serious candida infections. **Oral: >40 kg body weight:** 400 mg po q12h, then 200 mg po q12h. **<40 kg body weight:** 200 mg po q12h, then 100 mg po q12h **Take oral dose 1 hour before or 1 hour after eating.** Oral suspension (40 mg per mL). Oral suspension dosing: Same as for oral tabs. Reduce to ½ maintenance dose for moderate hepatic insufficiency	A triazole with activity against Aspergillus sp., **including Ampho resistant strains of A. terreus.** Active vs Candida sp. (including krusei), Fusarium sp., & various molds. Steady state serum levels reach 2.5–4 mcg per mL. Up to 20% of patients with subtherapeutic levels with oral administration: check levels for suspected treatment failure, life threatening infections. 300 mg bid oral dose or 8 mg/kg/d IV dose may be required to achieve target steady-state drug concentrations of 1-6 mcg/mL. **Toxicity** similar to other azoles/triazoles including uncommon serious hepatic toxicity (hepatitis, cholestasis & fulminant hepatic failure. Liver function tests should be monitored during rx & drug dc'd if abnormalities develop. Photosensitivity is common and can be severe. Many reports of associated skin cancers. Strongly recommend sun protective measures. *CID 58:997, 2014* & hallucinations & anaphylactoid infusion reactions with fever and hypertension. 1 case of QT prolongation with ventricular tachycardia in a 15 y/o pt with ALL reported. **Approx. 21% experience a transient visual disturbance** following IV or po ("altered/enhanced visual perception", blurred or colored visual change or photophobia) within 30–60 minutes. Visual changes resolve within 30–60 min. after administration & are attenuated with repeated doses **(do not drive at night for outpatient rx).** Persistent visual changes occur rarely. Cause unknown. In patients with ClCr <50 mL per min., the intravenous vehicle (SBECD-sulfobutylether-B cyclodextrin) may accumulate but not obviously toxic *(CID 54:913, 2012).* Hallucinations, hypoglycemia, electrolyte disturbance & pneumonitis attributed to ↑ drug concentrations. Potential for drug drug interactions high—*see Table 22.* **With prolonged use, fluoride in drug can cause a painful periostitis.** *(CID 59:1237, 2014)* **NOTE: Not in urine in active form. No activity vs. mucormycosis.**

See page 2 for abbreviations. All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 12A – TREATMENT OF MYCOBACTERIAL INFECTIONS*

Tuberculin skin test (TST). Same as PPD *[Chest 138:1456, 2010].*

Criteria lor positive TST after 5 tuberculin units (intermediate PPD) read at 48–72 hours:

- ≥5 mm indurafion: + HIV, immunosuppressed, ≥15 mg prednisone per day, healed TBc on chest x-ray, recent close contact
- ≥10 mm induration: loreign-born, countries with high prevalence; IVD Users; low income; NH residents; chronic illness; silicosis
- ≥15 mm induration: otherwise healthy

Two-sfage to detecf sluggish positivity: If 1st PPD + buf <10 mm, repeat intermediate PPD in 1 wk. Response to 2nd PPD can also happen il pt received BCG in childhood.

BCG vaccine as child: if ≥10 mm induration, & from country with TBc, should be attributed to MTB. Prior BCG may result in boosfer ellect in 2-stage TST.

Routine anergy testing not recommended.

Interferon Gamma Release Assays (IGRAs): IGRAs detect sensitivities to MTB by measuring IFN-γ release in response to MTB antigens. May be used in place of TST in all situations in which TST may be used *(MMWR 59 (RR-5), 2010)*. FDA approved tests available in the U.S.:

- OuantiFERON-TB Gold (OFT-G) (approved 2005)
- OuantiFERON-TB Gold In-Tube Test (OFT-GIT) (approved 2007)
- T-Spot (approved 2008)

IGRAs are relatively specific for MTB and do not cross-react with BCG or most nontuberculous mycobacteria. CDC recommends IGRA over TST for persons unlikely to return lor reading TST & for persons who have received BCG. TST is prelerred in children age < 5 yrs (but IGRA is acceptable). IGRA or TST may be used without preference for recent contacts of TB with special utility for follow-up tesfing since IGRAs do not produce "booster effect". May also be used without preference over TBc for occupational exposures. As with TST, testing with IGRAs in low prevalence populations will result in false-positive results *(CID 53:234, 2011)*. Manufacturer's IFN-gamma cutoff ≥0.35 IU/ml for OFT-GIT may be too low for low prevalence settings, inflating positivity and conversion rates, and a higher cut-off may be more appropriate *(Am J Respir Crit Care Med 188:1005, 2013)*. For detailed discussion of IGRAs, see *MMWR 59 (RR-5), 2010 and JAMA 308:241, 2012.*

Rapid (24-hr or less) diagnostic tests lor MTB: (1) the Amplilied Mycobacterium tuberculosis Direct Test amplifies and defects MTB ribosomal RNA; (2) the AMPLICOR Mycobacterium tuberculosis Test amplifies and detects MTB DNA. Both tests have sensitivities & specificifies >95% in sputum samples that are AFB-positive. In negative smears, specificity remains >95% but sensitivity is 40–77% *(MMWR 58:7, 2009; CID 49:46, 2009)* to 60-90% *(see: http://www.cdc.gov/tb/publications/guidelines/amplification_tests/default.htm (3)* COBAS TaqMan MTB Test: real-time PCR test for detection of M. tuberculosis in respiratory specimens (not available in the U.S.) with performance characteristics similar to other rapid tests *(J Clin Microbiol 51:3225, 2013)*.

Xpert MTB/RIF is a rapid test (2 hrs) for MTB in sputum samples which also detects RIF resistance with specificity of 99.2% and sensitivity of 72.5% in smear negative patients *(NEJM 363:1005, 2010)*. Current antibody-based and ELISA-based rapid tests for TBc not recommended by WHO because they are less accurate than microscopy ± culture *(Lancet ID 11:736, 2011)*.

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS	
		INITIAL THERAPY	CONTINUATION PHASE OF THERAPY
I. **Mycobacterium tuberculosis exposure baseline TST/IGRA negative** (household members & other close contacts of potentially infectious cases)	Neonate- Rx essential NOTE: If fever, abnormal CXR (pleural effusion, hilar adenopathy, infiltrafe) at baseline, treat for acfive TBc and not with INH alone.	**INH** (10 mg/kg/ day lor 8-10 wks)	Repeat fuberculin skin test (TST) in 8-12 wks: if TST neg & CXR normal & inlant age at exposure > 6 mos., stop INH, if TST (≥ 5 mm) or age ≤ 6 mos, treat with INH for total ol 9 mos. Il follow-up CXR abnormal, treat lor active TBc.
	Children <5 years of age—Rx indicated	As for neonate for 1st 8-10 wks.	If repeat TST at 8-10 wks is negative, stop. If repeat TST ≥ 5 mm, continue INH lor total of 9 mos. If INH not given initially, repeat TST at 3 mos, **if + rx** with INH for 9 mos. *(see Category II below)*.
	Older children & adults— Risk 2–4% 1st yr		Pts at high risk of progression (e.g., HIV+, immunosuppressed or on immunosuppressive therapy) and no evidence of active infection should be treated lor LTBI (see below). For others repeat TST/IGRA at 8-10 wks: no rx if repeat TST/IGRA neg.

See page 2 for abbreviations

* Dosages are for adults (unless otherwise indicated) and assume normal renal function

† **DOT** = directly observed therapy

TABLE 12A (2)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS	
		INITIAL THERAPY	ALTERNATIVE
II. Tuberculosis (LTBI, positive TST or IGRA as above, active TB ruled out) *See FIGURE 1 for treatment algorithm for pt with abnormal baseline CXR (e.g., upper lobe fibronodular disease) suspected active TBc.)* *Review:* *NEJM 372:2127, 2015* Estimating risk of active M.TBc in pts with positive TST or IGRA (www.tst3d.com)	Age no longer an exclusion, all persons with LTBI should be offered therapy. If pre-anti-TNF therapy, recommend at least one month of treatment for LBTI prior to start of anti-TNF therapy *(Arth Care & Res 64:625, 2012)*. Overall, regimens containing a rifamycin (RIF, RFB or RFP) are most effective at preventing active tuberculosis *(AnUM 161:419 & 449, 2014)*. For patients on **Isoniazid** educate and monitor clinically for signs and symptoms of hepatitis. Baseline lab testing of liver function at start of therapy not routinely indicated but is indicated for patients with HIV infection, pregnant women, and women within 3 mo of delivery, persons with a history of chronic liver disease, persons who use alcohol regularly, and persons at risk for chronic liver disease. Lab monitoring of liver function during therapy is indicated if baseline liver function tests are abnormal, if risk factors for hepatic disease are present, or to evaluate for possible adverse effects.	**INH** po once daily (adult: 5 mg/kg/day, max 300 mg/day; child: 10-15 mg/kg/day not to exceed 300 mg/day) x 9 mos. For current recommendations for monitoring hepatotoxicity on INH see *MMWR 59:227, 2010*. Supplemental pyridoxine 50 mg/day for HIV+ patients. A 12 dose once weekly DOT[†] **INH** + **Rifapentine** (RFP): **INH** po 15 mg/kg (max dose 900 mg); **RFP** po (wt-based dose): 10-14 kg: 300 mg; 14.1-25 kg: 450 mg; 25.1-32 kg: 600 mg; 32.1-49.9 kg: 750 mg; ≥50 kg: 900 mg. Not recommended for children age < 2 yrs; pts with HIV/AIDS on ART; pregnant women; or pts presumed infected with INH- or RIF-resistant MTB *(MMWR 60:1650, 2011, NEJM 365:2155, 2011)*.	**INH** 300 mg once daily for 6 mo (but slightly less effective than 9 mos.; not recommended in children, HIV+ persons, or those with fibrotic lesions on chest film). **INH** 2x/wk (adult: 15 mg/kg, max 900 mg; child: 20-30 mg/kg, max dose 900 mg) x 9 mo. **RIF** once daily po (adult: 10 mg/kg/day, max dose 600 mg/day; child: 10-20 mg/kg/day, max dose 600 mg/day) for 4 mos. **INH** + **RIF** once daily x 3 mos. Rates of flu-like symptoms, cutaneous reactions, and severe drug reactions (rare, 0.3%) higher with 3 mo INH+RFP than with 9 mo INH *(CID 61:527, 2015)*, but hepatotoxicity higher with INH (1.8% vs. 0.4%) *(Int J Tuberc Lung Dis 19:1039, 2015)*.
	Pregnancy	Regimens as above. Once active disease is excluded may delay initiation of therapy until after delivery unless patient is recent contact to an active case, HIV+. Supplemental pyridoxine 10-25 mg/d recommended	
LTBI, suspected INH-resistant organism		**RIF** once daily po (adult: 10 mg/kg/day, max dose 600 mg/day; child: 10-20 mg/kg/day, max dose 600 mg/day) for 4 mos.	**RFB** 300 mg once daily po may be substituted for RIF (in HIV+ patient on anti-retrovirals, dose may need to be adjusted for drug interactions).
LTBI, suspected INH and RIF resistant organism		**Moxi**. 400 mg ± **EMB** 15 mg/kg once daily x 12 months	**Levo**. 500 mg once daily + (**EMB** 15 mg/kg or **PZA** 25 mg/kg) once daily x 12 months.

See page 2 for abbreviations

* Dosages are for adults (unless otherwise indicated) and assume normal renal function

[†] **DOT** = directly observed therapy

TABLE 12A (3)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUM-STANCES	SUGGESTED REGIMENS							COMMENTS
		INITIAL THERAPY			CONTINUATION PHASE OF THERAPY (in vitro susceptibility known)				
		SEE COMMENTS FOR DOSAGE AND DIRECTLY OBSERVED THERAPY (DOT) REGIMENS							
		Regimen: in order of preference	Drugs	Interval/Doses (min. duration)	Regimen	Drugs	Interval/Doses (min. duration)	Range of Total Doses (min. duration)	
III. Mycobacterium tuberculosis **A. Pulmonary TB** General reference on rx in adults & children: *MMWR 52 (RR-11):1,* 2003. In pts with newly diagnosed HIV and TB, Rx for both should be started as soon as possible *(NEJM 362:697, 2010).* **Isolation essential!** Hospitalized pts with suspected or documented active TB should be isolated in single rooms using airborne precautions until deemed non-infectious. DC isolation if 3 negative AFB smears or 1-2 neg NAAT (Xpert MTB/RIF) *(CID 59:1353 & 1361, 2014).* **USE DOT REGIMENS IF POSSIBLE** *(continued on next page)*	**Rate of INH resistance known to be <4%** (drug-susceptible organisms)	1 *(See Figure 2 page 143)*	INH RIF PZA EMB	7 days per wk times 56 doses (8 wks) or 5 days per wk (DOT) times 40 doses (8 wks) If cavitary disease, treat for 9 mos. Fixed dose combination of INH, RIF, PZA & EMB currently being evaluated *(JAMA 305:1415, 2011).*	1a	INH/ RIF[a]	7 days per wk times 126 doses (18 wks) or 5 days per wk (DOT) times 90 doses (18 wks). If cavitary disease, treat for 9 mos.	182–130 (26 wks)	**Dose in mg per kg (max. q24h dose)** **Regimen* INH RIF PZA EMB SM RFB** **Q24h:** Child 10–20 10–20 15–30 15–25 20–40 10–20 (300) (600) (2000) (1000) (300) Adult 5 (300) 10 (600) 15–30 (2000) 15–25 15 (1000) 5 (300) **2 times per wk (DOT):** Child 20–40 (900) 10–20 (600) 50–70 (4000) 50 25–30 (1500) 10–20 (300) Adult 15 (900) 10 (600) 50–70 (4000) 50 25–30 (1500) 5 (300) **3 times per wk (DOT):** Child 20–40 (900) 10–20 (600) 50–70 (3000) 25–30 25–30 (1500) NA Adult 15 (900) 10 (600) 50–70 (3000) 25–30 25–30 (1500) NA **Second-line anti-TB agents can be dosed as follows to facilitate DOT:** Cycloserine 500–750 mg po q24h (5 times per wk) Ethionamide 500–750 mg po q24h (5 times per wk) Kanamycin or capreomycin 15 mg per kg IM/IV q24h (3–5 times per wk) Ciprofloxacin 750 mg po q24h (5 times per wk) Ofloxacin 600–800 mg po q24h (5 times per wk) Levofloxacin 750 mg po q24h (5 times per wk) *(CID 21:1245, 1995)* **Risk factors for drug-resistant (MDR) TB:** Recent immigration from Latin America or Asia or living in area of † resistance (≥4%) or previous rx without RIF; exposure to known MDR TB. Incidence of MDR TB in **US steady** at 0.7%. Incidence of primary drug resistance is particularly high (>25%) in parts of China, Thailand, Russia, Estonia & Latvia; ~80% of US MDR cases in foreign born.
					1b	INH/ RIF	2 times per wk times 36 doses (18 wks)	92–76 (26 wks) (Not AIDS pts)	
					1c	INH/ RFP	1 time per wk times 18 doses (18 wks) (only if HIV-neg)	74–58 (26 wks)	
		2 *(See Figure 2 page 143)*	INH RIF PZA EMB	7 days per wk times 14 doses (2 wks), then 2 times per wk times 12 doses (6 wk) or 5 days per wk (DOT) times 10 doses (2 wks) then 2 times per wk times 12 doses (6 wks)	2a	INH/ RIF	2 times per wk times 36 doses (18 wks)	62–58 (26 wks) (Not AIDS pts)	
					2b[b]	INH/ RFP	1 time per wk times 18 doses (18 wks) (only if HIV-neg)	44–40 (26 wks)	
		3 *(See Figure 2 page 143)*	INH RIF PZA EMB	3 times per wk times 24 doses (8 wks)	3a	INH/ RIF	3 times per wk times 54 doses (18 wks)	78 (26 wks)	
		4 *(See Figure 2 page 143)*	INH RIF EMB	7 days per wk times 56 doses (8 wks) or 5 days per wk (DOT) times 40 doses (8 wks)	4a	INH/ RIF	7 days per wk times 217 doses (31 wks) or 5 days per wk (DOT) times 155 doses (31 wks)	273–195 (39 wks)	
					4b	INH/ RIF	2 times per wk times 62 doses (31 wks)	118–102 (39 wks)	

(continued on next page)

See page 2 for abbreviations

* Dosages are for adults (unless otherwise indicated) and assume normal renal function

† **DOT** = directly observed therapy

TABLE 12A (4)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUM-STANCES	SUGGESTED REGIMEN[a]	DURATION OF TREATMENT (mos.)[a]	SPECIFIC COMMENTS[a]	COMMENTS
III. Mycobacterium tuberculosis **A. Pulmonary TB** *(continued from previous page)* **Multidrug-Resistant Tuberculosis** (MDR TB): Defined as resistant to at least 2 drugs including INH & RIF. Pt clusters with high mortality *(NEJM 363:1050, 2010)*. **Extensively Drug-Resistant TB** (XDR-TB): Defined as resistant to INH & RIF plus any FQ and at least 1 of the 3 second-line drugs: capreomycin, kanamycin or amikacin *(MMWR 56:250, 2007; CID 51:379, 2010)*.	**INH (± SM) resistance**	**RIF, PZA, EMB** (a **FQ** may strengthen the regimen for pts with extensive disease).	*6*	INH should be stopped in cases of INH resistance. Outcome similar for drug susceptible and INH-mono-resistant strains *(CID 48:179, 2009)*.	*(continued from previous page)* **Alternatives for resistant strains: Moxi** and **levo** are **FQs of choice**, not CIP. FQ resistance may be seen in pts previously treated with FQ. WHO recommends using moxi (if MIC ≤ 2) if resistant to earlier generation FQs *(AAC 54:4765, 2010)*. **Linezolid** 600 mg once daily has excellent in vitro activity, including MDR strains and effective in selected cases of MDR TB and XDR TB but watch for toxicity *(NEJM 367:1508, 2012)*. **Clofazimine** 100 mg as one component of a multiple drug regimen may improve outcome *(CID 60:1361, 2015)*. **Bedaquiline** recently FDA approved for treatment of MDR TB based on efficacy in Phase 2 trials *(NEJM 360:2397, 2009; AAC 56:3271, 2012; NEJM 371:689, 723, 2014)*. Dose is 400 mg once daily for 2 weeks then 200 mg tiw for 22 weeks administered as directly observed therapy (DOT), taken with food, and always in combination with other anti-TB meds. The investigational agent, **delamanid** *(NEJM 366:2151, 2012; Eur Respir J 45:1498, 2015)* at a dose of 100 mg bid, granted conditional approval for treatment of MDR-TB as one component of an optimized background regimen by the European Medicines Agency. **Consultation with an expert in MDR-TB management** strongly advised before use of this agent. For MDR-TB and XDR-TB, do drug susceptibility testing for ethambutol, PZA & other 2nd line drugs if possible *(CID 59:1364, 2014)*
	Resistance to INH & RIF (± SM)	**FQ, PZA, EMB, AMK or capreomycin (SM only if confirmed susceptible)**, see *Comment*	18–24	Extended rx is needed to ↓ the risk of relapse. In cases with extensive disease, the use of an additional agent (alternative agents) may be prudent to ↓ the risk of failure & additional acquired drug resistance. Resectional surgery may be appropriate.	
	Resistance to INH, RIF (± SM), & EMB or PZA	**FQ** (**EMB** or **PZA** if active), **AMK or capreomycin (SM only if confirmed susceptible)**, see *Comment*	24	Use the first-line agents to which there is susceptibility. Add 2 or more alternative agents in case of extensive disease. Surgery should be considered. Survival ↑ in pts receiving active FO & surgical intervention *(AJRCCM 169:1103, 2004)*.	
	Resistance to RIF	**INH, EMB, FQ**, supplemented with **PZA** for the first 2 mos (an IA may be included for the first 2–3 mos. for pts with extensive disease)	12–18	Extended use of an IA may not be feasible. An all-oral regimen fimes 12–18 mos. should be effective but for more extensive disease &/or to shorten duration (e.g., to 12 mos.), an IA may be added in the initial 2 mos. of rx.	
	XDR-TB	Expert consultation strongly advised. See *comments*	18-24	Therapy requires administration of 4-6 drugs to which infecting organism is susceptible, including multiple second-line drugs *(MMWR 56:250, 2007)*. Increased mortality seen primarily in HIV+ patients. Cure with outpatient therapy likely in non-HIV+ patients when regimens of 4 or 5 or more drugs to which organism is susceptible are employed *(NEJM 359:563, 2008; CID 47:496, 2008)*. Successful sputum culture conversion correlates to initial susceptibility to FOs and kanamycin *(CID 46:42, 2008)*. Bedaquiline *(CID 60:188, 2015)* and Linezolid are options.	

See *page 2 for abbreviations*

* Dosages are for adults (unless otherwise indicated) and assume normal renal function

† **DOT** = directly observed therapy

TABLE 12A (5)

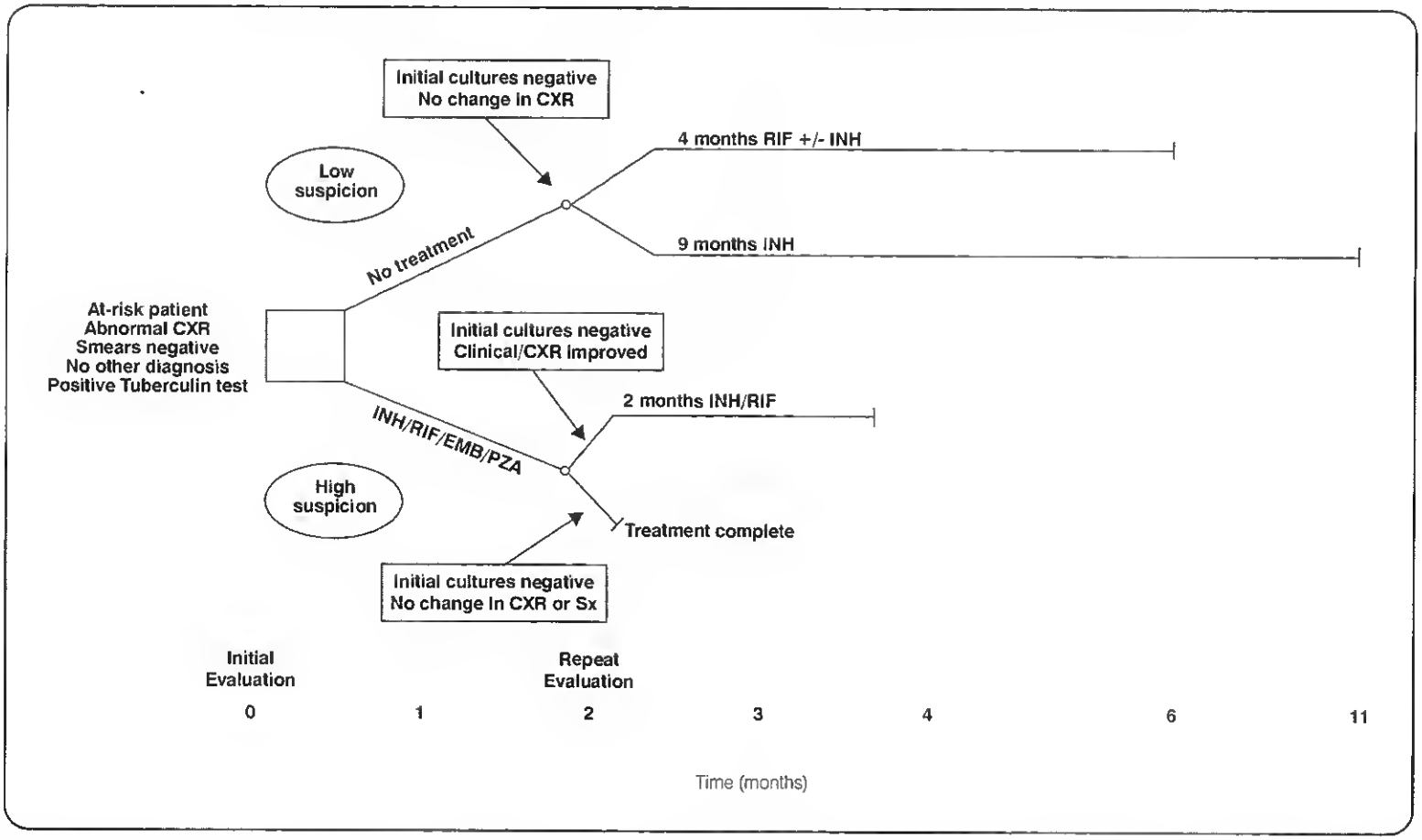
CAUSATIVE AGENT/DISEASE; MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS: INITIAL THERAPY	SUGGESTED REGIMENS: CONTINUATION PHASE OF THERAPY (in vitro susceptibility known)	COMMENTS
III. Mycobacterium tuberculosis *(continued)*			
B. Extrapulmonary TB **Steroids:** see Comment	**INH** + **RIF** (or **RFB**) + **PZA** + **EMB** q24h times 2 months Some add **pyridoxine** 25–50 mg po q24h to regimens that include INH.	**INH** + **RIF** (or **RFB**)	IDSA recommends 6 mos for lymph node, pleural, pericarditis, disseminated disease, genitourinary & peritoneal TBc; 6–9 mos for bone & joint; 9-12 mos for CNS (including meningeal) TBc. **Corticosteroids** "strongly rec" only for meningeal TBc *[MMWR 52(RR-11):1, 2003]*. Steroids not recommended for pericarditis *(NEJM 371:1121 & 1155, 2014)*.
C. Tuberculous meningitis Excellent summary of clinical aspects and therapy (including steroids): *CMR 21:243, 2008*. Also *J Infect 59:167, 2009*.	(**INH** + **RIF** + **EMB** + **PZA**) + prednisone 60 mg/day x 4 wks, then 30 mg/day x 4 wks, then 15 mg/day x 2 wks, then 5 mg/day x 1 wk	May omit **EMB** when susceptibility to **INH** and **RIF** established. Can D/C PZA after 2 months. Treat for total of 12 months. *See Table 9, page 94*, for CSF drug penetration. Initial reg of **INH** + **RIF** + **SM** + **PZA** also effective, even in patients with INH resistant organisms.	**3 drugs often rec for initial rx; we prefer 4** *(J Infect 59:167, 2009)*. Infection with MDR TB ↑ mortality & morbidity. **Dexamethasone** (for 1st mo) shown to ↓ complications & ↑ survival *(NEJM 351:1741, 2004)*. FQs (Levo, Gati, CIP) may be useful if started early *(AAC 55:3244, 2011)*.
D. Tuberculosis during pregnancy	**INH** + **RIF** + **EMB** for 9 mos	SM should not be substituted for EMB due to toxicity. AMK, capreomycin, kanamycin, FQs also contraindicated. PZA is recommended for routine use in pregnant women by the WHO but has not been recommended for general use in U.S. due to lack of safety data, although PZA has been used in some US health jurisdictions without reported adverse events. Breast-feeding should not be discouraged. If PZA is not included in the initial treatment regimen, the minimum duration of therapy is 9 months. Pyridoxine, 25 mg/ day, should be administered.	
E. Treatment failure or relapse: Usually due to poor compliance or resistant organisms, or subtherapeutic drug levels *(CID 55:169, 2012)*.	Directly observed therapy (DOT). Check susceptibilities. *(See section III. A, page 139 & above)*	Pts whose sputum is culture-positive after 5–6 mos. = treatment failures. Failures may be due to non-compliance or resistant organisms. Confirm susceptibilities of original isolates and obtain susceptibility to first and second line agents on current isolates. Non-compliance common, therefore institute DOT. If isolates show resistance, modify regimen to include at least 2 (preferably 3) new active agents, ones that the patient has not previously received if at all possible. Patients with MDR-TB usually convert sputum within 12 weeks of successful therapy.	
F. HIV infection or AIDS—pulmonary or extrapulmonary All HIV infected patients with TB should be treated with ARVs. If CD4 < 50, initiation of ARVs within 2 weeks of starting TB meds associated with improved survival *(Ann Intern Med 163:32, 2015)*. If CD4 > 50 no proven survival benefit with early ARVs: initiate ARVs at 2-4 weeks of TB meds for moderately severe or severe TB, 8-12 weeks for less severe TB.	**INH** + **RIF** (or **RFB**) + **PZA** q24h x 2 mos.	**INH** + **RIF** (or **RFB**) q24h times 4 months (total 6 mos.). Treat up to 9 mos. in pts with delayed response, cavitary disease. **Add pyridoxine 50 mg po q24h to regimens that include INH**	1. Co-administration of RIF not recommended for these anti-retroviral drugs: nevirapine, etravirine, rilpivirine; maraviroc, elvitegravir (integrase inhibitor in four drug combination Stribild®), all HIV protease inhibitors. Use RFB instead). 2. RIF may be coadministered with efavirenz; nucleoside reverse transcriptase inhibitors. Coadministration of RIF with raltegravir best avoided (use RFB instead) but if necessary increase raltegravir dose to 800 mg q12h: RIF + dolutegravir OK at 50 mg bid of latter. 3. Because of possibility of developing resistance to RIF or RFB in pts with low CD4 cell counts who receive wkly or biwkly (2x/wk) therapy, daily dosing (preferred), or at a min 3x/wk dosing (failure rate likely higher) recommended for initial or continuation phase of rx. 4. Clinical & microbiologic response similar to that of HIV-neg patient 5. Post-treatment suppression not necessary for drug-susceptible strains. 6. Immune reconstitution inflammatory syndrome occurs in 10-20% of TB patients after initiation of ARVs.
Concomitant protease inhibitor (PI) therapy	**INH** 300 mg q24h + **RFB** (150 mg q24h or 300 mg tiw) + **EMB** 15 mg/kg q24h + **PZA** 25 mg/kg q24h x 2 mos.; then INH + RFB times 4 mos. (up to 7 mos.)	**INH** + **RFB** x 4 mos. (7 mos. in slow responders, cavitary disease)	Rifamycins induce cytochrome CYP450 enzymes (RIF > RFP > RFB) & reduce serum levels of concomitantly administered PIs. Conversely, PIs inhibit CYP450 & cause ↑ serum levels of RFP & RFB. If dose of RFB is not reduced, toxicity ↑.

* Dosages are for adults (unless otherwise indicated) and assume normal renal function

† **DOT** = directly observed therapy

TABLE 12A (6)

FIGURE 1 ALGORITHM FOR MANAGEMENT OF AT-RISK PATIENT WITH LOW OR HIGH SUSPICION OF ACTIVE TUBERCULOSIS WHILE CULTURES ARE PENDING *(modified from MMWR 52(RR-11):1, 2003).*



Patients at high clinical suspicion of active TB should be started on 4-drug therapy, pending results of cultures. If cultures are negative and there is no change in symptoms or CXR, the 4-drug regimen can be stopped and no further therapy is required. If cultures are negative and there is clinical or CXR improvement, continue INH/RIF for 2 additional months. For patients at low suspicion for active TB, treat for LTBI once cultures are negative.

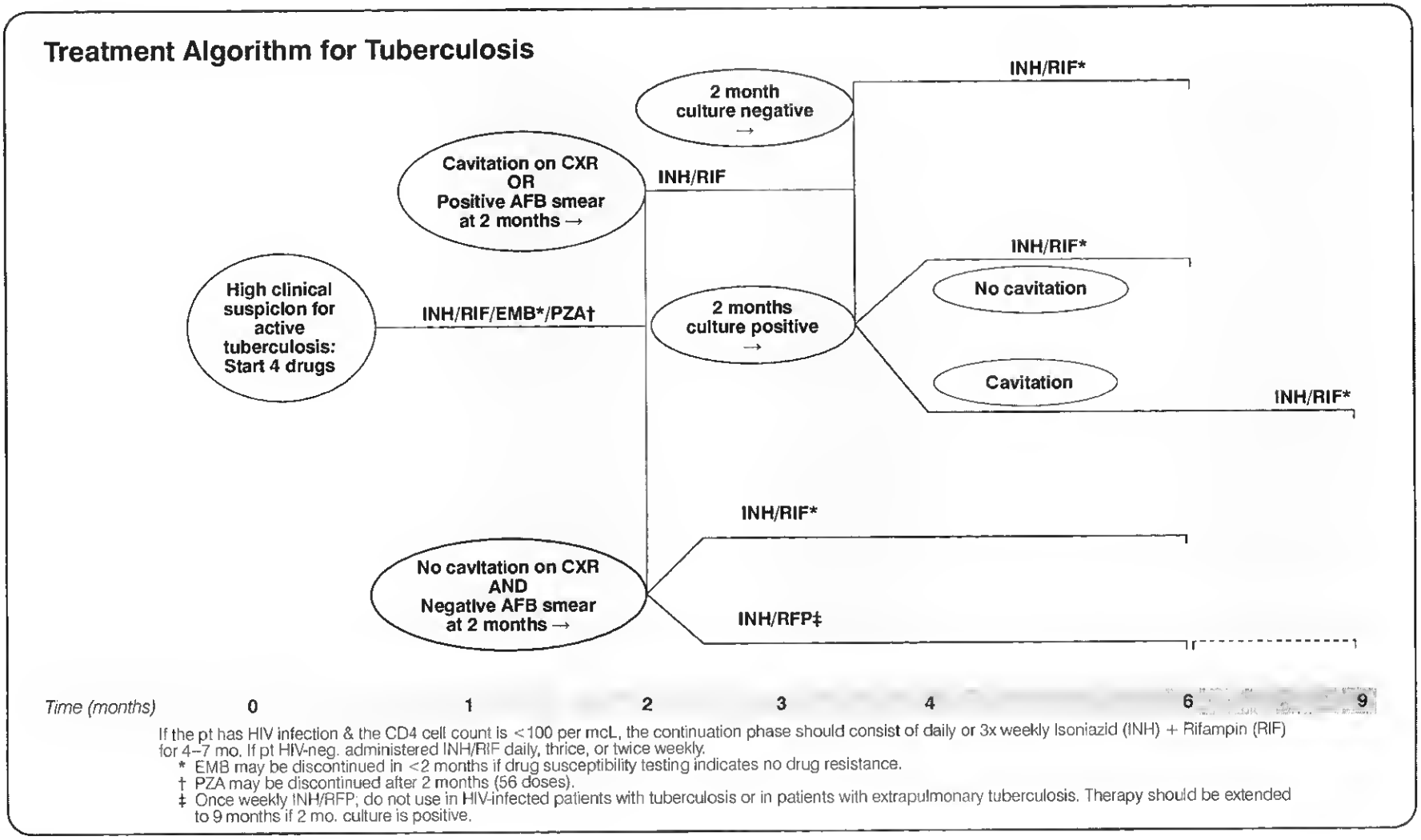
See page 2 for abbreviations

* Dosages are for adults (unless otherwise indicated) and assume normal renal function

† **DOT** directly observed therapy

TABLE 12A (7)

FIGURE 2 *[Modified from MMWR 52(RR-11):1, 2003]*



If the pt has HIV infection & the CD4 cell count is <100 per mcL, the continuation phase should consist of daily or 3x weekly Isoniazid (INH) + Rifampin (RIF) for 4–7 mo. If pt HIV-neg. administered INH/RIF daily, thrice, or twice weekly.

* EMB may be discontinued in <2 months if drug susceptibility testing indicates no drug resistance.

† PZA may be discontinued after 2 months (56 doses).

‡ Once weekly INH/RFP; do not use in HIV-infected patients with tuberculosis or in patients with extrapulmonary tuberculosis. Therapy should be extended to 9 months if 2 mo. culture is positive.

See page 2 for abbreviations.

TABLE 12A (8)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS PRIMARY/ALTERNATIVE		COMMENTS
IV. Nontuberculous Mycobacteria (NTM) *(See ATS Consensus: AJRCCM 175:367, 2007; EID 17:506, 2011)*				
A. M. bovis		**INH + RIF + EMB** for 2 months then INH + RIF for 7 months		The M. tuberculosis complex includes M. bovis and regimens effective for MTB (except PZA based) also likely to be effective for M. bovis. **All isolates resistant to PZA.** Isolation not required. Increased prevalence of extrapulmonary disease in U.S. born Hispanic populations and elsewhere *(CID 47:168, 2008; EID 14:909, 2008; EID 17:457, 2011).*
B. Bacillus Calmette-Guerin (BCG) (derived from M. bovis)	Only fever (>38.5°C) for 12–24 hrs	**INH** 300 mg q24h times 3 months		Intravesical BCG effective in superficial bladder tumors and carcinoma in situ. With sepsis, consider initial adjunctive prednisolone. Also susceptible to RFB, CIP, oflox, levo, moxi, streptomycin, amikacin, capreomycin *(AAC 53:316, 2009)*. BCG may cause regional adenitis or pulmonary disease in HIV-infected children *(CID 37:1226, 2003)*. **Resistant to PZA.**
	Systemic illness or sepsis	Same as for M. bovis.		
C. M. avium-intracellulare complex (MAC, MAI, or Battey bacillus) *ATS/IDSA Consensus Statement: AJRCCM 175:367, 2007; See http://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/0 for updated CDC recommendations for AIDS patients.*	**Immunocompetent patients**			See AJRCCM 175:367, 2007 for details of dosing and duration of therapy. Intermittent (tiw) therapy not recommended for patients with cavitary disease, patients who have been previously treated or patients with moderate of severe disease. Intermittent therapy may be an option in nodular bronchiectatic form of the disease *(Am J Respir Crit Care Med 191:96, 2015)*. The primary microbiologic goal of therapy is 12 months of negative sputum cultures on therapy.
	Nodular/Bronchiectatic disease	[**Clarithro** 1000 mg or **azithro** 500 mg] tiw + **EMB** 25 mg/kg tiw + [**RIF** 600 mg or **RFB** 300 mg] tiw		
	Cavitary disease or severe nodular/bronchiectatic disease [**Clarithro** 500-1000 mg/day (lower	dose for wt <50 kg) or **azithro** 250 mg/day] + **EMB** 15 mg/kg/day + [**RIF** 600 mg/day or **RFB** 150-300 mg/day] ± [**strep** or **AMK**]		**"Classic" pulmonary MAC:** Men 50–75, smokers, COPD. May be associated with hot tub use *(Clin Chest Med 23:675, 2002)*. **"New" pulmonary MAC:** Women 30–70, scoliosis, mitral valve prolapse, (bronchiectasis), pectus excavatum ("Lady Windermere syndrome") and fibronodular disease in elderly women *(EID 16:1576, 2010)*. May also be associated with interferon gamma deficiency *(AJM 113:756, 2002)*. For cervicofacial lymphadenitis (localized) in immunocompetent children, surgical excision is as effective as chemotherapy *(CID 44:1057, 2007)*. Moxifloxacin and gatifloxacin, active in vitro & in vivo *(AAC 51:4071, 2007)*.
	HIV infection: **Primary prophylaxis**—Pt's CD4 count <50–100 per mm^3 Discontinue when CD4 count >100 per mm^3 in response to ART	**Azithro** 1200 mg po weekly OR **Clarithro** 500 mg po bid	**RFB** 300 mg po q24h OR **Azithro** 1200 mg po weekly + **RIF** 300 mg po q24h	**Many drug-drug interactions,** see *Table 22, page 237*. Drug-resistant MAI disease seen in 29–58% of pts in whom disease develops while taking clarithro prophylaxis & in 11% of those on azithro but has not been observed with RFB prophylaxis. Clarithro resistance more likely in pts with extremely low CD4 counts at initiation. Need to be sure no active MTB; RFB used for prophylaxis may promote selection of rifamycin-resistant MTB.
	Treatment Either presumptive dx or after + culture of blood, bone marrow, or usually, sterile body fluids, eg liver	(**Clarithro** 500 mg* po bid + **EMB** 15 mg/kg/day ± **RFB** 300 mg po q24h (adjust dose) *** Higher doses of clari (1000 mg bid) may be associated with ↑ mortality**	**Azithro** 500 mg po/day + **EMB** 15 mg/kg/day +/- **RFB** 300-450 mg po/day	Adjust RFB dose as needed for drug-drug interactions.

(continued on next page)

* Dosages are for adults (unless otherwise indicated) and assume normal renal function

† **DOT** directly observed therapy

TABLE 12A (9)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS PRIMARY/ALTERNATIVE		COMMENTS
IV. Nontuberculous Mycobacteria (NTM) *(continued)*				
C. M. avium-intracellulare complex *(continued)*				*(continued from previous page)* Addition of a third or fourth drug should be considered for patients with advanced immunosuppression (CD4+ count <50 cells/μL), high mycobacterial loads (>2 log CFU/mL of blood), or in the absence of effective ART: AMK 10–15 mg/kg IV daily; Strep 1 gm IV or IM daily; CIP 500–750 mg PO bid; Levo 500 mg PO daily; Moxi 400 mg PO daily. Testing of susceptibility to clarithromycin and azithromycin is recommended. Short term (4–8 weeks) of systemic corticosteroid (equivalent to 20–40 mg of prednisone) can be used for IRIS.
	Chronic post-treatment suppression—secondary prophylaxis	**Always necessary.** [**Clarithro** or azithro] + **EMB** 15 mg/ kg/day *(dosage above)*	**Clarithro** or **azithro** or **RFB** *(dosage above)*	Recurrences almost universal without chronic suppression. Can discontinue if no signs and symptoms of MAC disease and sustained (>6 months) CD4 count >100 cells/μL in response to ART.
D. Mycobacterium celatum	Treatment; optimal regimen not defined	May be susceptible to **clarithro**, **FQ** Treat as if MAC.		Isolated from pulmonary lesions and blood in AIDS patients. Easily confused with M. xenopi (and MAC).
E. Mycobacterium abscessus **Mycobacterium chelonae**	Treatment; Surgical excision may facilitate clarithro rx in subcutaneous abscess and is important adjunct to rx. For role of surgery in M. abscessus pulmonary disease, see *CID 52:565, 2011.*	Cutaneous: **Clarithro** 500 mg po bid x 6 months. Pulmonary/disseminated: 2 or 3 IV drugs (check susceptibility) (**Amikacin, IMP, Cefoxitin, Tigecycline**). Watch out for inducible resistance to Clarithro		M. abscessus susceptible in vitro to AMK (70%), clarithro (95%), cefoxitin (70%), CLO, cefmetazole, RFB, FO, IMP, azithro, CIP, Doxy, Mino, tigecycline *(CID 42:1756, 2006; JIC 15:46, 2009)*. M. abscesses actually a complex of 3 species: M. abscessus, M. massiliense, M bolletii; M. massiliense does not exhibit inducible resistance to macrolides and outcomes of medical therapy for infection with this organism may be better than with other species *(Int J Tuberc Lung Dis 18:1141, 2014)*. Culture-conversion may not be achievable in M. abscessus pulmonary infection; suppressive therapy may be required to control disease progression. Tigecycline effective in combination with other drugs in salvage therapy *(J Antimicrob Chemother 69:1945, 2014)*. Disseminated disease associated with auto-antibodies to interferon-γ *(Immunobiology 218: 762, 2013)*. Tigecycline effective in combination with other drugs in salvage therapy *(J Antimicrob Chemother 69:1945, 2014)*. In animal model, Cefoxitin & Tigecycline active *(JID 209:905, 2014)*. M. chelonae susceptible to AMK (80%), clarithro, azithro, tobramycin (100%), IMP (60%), moxifloxacin, CIP, Mino, Doxy, linezolid (94%) *(CID 42:1756, 2006)*. Resistant to cefoxitin, FO. Tigecycline highly active in vitro and successfully used as salvage for M. chelonae infection in combination regimens *(J Antimicrob Chemother 69:1945, 2014)*.
F. Mycobacterium fortuitum	Treatment; optimal regimen not defined. Surgical excision of infected areas.	**AMK** + **cefoxitin** + **probenecid** 2–6 wks, then po **TMP- SMX**, or **doxy** 2–6 mos. Usually responds to 6–12 mos of oral rx with 2 drugs to which it is susceptible.		**Resistant to all standard anti-TBc drugs.** Sensitive in vitro to doxycycline, minocycline, cefoxitin, IMP, AMK, TMP-SMX, CIP, oflox, azithro, clarithro, linezolid, tigecycline, but some strains resistant to azithromycin, rifabutin. For M. fortuitum pulmonary disease treat with at least 2 agents active in vitro until sputum cultures negative for 12 months *(AJRCCM 175:367, 2007)*. Disseminated disease associated with auto-antibodies to interferon-γ *(Intern Med 53:1361, 2014)*.
G. Mycobacterium haemophilum	Regimen(s) not defined. In animal model, **clarithro** + **rifabutin** effective. Combination of **CIP** + **RFB** + **clarithro** reported effective but clinical experience limited *(CID 52:488, 2011)*. Surgical debridement may be necessary.			Clinical: Ulcerating skin lesions, synovitis, osteomyelitis, cervicofacial lymphadenitis in children. Associated with permanent eyebrow makeup *(CID 52:488, 2011)*. Lab: Requires supplemented media to isolate. Sensitive in vitro to: CIP, cycloserine, rifabutin, moxifloxacin. Over ½ resistant to: INH, RIF, EMB, PZA. For localized cervicofacial lymphadenitis in immunocompetent children, surgical excision as effective as chemotherapy *(CID 44:1057, 2007)* or "watchful waiting" *(CID 52:180, 2011)*.

See page 2 for abbreviations

* Dosages are for adults (unless otherwise indicated) and assume normal renal function

† **DOT** = directly observed therapy

TABLE 12A (10)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS PRIMARY/ALTERNATIVE	COMMENTS
IV. Nontuberculous Mycobacteria (NTM) *(continued)*			
H. Mycobacterium genavense	2 or more drugs: **Clarithro**, **EMB**, **RFB**; **CLO**, **Amikacin**, Moxifloxacin as alternatives.		Seen in AIDS patients with CD4 < 50 and in non-HIV severely immunocompromised hosts. *For review see Clin Microbiol Infect 19:432, 2013.*
I. Mycobacterium gordonae	Regimen(s) not defined, but consider **RIF** + **EMB** + **KM** or **CIP** *(or* **linezolid** *(AJRCCM 175:367, 2007)*		Frequent colonizer, not associated with disease. In vitro: sensitive to EMB, RIF, AMK, CIP, clarithro, linezolid. Resistant to INH. Surgical excision.
J. Mycobacterium kansasii	O24h po: **INH** (300 mg) + **RIF** (600 mg) + **EMB** (25 mg per kg times 2 mos., then 15 mg per kg). Rx for 18 mos. (until culture-neg. sputum times 12 mos; 15 mos. If HIV+ pt.) *(See Comment)*	For **RIF** resistant organism: (**INH** 900 mg + **pyridoxine** 50 mg + **EMB** 25 mg/kg) po q24h + **Sulfamethoxazole** 1000 mg tid (if sulfamethoxazole is unavailable options include **TMP-SMX** two double strength tablets (320 mg **TMP** and 1600 mg SMX) bid OR **Clarithromycin** 500 mg po bid OR **Moxifloxacin** 400 mg po once daily. Treat for 12-15 mos or until 12-15 mos of culture-negative sputum.	**All Isolates are resistant to PZA.** Highly susceptible to linezolid in vitro *(AAC 47:1736, 2003)* and to clarithro and moxifloxacin *(JAC 55:950, 2005)*. If HIV+ pt taking protease inhibitor, substitute either clarithro (500 mg bid) or RFB (150 mg per day) for RIF. Because of variable susceptibility to INH, some substitute clarithro for INH. Resistance to clarithro reported.
K. Mycobacterium marinum	Two active agents for 1-2 months after surgical incision: **Clarithro** 500 mg bid + **EMB** 25 mg/kg q24h or **RIF** 600 mg q24h + **EMB** 25 mg/kg q24h Surgical excision.		For deep tissue involvement a three drug combination therapy with Rifampin 600 mg q24h + [Minocycline 100–200 mg q24h or Doxycycline 100–200 mg q24h] + Clarithromycin 500 mg bid. Monotherapy may be considered for minimal disease: Minocycline 100–200 mg q24h or Doxycycline 100–200 mg q24h or TMP-SMX 160/800 mg po bid.
L. Mycobacterium scrofulaceum	Surgical excision. Chemotherapy seldom indicated. Although regimens not defined, **clarithro** + **CLO** with or **without EMB**. **INH**, **RIF**, **strep** + **cycloserine** have also been used.		In vitro resistant to INH, RIF, EMB, PZA, AMK, CIP. Susceptible to clarithro, strep, erythromycin.
M. Mycobacterium simiae	Regimen(s) not defined. Start 4 drugs as for disseminated MAC		Most isolates resistant to all 1st-line anti-TBc drugs. Isolates often not clinically significant.
N. Mycobacterium ulcerans (Buruli ulcer)	WHO recommends **RIF** + **SM** for 8 weeks. **RIF**+ **CIP** recommended as alternatives by WHO *(CMN 31:119, 2009)*.		Susceptible in vitro to RIF, strep, CLO, clarithro, CIP, oflox, amikacin, moxi, linezolid. Australian guidelines (MJA 200:267, 2014) recommend oral combination of RIF + Clarithro or RIF + a FO (moxifloxacin or CIP). Surgery not required for cure and reserved for those declining or intolerant of antibiotic, debridement of necrotic tissue, large defects.
O. Mycobacterium xenopi	Regimen(s) not defined. **Clarithro** 500 mg bid + **RIF** 600 mg or **Rifabutin** 300 mg + **EMB** 15 mg/kg once daily + **INH** 300 mg once daily.		In vitro: sensitive to clarithro and many standard antimycobacterial drugs. MOXI active in vitro and may be an alternative.
V. Mycobacterium leprae (leprosy) Classification: *CID 44:1096, 2007*. Overview: *Lancet ID 11:464, 2011.*	There are 2 sets of therapeutic recommendations here: one from USA (National Hansen's Disease Programs [NHDP], Baton Rouge, LA) and one from WHO. Both are based on expert recommendations and neither has been subjected to controlled clinical trial.		

* Dosages are for adults (unless otherwise indicated) and assume normal renal function ! **DOT** directly observed therapy

TABLE 12A (11)

Type of Disease	NHDP Regimen	WHO Regimen	COMMENTS
Paucibacillary Forms: (Intermediate, Tuberculoid, Borderline tuberculoid)	(**Dapsone** 100 mg/day + **RIF** 600 mg po/day) for 12 months	(**Dapsone** 100 mg/day (unsupervised) + **RIF** 600 mg 1x/mo (supervised)) for 6 mos	Side effects overall 0.4%
Single lesion paucibacillary	Treat as paucibacillary leprosy for 12 months.	Single dose ROM therapy: (RIF 600 mg + Oflox 400 mg + Mino 100 mg) *(Ln 353:655, 1999).*	
Multibacillary forms: Borderline Borderline-lepromatous Lepromatous *See Comment for erythema nodosum leprosum* Rev.: *Lancet 363:1209, 2004*	(**Dapsone** 100 mg/day + **CLO** 50 mg/day + **RIF** 600 mg/day) for 24 mos **Alternative regimen:** (**Dapsone** 100 mg/day + **RIF** 600 mg/day + **Minocycline** 100 mg/day) for 24 mos if **CLO** is refused or unavailable.	(**Dapsone** 100 mg/day + **CLO** 50 mg/day (both unsupervised) + **RIF** 600 mg + **CLO** 300 mg once monthly (supervised)). Continue regimen for 12 months.	Side-effects overall 5.1%. For **erythema nodosum leprosum:** prednisone 60–80 mg/day or thalidomide 100-400 mg/day. Thalidomide available in US at 1-800-4-CELGENE. Altho thalidomide effective, WHO no longer rec because of potential toxicity however the majority of leprosy experts feel thalidomide remains drug of choice for ENL under strict supervision. **CLO (Clofazimine)** available from NHDP under IND protocol; contact at 1-800-642-2477. **Ethionamide** (250 mg q24h) or prothionamide (375 mg q24h) may be subbed for CLO. Etanercept effective in one case refractory to above standard therapy *(CID 52:e133, 2011).* Regimens incorporating clarithro, minocycline, dapsone monotherapy have been abandoned due to emergence of resistance *(CID 52:e127, 2011),* but older patients previously treated with dapsone monotherapy may remain on lifelong maintenance therapy. Moxi highly active in vitro and produces rapid clinical response *(AAC 52:3113, 2008).*

* Dosages are for adults (unless otherwise indicated) and assume normal renal function

† **DOT** = directly observed therapy

TABLE 12B – DOSAGE AND ADVERSE EFFECTS OF ANTIMYCOBACTERIAL DRUGS

AGENT (TRADE NAME)[1]	USUAL DOSAGE*	ROUTE/1° DRUG RESISTANCE (RES) US[2,§]	SIDE-EFFECTS, TOXICITY AND PRECAUTIONS	SURVEILLANCE
FIRST LINE DRUGS				
Ethambutol (Myambutol) (100, 400 mg tab)	25 mg/kg/day for 2 mos then 15 mg/ kg/day q24h as 1 dose (<10% protein binding) [Bacteriostatic to both extracellular & intracellular organisms]	RES: 0.3% (0–0.7%) po 400 mg tab	**Optic neuritis** with decreased visual acuity, central scotomata, and loss of green and red perception; peripheral neuropathy and headache (~1%), rashes (rare), arthralgia (rare), hyperuricemia (rare). Anaphylactoid reaction (rare). *Comment:* Primarily used to inhibit resistance. Disrupts outer cell membrane in M. avium with ↑ activity to other drugs.	Monthly visual acuity & red/ green with dose >15 mg/kg/ day. ≥10% loss considered significant. Usually reversible if drug discontinued.
Isoniazid (INH) (Nydrazid, Laniazid, Teebaconin) (50, 100, 300 mg tab)	Q24h dose: 5–10 mg/kg/day up to 300 mg/day as 1 dose. 2x/wk dose: 15 mg/kg (900 mg max dose) (< 10% protein binding) [Bactericidal to both extracellular and intracellular organisms] Add pyridoxine in alcoholic, pregnant, or malnourished pts.	RES: 4.1% (2.6–8.5%) po 300 mg tab IM 100 mg/mL in 10 mL (IV route not FDA-approved but has been used, esp. in AIDS)	Overall ~1%. Liver: **Hep** (children 10% mild ↑ SGOT, normalizes with continued rx, age <20 yrs rare, 20–34 yrs 1.2%, ≥50 yrs 2.3%) [also ↑ with q24h alcohol & previous exposure to Hep C (usually asymptomatic—*CID 36:293, 2003*)]. May be fatal. With prodromal sx, dark urine do LFTs; discontinue if SGOT >3–5x normal. **Peripheral neuropathy** (17% on 6 mg/kg per day, less on 300 mg, incidence ↑ in slow acetylators); **pyridoxine 10 mg q24h will decrease incidence;** other neurologic sequelae, convulsions, optic neuritis, toxic encephalopathy, psychosis, muscle twitching, dizziness, coma (all rare); allergic skin rashes, fever, minor disulfiram-like reaction, flushing after Swiss cheese; blood dyscrasias (rare); + antinuclear (20%). **Drug-drug interactions** common, *see Table 22.*	Pre-rx liver functions. Repeat if symptoms (fatigue, weakness, malaise, anorexia, nausea or vomiting) >3 days *(AJRCCM 152: 1705, 1995).* Some recommend SGOT at 2, 4, 6 mos esp. if age >50 yrs. Clinical evaluation every mo.
Pyrazinamide (500 mg tab)	25 mg per kg per day (maximum 2.5 gm per day) q24h as 1 dose [Bactericidal for intracellular organisms]	po 500 mg tab	**Arthralgia; hyperuricemia** (with or without symptoms); hepatitis (not over 2% if recommended dose not exceeded); gastric irritation; photosensitivity (rare).	Pre-rx liver functions. Monthly SGOT, uric acid. Measure serum uric acid if symptomatic gouty attack occurs.
Rifamate®— combination tablet	2 tablets single dose q24h	po (1 hr before meal)	1 tablet contains 150 mg INH, 300 mg RIF	As with individual drugs
Rifampin (Rifadin, Rimactane, Rifocin) (100, 300, 450, 600 mg cap)	10.0 mg per kg per day up to 600 mg per day q24h as 1 dose (60–90% protein binding) [Bactericidal to all populations of organisms]	RES: 0.2% (0–0.3%) po 300 mg cap (IV available, Merrell-Dow)	INH/RIF dc'd in ~3% for toxicity; gastrointestinal irritation, antibiotic-associated colitis, drug fever (1%), pruritus with or without skin rash (1%), anaphylactoid reactions in HIV+ pts, mental confusion, thrombocytopenia (1%), leukopenia (1%), hemolytic anemia, transient **abnormalities in liver function. "Flu syndrome"** (fever, chills, headache, bone pain, shortness of breath) seen if RIF taken irregularly or if q24h dose restarted after an interval of no rx. **Discolors urine, tears, sweat, contact lens an orange-brownish color.** May cause drug-induced lupus erythematosus *(Ln 349: 1521, 1977).*	Pre-rx liver function. Repeat if symptoms. **Multiple significant drug-drug interactions,** see *Table 22.*
Rifater®— combination tablet *(See Side-Effects)*	Wt ≥55 kg, 6 tablets single dose q24h	po (1 hr before meal)	1 tablet contains 50 mg INH, 120 mg RIF, 300 mg PZA. Used in 1st 2 months of rx (PZA 25 mg per kg). Purpose is convenience in dosing, ↑ compliance *(AnIM 122: 951, 1995)* but cost 1.58 more. Side-effects = individual drugs.	As with individual drugs, PZA 25 mg per kg
Streptomycin (IV/IM sol'n)	15 mg per kg IM q24h, 0.75–1.0 gm per day initially for 60–90 days, then 1.0 gm 2–3 times per week (15 mg per kg per day) q24h as 1 dose	RES: 3.9% (2.7–7.6%) IM (or IV)	Overall 8%. **Ototoxicity:** vestibular dysfunction (vertigo); paresthesias; dizziness & nausea (all less in pts receiving 2–3 doses per week); tinnitus and high frequency loss (1%); nephrotoxicity (rare); peripheral neuropathy (rare); allergic skin rashes (4–5%); drug fever. Available from X-Gen Pharmaceuticals, 607-732-4411. Ref. re: IV—*CID 19:1150, 1994.* Toxicity similar with qd vs tid dosing *(CID 38:1538, 2004).*	Monthly audiogram. In older pts, serum creatinine or BUN at start of rx and weekly if pt stable

[1] Note: Malabsorption of antimycobacterial drugs may occur in patients with AIDS enteropathy. For review of adverse effects, see *AJRCCM 167:1472, 2003.*

[2] **RES** = % resistance of M. tuberculosis

See page 2 for abbreviations.

* Dosages are for adults (unless otherwise indicated) and assume normal renal function

§ Mean (range) (higher in Hispanics, Asians, and patients <10 years old)

† **DOT** = directly observed therapy

TABLE 12B (2)

AGENT (TRADE NAME)[1]	USUAL DOSAGE*	ROUTE/1° DRUG RESISTANCE (RES) US[2,§]	SIDE-EFFECTS, TOXICITY AND PRECAUTIONS	SURVEILLANCE
SECOND LINE DRUGS (more difficult to use and/or less effective than first line drugs)				
Amikacin (Amikin) (IV soln)	7.5–10.0 mg per kg q24h [Bactericidal for extracellular organisms]	RES: (est. 0.1%) IM/IV 500 mg vial	*See Table 10B, pages 115 & 118* Toxicity similar with qd vs tid dosing *(CID 38:1538, 2004).*	Monthly audiogram. Serum creatinine or BUN weekly if pt stable
Bedaquiline (Sirturo) (100 mg tab) Ref: *JAC 69:2310, 2014; NEJM 371:723, 2014; CID 60:188, 2015.*	Directly observed therapy (DOT): 400 mg once daily for 2 weeks, then 200 mg 3 times weekly for 22 weeks, taken with food and always used in combination with other anti-TB medications.	Does not exhibit cross-resistance to other TB drugs; always use in combination with other TB drugs to prevent selection of resistant mutants	Most common: nausea, vomiting, arthralgia, headache, hyperuricemia. Elevated transaminases. Bedaquiline in clinical trials was administered as one component of a multiple drug regimen, so side-effects were common, yet difficult to assign to a particular drug.	Moderate QTc increases (average of 10-16 ms over the 24 weeks of therapy. Potential risks of pancreatitis, myopathy, myocardial injury, severe hepatotoxicity.
Capreomycin sulfate (Capastat sulfate)	1 gm per day (15 mg per kg per day) q24h as 1 dose	RES: 0.1% (0–0.9%) IM/IV	Nephrotoxicity (36%), ototoxicity (auditory 11%), eosinophilia, leukopenia, skin rash, fever, hypokalemia, neuromuscular blockade.	Monthly audiogram, biweekly serum creatinine or BUN
Ciprofloxacin (Cipro) (250, 500, 750 mg tab)	750 mg bid	500 mg or 750 mg po IV 200-400 mg vial	TB not a FDA-approved indication for CIP. Desired CIP serum levels 4–6 mcg per mL. See *Table 10A, page 110 & Table 10B, page 116 for adverse effects.*	None
Clofazimine (Lamprene) (50, 100 mg cap)	50 mg per day (unsupervised) + 300 mg 1 time per month supervised or 100 mg per day	50 mg (with meals)	Skin: **pigmentation (pink-brownish black)** 75–100%, dryness 20%, pruritus 5%. GI: abdominal pain 50% (rarely severe leading to exploratory laparoscopy), splenic infarction (VR), bowel obstruction (VR), GI bleeding (VR). Eye: conjunctival irritation, retinal crystal deposits.	None
Cycloserine (Seromycin) (250 mg tab)	750–1000 mg per day (15 mg per kg per day) 2–4 doses per day [Bacteriostatic for both extra-cellular & intracellular organisms]	RES: 0.1% (0–0.3%) 250 mg cap	Convulsions, **psychoses** (5–10% of those receiving 1.0 gm per day); headache; somnolence; hyperreflexia; increased CSF protein and pressure, **peripheral neuropathy.** 100 mg pyridoxine (or more) q24h should be given concomitantly. Contraindicated in epileptics.	None
Dapsone (25, 100 mg tab)	100 mg per day	100 mg tab	Blood: ↓ hemoglobin (1–2 gm) & ↑ retics (2–12%), in most pts. Hemolysis in G6PD deficiency. ↑ hemolysis due to concomitant atazanavir *(AAC 56:1081, 2012).* **Methemoglobinemia.** CNS: peripheral neuropathy (rare). GI: nausea, vomiting. Renal: albuminuria, nephrotic syndrome. Erythema nodosum leprosum in pts rx for leprosy (½ pts 1st year). Hypersensitivity syndrome in 0.5-3.6% *(See Surveillance).*	Hypersensitivity syndrome: fever, rash, eosinophilia, lymphadenopathy, hepatitis, pneumonitis. Genetic marker identified *(NEJM 369:1620, 2013).*
Ethionamide (Trecator-SC) (120, 250 mg tab)	500–1000 mg per day (15–20 mg per kg per day) divided 1–3 doses per day [Bacteriostatic for extracellular organisms only]	RES: 0.8% (0–1.5%) 250 mg tab	**Gastrointestinal irritation** (up to 50% on large dose); goiter; peripheral neuropathy (rare); convulsions (rare); changes in affect (rare); difficulty in diabetes control; rashes; hepatitis; purpura; stomatitis; gynecomastia; menstrual irregularity. Give drug with meals or antacids; 50–100 mg pyridoxine per day concomitantly; SGOT monthly. Possibly teratogenic.	

See *page 2 for abbreviations.*

* Dosages are for adults (unless otherwise indicated) and assume normal renal function

§ Mean (range) (higher in Hispanics, Asians, and patients <10 years old)

† **DOT** = directly observed therapy

TABLE 12B (3)

AGENT (TRADE NAME)[1]	USUAL DOSAGE*	ROUTE/1° DRUG RESISTANCE (RES) US[2, §]	SIDE-EFFECTS, TOXICITY AND PRECAUTIONS	SURVEILLANCE
SECOND LINE DRUGS *(continued)*				
Linezolid (Zyvox) (600 mg tab, oral suspension 100 mg/mL)	600 mg once daily	PO or IV	Not FDA-approved indication. High rate of adverse events (>80% with 4 months or longer of therapy: myelosuppression, peripheral neuropathy, optic neuropathy. Avoid tyramine-containing foods, soy products, adrenergic agents (e.g., pseudoephedrine, phenylpropanolamine) MOA inhibitors, SSRIs. 600 mg > 300 mg dose for toxicity; consider reducing dose to 300 mg for toxicity or after 4 mos of therapy or culture-conversion to reduce toxicity.	Baseline and monthly complete blood count, visual acuity checks, screen for symptoms of peripheral neuropathy, neurologic examination.
Moxifloxacin (Avelox) (400 mg tab)	400 mg qd	400 mg cap	Not FDA-approved indication. Concomitant administration of rifampin reduces serum levels of moxi *(CID 45:1001, 2007)*.	None
Ofloxacin (Floxin) (200, 300, 400 mg tab)	400 mg bid	400 mg cap	Not FDA-approved indication. Overall adverse effects 11%, 4% discontinued due to side-effects. GI: nausea 3%, diarrhea 1%. **CNS:** insomnia 3%, headache 1%, dizziness 1%.	
Para-aminosalicylic acid (PAS, Paser) (Na^+ or K^+ salt) (4 gm cap)	4–6 gm bid (200 mg per kg per day) [Bacteriostatic for extracellular organisms only]	RES: 0.8% (0–1.5%) 450 mg tab *(see Comment)*	**Gastrointestinal irritation** (10–15%); goitrogenic action (rare); depressed prothrombin activity (rare); G6PD-mediated hemolytic anemia (rare), drug fever, rashes, hepatitis, myalgia, arthralgia. Retards hepatic enzyme induction, may ↓ INH hepatotoxicity. Available from CDC, (404) 639-3670, Jacobus Pharm. Co. (609) 921-7447.	None
Rifabutin (Mycobutin) (150 mg cap)	300 mg per day (prophylaxis or treatment)	150 mg tab	Polymyalgia, polyarthralgia, leukopenia, granulocytopenia. Anterior uveitis when given with concomitant clarithromycin; avoid 600 mg dose *(NEJM 330:438, 1994)*. Uveitis reported with 300 mg per day *(AnIM 12:510, 1994)*. Reddish urine, orange skin (pseudojaundice).	None
Rifapentine (Priftin) (150 mg tab)	600 mg twice weekly for 1st 2 mos., then 600 mg q week	150 mg tab	Similar to other rifabutins. *(See RIF, RFB)*. Hyperuricemia seen in 21%. Causes red-orange discoloration of body fluids. Flu-like illness in pts given weekly Rifapentine + INH for latent MTB *(CID 61:527, 2015)*.	None
Thalidomide (Thalomid) (50, 100, 200 mg cap)	100–300 mg po q24h (may use up to 400 mg po q24h for severe erythema nodosum leprosum)	50 mg tab	**Contraindicated in pregnancy. Causes severe life-threatening birth defects. Both male and female patients must use barrier contraceptive methods (Pregnancy Category X).** Frequently causes drowsiness or somnolence. May cause peripheral neuropathy. *(AJM 108:487, 2000)* For review, see *Ln 363:1803, 2004*.	In US: contact Celgene (800-4-CELGENE)

See page 2 for abbreviations.

* Dosages are for adults (unless otherwise indicated) and assume normal renal function

§ Mean (range) (higher in Hispanics, Asians, and patients <10 years old)

[1] **DOT** directly observed therapy

TABLE 13A– TREATMENT OF PARASITIC INFECTIONS

- **See *Table 13D* for sources for antiparasitic drugs not otherwise commercially available.**
- The following resources are available through the Centers for Disease Control and Prevention (CDC) in Atlanta. Website is www.cdc.gov. General advice for parasitic diseases other than malaria: (+1) (404) 718-4745 (day), (+1) (770) 488-7100 (after hours). For CDC Drug Service 8:00 a.m. 4:30 p.m. EST: (+1) (404) 639-3670; fax: (+1) (404) 639-3717. *See www.cdc.gov/laboratory/drugservice/index.html* For malaria: Prophylaxis advice (+1) (770) 488-7788; treatment (+1) (770) 488-7788; or after hours (+1) (770) 488-7100; toll-free (US) 1-855-856-4713; website: *www.cdc.gov/malaria*
- **NOTE: All dosage regimens are for adults with normal renal function unless otherwise stated.** Many of the suggested regimens are not FDA approved.
- For licensed drugs, suggest checking package inserts to verify dosage and side-effects. Occasionally, post-licensure data may alter dosage as compared to package inserts.

INFECTING ORGANISM	SUGGESTED REGIMENS		COMMENTS
	PRIMARY	ALTERNATIVE	
PROTOZOA—INTESTINAL (non-pathogenic: E. hartmanni, E. dispar, E. moshkovskii, E. coli, Iodamoeba bütschlii, Endolimax nana, Chilomastix mesnili)			
Balantidium coli	**Tetracycline** 500 mg po qid x 10 days	**Metronidazole** 750 mg po tid times 5 days	Another alternative: Iodoquinol 650 mg po tid x 20 days.
Blastocystis hominis Ref: *Trends Parasitol 28:305, 2012*	**Metronidazole** 1.5 gm po 1x/day x 10 days or 750 mg po tid x 10 days (need to treat is dubious).	**Alternatives: iodoquinol*** 650 mg po tid x 20 days or **TMP-SMX-DS,** one bid x 7 days or **Nitazoxanide** 500 mg po bid x 3 days	Role as pathogen unclear; may serve as marker of exposure to contaminated food/water. Some genotypes may be more virulent.
Cryptosporidium parvum & hominis Treatment is unsatisfactory Ref.: *Curr Opin Infect Dis 23:494, 2010*	**Immunocompetent—No HIV: Nitazoxanide** 500 mg po bid x 3 days (expensive)	**HIV with immunodeficiency**: Effective antiretroviral therapy best therapy. **Nitazoxanide** no clinical or parasite response compared to placebo.	**Nitazoxanide:** Approved in liquid formulation for rx of children & 500 mg tabs for adults who are immunocompetent. Ref.: *CID 40:1173, 2005.* **C. hominis** assoc. with ↑ in post-infection eye & joint pain, recurrent headache, & dizzy spells *(CID 39:504, 2004).*
Cyclospora cayetanensis; cyclosporiasis *(Clin Micro Rev 23:218, 2010)*	**Immunocompetent pts: TMP-SMX-DS** tab 1 po bid x 7–10 days. Other options: see *Comments.*	**AIDS pts: TMP-SMX-DS** tab 1 po qid for up to 3-4 wks. Immunocompromised pts: may require suppressive rx with **TMP-SMX** DS 1 tab 3x/wk	If sulfa-allergic: **CIP** 500 mg po bid x 7 days but results inconsistent. Anecdotal success with nitazoxanide. Biliary disease described in HIV pts.
Dientamoeba fragilis *See AJTMH 82:614, 2010; Clin Micro Infect 14:601, 2008.*	**Iodoquinol*** 650 mg po tid x 20 days or **Paromomycin*** 25-35 mg/kg/day po in 3 div doses x 7 days or **Metronidazole** 750 mg tid x 10 days.	For treatment failures: **Tetracycline** 500 mg po qid x 10 days + **Iodoquinol*** 650 mg po tid x 10 days OR (**Iodoquinol*** + **Paromomycin***) May try second course of Iodoquinol	**Metronidazole** failed in prospective random placebo-control DB study *(CID 58:1692, 2014).* *In vitro tinidazole, metronidazole most active. AAC 56:487, 2012*
Entamoeba histolytica; ameblasis. If available, use stool PCR for diagnosis.			
Asymptomatic cyst passer	**Paromomycin*** 25-35 mg/kg/day po in 3 divided doses x 7 days OR **iodoquinol*** 650 mg po tid x 20 days	**Diloxanide furoate*** (Furamide) 500 mg po tid x 10 days.	Note: E. hartmanni and E. dispar are non-pathogenic.
Patient with diarrhea/dysentery; mild/moderate disease. Oral therapy possible	**Metronidazole** 500–750 mg po tid x 7-10 days or **tinidazole** 2 gm po daily x 3 days, followed by:		Colitis can mimic ulcerative colitis; ameboma can mimic adenocarcinoma of colon.
	Either [**paromomycin*** 25-35 mg/kg/day po divided in 3 doses x 7 days] or [**iodoquinol*** 650 mg po tid x 20 days] to clear intestinal cysts. See *comment.*		**Nitazoxanide** 500 mg po bid x 3 days may be effective *(JID 184:381, 2001 & Tran R Soc Trop Med & Hyg 101:1025, 2007)*
Severe or extraintestinal infection, e.g., hepatic abscess	(**Metronidazole** 750 mg **IV to PO** tid x 10 days or **tinidazole** 2 gm 1x/day x 5 days) followed by **paromomycin*** 25-35 mg/kg/day po divided in 3 doses x 7 days or **Iodoquinol*** 650 mg po tid x 20 days.		**Serology positive (antibody present) with extraIntestinal disease.**
Giardia intestinalis also known as **Giardia lamblia, Giardia duodenalis.**	(**Tinidazole** 2 gm po x 1) OR (**nitazoxanide** 500 mg po bid x 3 days). **Metro** & **Paromomycin** are alternatives	**Metronidazole** 250 mg po tid x 5 days; Albendazole 400 mg po once daily with food x 5 days. Cochrane Database Syst *Rev.2012 Dec 12; 12:CD007787.* **Pregnancy: Paromomycin*** 25-35 mg/kg/day po in 3 divided doses x 5-10 days.	**Refractory pts: (metro 750 mg po + quinacrine 100 mg po)** or (**Paromomycin** 10 mg/kg po) 3x/day x 3 wks *(CID 33:22, 2001)* giardia genetically heterogeneous *(J Clin Invest 123:2346, 2013)*

* For source of drug, see *Table 13D, page 165.*

TABLE 13A (2)

INFECTING ORGANISM	SUGGESTED REGIMENS		COMMENTS
	PRIMARY	ALTERNATIVE	
PROTOZOA—INTESTINAL *(continued)*			
Cystoisospora belli (formerly Isospora belli) (AIDS ref: MMWR 58 (RR-4):1, 2009)	**Immunocompetent: TMP-SMX-DS** tab 1 po bid x 7-10 days; **Immunocompromised: TMP-SMX-DS** qid for up to 4 wks. If CD4<200 may not respond; need ART.	**CIP** 500 mg po bid x 7 days is second-line alternative *(AnIM 132:885, 2000)* OR **Pyrimethamine** 50-75 mg/day + **Folinic acid** 10-25 mg/day (po).	**Chronic suppression in AIDS pts:** either **TMP-SMX-DS** 1 tab po 3x/wk OR tab 1 po daily OR (**pyrimethamine** 25 mg/day po + **folinic acid** 10 mg/day po) OR as 2nd-line alternative: **CIP** 500 mg po 3x/wk.
Microsporidiosis	For HIV pts: antiretroviral therapy key		
Ocular: Encephalitozoon hellum or cuniculi, Vittaforma (Nosema) corneae, Nosema ocularum	**Albendazole** 400 mg po bid x 3 wks plus fumagillin eye drops *(see Comment)*.	In HIV+ pts, reports of response of E. hellum to **fumagillin*** eyedrops *(see Comment)*. For V. corneae, may need keratoplasty	To obtain fumagillin: 800-292-6773 or *www.leiterrx.com*. Neutropenia & thrombocytopenia serious adverse events.
Intestinal (diarrhea): Enterocytozoon bieneusi, Encephalitozoon (Septata) intestinalis	**Albendazole** 400 mg po bid x 3 wks; peds dose: 15 mg/kg per day div. into 2 daily doses x 7 days for **E. intestinalis.** Fumagillin equally effective.	Oral **fumagillin* 20 mg po tid** reported effective for **E. bieneusi** *(NEJM 346:1963, 2002)* — see *Comment*	Dx: Most labs use modified trichrome stain. Need electron micrographs for species identification. FA and PCR methods in development. Peds dose ref.: *PIDJ 23:915, 2004*
Disseminated: E. hellum, cuniculi or intestinalis; Pleistophora sp., *others in Comment. Ref: JCM 52:3839, 2014.*	**Albendazole** 400 mg po bid x 3 wks. Fumagillin 20 mg po tid (not available in US)	No established rx for Pleistophora sp.	For Trachipleistophora sp., try itraconazole + albendazole *(NEJM 351:42, 2004)*. Other pathogens: Brachiola vesicularum & algerae *(NEJM 351:42, 2004)*.
PROTOZOA—EXTRAINTESTINAL			
Amebic meningoencephalitis *(Clin Infect Dis 51:e7, 2010 (Balamuthia))* Miltefosine available from CDC for all species of free-living ameba. *contact CDC Emergency Operations Center at 770-488-7100*			
Acanthamoeba sp.— no proven rx Rev.: *FEMS Immunol Med Micro 50:1, 2007*	IV therapy: [Pentamidine + Fluconazole + Miltefosine 50 mg po tid. May add TMP-SMX, Metronidazole, and a Macrolide		For Acanthamoeba keratitis: miltefosine or voriconazole.
Balamuthia mandrillaris	Pentamidine + Albendazole + (Fluconazole or Itraconazole) + Miltefosine 50 mg po tid		
Naegleria fowleri. >95% mortality. Ref. *MMWR 57:573, 2008.*	Amphotericin B 1.5 mg/kg/day ± 1.5 mg/day intrathecal + Rifampin 10 mg/kg/day + Fluconazole 10 mg/kg/day IV/po + Miltefosine 50 mg po tid		
Babesia microti (US) and **Babesia divergens** (EU) *(NEJM 366:366:2397, 2012)*	**For mild/moderate disease: Atovaquone** 750 mg po bid + **Azithro** 500 mg po on day 1, then 250-1000 mg po daily for total of 7-10 days. If relapse, treat x 6 wks & until blood smear neg x 2 wks.	**For severe babesiosis: (Clindamycin** 600 mg po tid) + (**quinine** 650 mg po tid) x 7–10 days For adults, can give **clinda** IV as 1.2 gm bid.	Overwhelming infection in asplenic patients. In immunocompromised patients, treat for 6 or more weeks *(CID 46:370, 2008)*. Transfusion related cases occur.
Leishmaniasis *(Suggest consultation – CDC (+1) 404-718-4745)* **Note: Miltefosine available directly from Profounda, Inc. (+1 407-270-7790), www.impavido.com. CDC IND does not cover leishmania.** Ref: Med Lett 56:89, 2014.			
Cutaneous: Mild Disease (< 4 lesions, none > 5 cm diameter, no lesions in cosmetically sensitive area, none over joints). Otherwise, consider Moderate Disease	**Mild Disease** (< 4 lesions, none > 5 cm): **Paromomycin*** ointment bid x 20 days (investigational); cryotherapy (freeze up to 3x with liquid nitrogen); intralesional Antimony 20 mg/kg into lesions weekly x 8-10 wks. CDC antimony IND does not cover intralesional use, common outside US. **Miltefosine** (w/food) 50 mg po bid (wt 30-44 kg); 50 mg tid (wt ≥ 45 kg). Treat for 28 days. Response in about 70% of pts.	**Moderate Disease:** **Sodium stibogluconate*** (Pentostam) or **Meglumine antimoniate** (Glucantime) 20 mg/kg/day IV/IM x 20 days. Dilute in 120 mL of D5W and infuse over 2 hrs. Alternatives: **Fluconazole** 200 mg po daily x 6 weeks (for *L. mexicana, L. panamensis, L. major*) or **Ketoconazole** 600 mg po daily x 30 days *(L. mexicana)* or **Miltefosine** (dose as for mild disease).Some experts use **liposomal amphotericin B** (regimens vary) with total cumulative dose of 20-60 mg/kg.	Oral therapy, Topical paromomycin* & other topical treatment only when low potential for mucosal spread; never use for *L. braziliensis* or *L. guyanensis* cutaneous lesions. Generic pentavalent antimony varies in quality and safety. Leishmania in travelers frequently responds to observation and local therapy *(CID 57:370, 2013)*. Miltefosine is preg cat D (do not use in pregnancy).

* For source of drug, see *Table 13D, page 165.*

TABLE 13A (3)

INFECTING ORGANISM	SUGGESTED REGIMENS		COMMENTS
	PRIMARY	ALTERNATIVE	
PROTOZOA—EXTRAINTESTINAL *(continued)*			
Leishmaniasis, Mucosal (Espundia). All cutaneous lesions due to L. brasiliensis. High cure rate with Lipo Ampho B *(Trans R Soc Trop Med Hyg 108:176, 2014).*	**Pentavalent antimony (Sb)*** 20 mg/kg/day IV or IM x 28 days for mucosal disease, 20 days for cutaneous disease or **liposomal amphotericin B** (regimens vary) with total cumulative dose of 20-60 mg/kg or **amphotericin B** 0.5-1 mg/kg IV daily or qod to total dose of 20-40 mg/kg. *See J Am Acad Dermatol 68:284, 2013.*	**Miltefosine*** (w/food) 50 mg po bid (wt 30-44 kg); 50 mg tid (wt ≥ 45 kg). Treat for 28 days. Complete resolution in 62% of pts.	Antimony available from CDC drug service; miltefosine FDA approved for leishmania in 2014 but not marketed in US at present. See *Table 13D for contact information.*
Visceral leishmaniasis – Kala-Azar – New World & Old World *L. donovani*: India, Africa *L. infantum*: Mediterranean *L. chagasi*: New World	Immunocompetent: **Liposomal ampho B** 3 mg/kg once daily days 1-5 & days 14, 21 **or Miltefosine** (w/food) 50 mg po bid (wt 30-44 kg); 50 mg tid (wt ≥ 45 kg). Treat for 28 days. HIV/AIDS: **Liposomal Ampho B** 4 mg/kg qd on days 1-5, 10, 17, 24, 31, 38 *(Curr Opin Infect Dis 26:1, 2013).*	**Standard Ampho B** 1 mg/kg IV daily x 15-20 days or qod x 8 wks (to total of 15-20 mg/kg) **or Miltefosine** (w/food) 50 mg po bid (wt 30-44 kg); 50 mg tid (wt ≥ 45 kg). Treat for 28 days. HIV/AIDS: **Liposomal Ampho B** 4 mg/kg qd on days 1-5, 10, 17, 24, 31, 38 (Curr Opin Infect Dis 26:1, 2013).OR **pentavalent antimony*** 20 mg/kg/day IV/IM x 28 days.	In HIV patients, may need lifelong suppression with Amphotericin B q 2-4 wks.
Malaria (Plasmodia species) —NOTE: CDC Malaria info— prophylaxis/treatment (770) 488-7788. After hours: 770-488-7100. US toll-free 1-855-856-4713. CDC offers species confirmation and drug resistance testing. Refs: *JAMA 297:2251, 2264 & 2285, 2007.* Websites: *www.cdc.gov/malaria; http://www.who.int/ith/ITH_chapter_7.pdf?ua=1* Review of rapid diagnostic tests: *CID 54:1637, 2012.*			
Prophylaxis—Drugs plus personal protection: screens, nets, 30–35% DEET skin repellent (avoid > 50% DEET) *(Med Lett 54:75, 2012)*, permethrin spray on clothing and mosquito nets. Country risk in CDC Yellow Book.			
For areas free of chloroquine (CQ)-resistant P. falciparum: Central America (west of Panama Canal), Caribbean, Korea, Middle East (most)	**CQ** phosphate 500 mg (300 mg base) po per wk starting 1–2 wks before travel, during travel, & 4 wks post-travel **or atovaquone-proguanil (AP)** 1 adult tab per day (1 day prior to, during, & 7 days post-travel). Another option for P. vivax only countries: **primaquine (PQ)** 30 mg base po daily in non-pregnant. G6PD-normal travelers; >92% effective vs P. vivax *(CID 33:1990, 2001).* Note: **CQ** may exacerbate psoriasis.	**CQ Peds dose:** 8.3 mg/kg (5 mg/kg of base) po 1x/wk up to 300 mg (base) max. dose **or AP** by weight (peds tabs): 11–20 kg, 1 tab; 21–30 kg, 2 tabs; 31–40 kg, 3 tabs; >40 kg, 1 adult tab per day. **Adults**: **Doxy** or **MQ** as below.	CQ safe during pregnancy. **The areas free of CQ-resistant falciparum malaria continue to shrink:** *See CDC or WHO maps for most current information on CQ resistance.* **Doxy AEs:** photosensitivity, candida vaginitis, gastritis.
For areas with CQ-resistant P. falciparum	**Atovaquone** 250 mg—**proguanil** 100 mg **(Malarone)** comb. tablet, 1 per day with food 1–2 days prior to, during, & 7 days post-travel. Peds dose in footnote[1]. **Not in pregnancy**. Malarone preferred for trips of a week or less; expense may preclude use for longer trips. Native population: intermittent pregnancy prophylaxis/treatment programs in a few countries. Fansidar 1 tab po 3 times during pregnancy *(Expert Rev Anti Infect Ther 8:589, 2010).*	**Doxycycline** 100 mg po daily for adults & children > 8 yrs of age[1]. Take 1-2 days before, during & for 4 wks after travel. **OR** **Mefloquine (MQ)**[1] 250 mg (228 mg base) po once per wk, 1-2 wks before, during, & for 4 wks after travel *(see Comment).* *Peds dose in footnote[1]* **Doxy AEs:** photosensitivity, candida vaginitis, gastritis.	**Pregnancy: MQ current best option.** Insufficient data with **Malarone. Avoid doxycycline and primaquine.** **Primaquine: Can cause hemolytic anemia if G6PD deficiency present.** **MQ not recommended** if cardiac conduction abnormalities, seizures, or psychiatric disorders, e.g., depression, psychosis. MQ outside U.S.: 275 mg tab, contains 250 mg of base. If used, can start 3 wks before travel to assure tolerability.

[1] **Peds prophylaxis dosages: Mefloquine** weekly dose by **weight** in kg: <9 kg = 5 mg/kg weekly; 10–19 kg = ¼ adult tab weekly; 20–30 kg = ½ adult tab weekly; 31–45 kg = ¾ adult tab weekly; >45 kg = 1 tab weekly **Atovaquone/proguanil** by **weight** in kg, single daily dose using peds tab (62.5 mg atovaquone & 25 mg proguanil): 5-8 kg, 1/2 tab; 8-10 kg, 3/4 tab; 11–20 kg, 1 tab; 21–30 kg, 2 tabs; 31-40 kg, 3 tabs; ≥41 kg, one adult tab. **Doxycycline,** ages >8–12 yrs: 2 mg per kg per day up to 100 mg/day. Continue daily x 4 wks after leaving risk area.

* For source of drug, see *Table 13D, page 165.*

TABLE 13A (4)

INFECTING ORGANISM	SUGGESTED REGIMENS		COMMENTS
	PRIMARY	ALTERNATIVE	

PROTOZOA—EXTRAINTESTINAL/Malaria (Plasmodia species) *(continued)*

Treatment of Malaria. Diagnosis is by microscopy. Alternative: rapid antigen detection test (Binax NOW): detects 96-100% of P. falciparum and 50% of other plasmodia *(CID 49:908, 2009; CID 54:1637, 2012)*. Need microscopy to speciate. Can stay positive for over a month after successful treatment.

Clinical Severity/ Plasmodia sp.	Region Acquired	Suggested Treatment Regimens (Drug)		Comments
		Adults	Peds	
Uncomplicated/ P. falciparum (or species not identified) 2015 WHO Guidelines suggest artemisinin combination therapy for adults (except in pregnancy) for all malaria species. E.g., Artemether-lumefantrine.	Cen. Amer., west of Panama Canal; Haiti, Dom. Repub., & most of Mid-East **CQ-sensitive**	**CQ phosphate** 1 gm salt (600 mg base) po, then 0.5 gm in 6 hrs, then 0.5 gm daily x 2 days. Total: 2500 mg salt	**Peds: CQ** 10 mg/kg of base po; then 5 mg/kg of base at 6, 24, & 48 hrs. Total: 25 mg/kg base	Other chloroquine salts available in some countries, total dose may differ **Peds dose should never exceed adult dose. CQ + MQ prolong QTc. Doses > 2x recommended may be fatal.**
	CQ-resistant or unknown resistance. Note: If >5% parasitemia or Hb <7, treat as severe malaria regardless of clinical findings or lack thereof.	**Adults: Atovaquone-proguanil** 1 gm–400 mg (4 adult tabs) po 1x/day x 3 days w/ food **OR [QS** 650 mg po tid x 3 days (7 days if SE Asia)**]** + **[(Doxy** 100 mg po bid) or (**tetra** 250 mg po qid) or **clinda** 20 mg/kg/d divided tid) x 7 days**] OR Artemether-lumefantrine*** tabs 20/120 mg: 4 tabs po (at 0, 8 hrs) then bid x 2 days (total 6 doses); take with food **OR** a less desirable adult alternative, **mefloquine** 750 mg po x 1 dose, then 500 mg po x 1 dose 6-12 hr later. **MQ** is 2nd line alternative due to neuropsychiatric reaction and cannot use in SE Asia due to resistance. Clinda or tetracycline only if doxy not available.	**Peds:** (**QS** 10 mg/kg po tid x 3 days) + (**clinda** 20 mg/kg per day div. tid) —both x 7 days. Use doxy >8 yrs of age 2.2 mg/kg/ bid up to 100 mg per dose OR **Atovaquone-proguanil** (all once daily x 3 d) by weight: 5-8 kg: 2 peds tabs; 9-10 kg: 3 peds tabs; 11-20 kg: 1 adult tab; 21-30 kg: 2 adult tabs; 31-40 kg: 3 adult tabs; >40 kg: 4 adult tabs. OR **MQ Salt:** 15 mg/kg x 1, then 6-12 hrs later, 10 mg/kg ALL po. OR **Artemether-lumefantrine*** • 5 kg to < 15 kg: 1 tablet (20 mg/ 120 mg) as a single dose, then 1 tablet again after 8 hours, then 1 tablet every 12 hours for 2 days • 15 kg to < 25 kg: 2 tablets (40 mg/ 240 mg) as a single dose, then 2 tablets again after 8 hours, then 2 tablets every 12 hours for 2 days • 25 kg to < 35 kg: 3 tablets (60 mg/ 360 mg) as a single dose, then 3 tablets again after 8 hours, then 3 tablets every 12 hours for 2 days • ≥35 kg: as per adult dose	**Pregnancy:** • Artemether-lumefantrine 4 tablets (80 mg/480 mg) as a single dose, then 4 tablets again after 8 hours, then 4 tablets every 12 hours for 2 days (take with food)). Drug of choice in 2nd/3rd trimester. Artemether-lumefantrine is safer than quinine in the first trimester of pregnancy. *Malar J. 13:197, 2014* OR • Quinine sulfate 10 mg/kg po tid x 3 days (7 days if SE Asia)) + Clindamycin 20 mg/kg/day divided tid x 7 days • Do not delay therapy if quinine available and artemether-lumefantrine is not In U.S., QS is only available as quinine 324 mg capsule, thus hard to use to treat children. **Note: Oral Artemether-lumefantrine tabs FDA-approved but not widely stocked. Call 1-800-COARTEM to obtain.** Wt-based dose of Artesunate IV in children: Wt < 20 kg: 3 mg/kg; Wrt > 20 kg: 2.4 mg/kg.
Uncomplicated / P. malariae or P. knowlesi *(JID 199: 1107 & 1143, 2009)*.	All regions – **CQ-sensitive**	**CQ** as above: adults & peds. In South Pacific, beware of P. knowlesi: looks like P. malariae, but behaves like P. falciparum *(CID 46:165, 2007)*.	**Artemether-lumefantrine*** (20/120 mg tab) 4 tabs po x 1 dose, repeat in 8 hrs, then repeat q12h x 2 days (take with food) OR **Atovaquone-proguanil** (1000/400 mg) 4 adult tabs po daily x 3 days	

* For source of drug, *see Table 13D, page 165*.

TABLE 13A (5)

INFECTING ORGANISM	SUGGESTED REGIMENS		COMMENTS
	PRIMARY	ALTERNATIVE	

PROTOZOA—EXTRAINTESTINAL/Malaria (Plasmodia species) /Treatment of Malaria *(continued)*

Clinical Severity/ Plasmodia sp.	Region Acquired	Suggested Treatment Regimens (Drug)		Comments
		Adults	Peds	
Uncomplicated/ P. vivax or P. ovale	**CQ-sensitive** (except Papua New Guinea, Indonesia which are CQ-resistant-see *below*)	**CQ** as above + **PQ** base: 30 mg po once daily x 14 days Each primaquine phosphate tab is 26.3 mg of salt and 15 mg of base. 30 mg of base = 2 26.3 mg tabs prim. phos.	**Peds: CQ** as above + **PQ** base 0.5 mg po once daily x 14 days	PQ added to eradicate latent parasites in liver. **Screen for G6PD def. before starting PQ;** if G6PD deficient dose PQ as 45 mg po once weekly x 8 wks. **Note: rare severe reactions.** Avoid PQ in pregnancy. If P. vivax or P. ovale, after pregnancy check for G6PD deficiency & give PQ 30 mg po daily times14 days.
Uncomplicated/ P. vivax	**CQ-resistant:** Papua, New Guinea & Indonesia	[**QS** + (**doxy** or **tetra**) ± **PQ**] as above or **Artemether-Lumefantrine** (same dose as for P. falciparum)	**MQ** + **PQ** as above. **Peds** (<8 yrs old): **QS** alone x 7 days or **MQ** alone. If latter fail, add **doxy** or **tetra**	Rarely acute. Lung injury and other serious complications: *LnID 8:449, 2008.*

Clinical Severity/ Plasmodia sp.	Region Acquired	Suggested Treatment Regimens (Drug)		Comments
		Primary—Adults	Alternative & Peds	
Uncomplicated Malaria/Alternatives for Pregnancy Ref: *LnID 7:118 & 136, 2007*	CQ-sensitive areas	**CQ** as above		Doxy or tetra used if benefits outweigh risks. No controlled studies of AP in pregnancy. If P. vivax or P. ovale, after pregnancy check for G6PD deficiency & give PQ 30 mg po daily times 14 days.
	CQ-resistant P. falciparum	**QS** + **clinda** as above	If failing or intolerant, **QS** + **doxy**	
	CQ-resistant P. vivax	**QS** 650 mg po tid x 7 days		
	Intermittent pregnancy treatment (empinc)	Give treatment dose of [Sulfadoxine 500 mg + Pyrimethamine 25 mg (Fansidar) po] at 3 times during pregnancy to decrease maternal & fetal morbidity & mortality		
Severe malaria, i.e., impaired consciousness, severe anemia, renal failure, pulmonary edema, ARDS, DIC, jaundice, acidosis, seizures, parasitemia >5%. One or more of latter. **Almost always P. falciparum.** *Ref: NEJM 358:1829, 2008; Science 320:30, 2008.*	All regions Note: •IV Artesunate is drug of choice but not FDA-approved. Available from CDC Drug Service under specific conditions, need to state quinidine not available or not tolerated. •IV quinidine uncommonly available. Possible emergency availability from Eli Lilly.	**Quinidine gluconate** in normal saline: 10 mg/kg (salt) IV over 1 hr then 0.02 mg/ kg/min by constant infusion QR 24 mg/kg IV over 4 hrs & then 12 mg/kg over 4 hrs q8h. Continue until parasite density <1% & can take po QS. **QS** 650 mg po **tid** x 3 days (7 days if SE Asia) + [(**Doxy** 100 mg IV q12h x 7 days) QR Artesunate* 2.4 mg/kg IV at 0, 12, 24, 48 hrs, and Doxy 100 mg IV q12h x 7 days)	**Peds: Quinidine gluconate IV**—same mg/kg dose as for adults **PLUS** (**Doxy:** if <45 kg, 4 mg per kg IV q12h; if ≥45 kg, dose as for adults) QR **Clinda, Clindamycin** 10 mg/kg IV loading dose, then 5 mg/kg IV or po (as tolerated) q8h x 7 days **Follow IV artesunate with a complete oral course of one of: Doxycycline**, Atovaquone/proguanil, Artemether/lumefantrine **or Dihydroartemisinin/piperaquine (not available in US)**	During quinidine IV: monitor BP, EKG (prolongation of QTc), & blood glucose (hypoglycemia). Exchange transfusion no longer recommended. Switch to QS po + (Doxy or Clinda) when patient able to take oral drugs. **Steroids not recommended for cerebral malaria.** IV artesunate from CDC (8 hr transport time post-approval), *see Table 13D (Ref: CID 44:1067 & 1075, 2007).* Can cause non-life threatening, but transfusion requiring, hemolytic anemia up to 15 days post-therapy *(AnIM 163:498, 2015).*

* For source of drug, *see Table 13D, page 165.*

TABLE 13A (6)

INFECTING ORGANISM	SUGGESTED REGIMENS		COMMENTS
	PRIMARY	ALTERNATIVE	
PROTOZOA—EXTRAINTESTINAL/Malaria (Plasmodia species) /Treatment of Malaria *(continued)*			
Malaria—self-initiated treatment: Only for people at high risk. Carry a reliable supply of recommended treatment (to avoid counterfeit meds). Use only if malaria is lab-diagnosed and no available reliable meds.	**Artemether-lumefantrine** (20/120 mg tab) 4 tabs po x 1 dose, repeat in 8 hrs, then repeat q12h x 2 days (take with food) OR **Atovaquone-proguanil (AP)** 4 adult tabs (1 gm/400 mg) po daily x 3 days	**Peds:** Using adult **AP** tabs for 3 consecutive days: 11–20 kg, 1 tab; 21–30 kg, 2 tabs; 31–40 kg, 3 tabs; >41 kg, 4 tabs. For Peds dosing of Artemether-lumefantrine, see *Uncomplicated/ P. falciparum, page 154.*	Do not use for renal insufficiency pts. Do not use if weight <11 kg, pregnant, or breast-feeding. **Artemether-lumefantrine:** sold as Riamet (EU) and Coartem (US & elsewhere).
Toxoplasma gondii (Reference: *Ln 363:1965, 2004*)			
Immunologically normal patients *(For pediatric doses, see reference)*			
Acute illness w/ lymphadenopathy	No specific rx unless severe/persistent symptoms or evidence of vital organ damage		
Acq. via transfusion (lab accident)	Treat as for active chorioretinitis.		
Active chorioretinitis; meningitis; lowered resistance due to steroids or cytotoxic drugs	[**Pyrimethamine** (pyri) 200 mg po once on 1st day, then 50–75 mg q24h] + [**sulfadiazine** *(see footnote[2])* S 1–1.5 gm po qid] + [**leucovorin (folinic acid)** 5–20 mg 3x/wk]—*see Comment.* Treat 1–2 wks beyond resolution of signs/symptoms; continue leucovorin 1 wk after stopping pyri.		For congenital Toxo, Toxo meningitis in adults, & chorioretinitis, **add prednisone 1 mg/kg/day in 2 div. doses** until CSF protein conc. falls or vision-threatening inflammation subsides. Adjust folinic acid dose by following CBC results.
Acute in pregnant women. Ref: *CID 47:554, 2008.*	**If <18 wks gestation at diagnosis: Spiramycin*** 1 gm po q8h until 16-18 wks; dc if amniotic fluid PCR is negative. Positive PCR: treat as below. **If >18 wks gestation & documented fetal infection by positive amniotic fluid PCR: (Pyrimethamine** 50 mg po q12h x 2 days, then 50 mg/day + **sulfadiazine** 75 mg/kg po x 1 dose, then 50 mg/kg q12h (max 4 gm/day) + **folinic acid** 10-20 mg po daily) for minimum of 4 wks or for duration of pregnancy.		Screen patients with IgG/IgM serology at commercial lab. IgG+ /IgM neg = remote past infection; IgG+/IgM+ = seroconversion. For Spiramycin, consult with Palo Alto Medical Foundation Toxoplasma Serology Lab: 650-853-4828 or toxlab@pamf.org
Fetal/congenital	Mgmt complex. Combo rx with pyrimethamine + sulfadiazine + leucovorin—*see Comment*		Details in *Ln 363:1965, 2004.* **Consultation advisable.**
AIDS			
Cerebral toxoplasmosis *Ref: MMWR 58(RR-4) 1, 2009.*	[**Pyrimethamine** (pyri) 200 mg x 1 po, then 75 mg/day po] + (**sulfadiazine** [Wt based dose: 1 gm if <60 kg, 1.5 gm if ≥60 kg] po q6h) + (**folinic acid** 10–25 mg/day po) for minimum of 6 wks after resolution of signs/ symptoms, and then suppressive rx *(see below)* OR **TMP-SMX** 10/50 mg/kg per day po or IV div. q12h x 30 days *(AAC 42:1346, 1998)*	[**Pyri** + **folinic acid** (as in primary regimen)] + 1 of the following: (1) **Clinda** 600 mg po/IV q6h or (2) **TMP=SMX** 5/25 mg/kg/day po or IV bid or (3) **atovaquone** 750 mg po q6h. Treat 4–6 wks after resolution of signs/symptoms, then suppression.	Use alternative regimen for pts with severe sulfa allergy. If multiple ring-enhancing brain lesions (CT or MRI), >85% of pts respond to 7–10 days of empiric rx; if no response, suggest brain biopsy. Pyri penetrates brain even if no inflammation; folinic acid prevents pyrimethamine hematologic toxicity.
Primary prophylaxis, AIDS pts—IgG Toxo antibody + CD4 count <100 per mcL	(**TMP-SMX-DS**, 1 tab po q24h or 3x/wk) or (**TMP-SMX-SS**, 1 tab po q24h)	[(**Dapsone** 50 mg po q24h) + (**pyri** 50 mg po q wk) + (**folinic acid** 25 mg po q wk)] OR **atovaquone** 1500 mg po q24h	Prophylaxis for pneumocystis also effective vs Toxo. *Ref: MMWR 58(RR-4):1, 2009.* **Another alternative:** (Dapsone 200 mg po + pyrimethamine 75 mg po + folinic acid 25 mg po) once weekly.
Suppression after rx of cerebral Toxo	(**Sulfadiazine** 2-4 gm po divided in 2-4 doses/day) + (**pyri** 25–50 mg po q24h) + (**folinic acid** 10–25 mg po q24h). DC if CD4 count >200 x 3 mos	[(**Clinda** 600 mg po q8h) + (**pyri** 25–50 mg po q24h) + (**folinic acid** 10–25 mg po q24h)] OR **atovaquone** 750 mg po q6–12h	(Pyri + sulfa) prevents PCP and Toxo; (clinda + pyri) prevents Toxo only. Additional drug needed to prevent PCP.
Trichomonas vaginalis	*See Vaginitis, Table 1, page 26.*		

[2] Sulfonamides for Toxo. Sulfadiazine now commercially available. Sulfisoxazole much less effective.

* For source of drug, *see Table 13D, page 165.*

INFECTING ORGANISM	SUGGESTED REGIMENS		COMMENTS
	PRIMARY	ALTERNATIVE	
PROTOZOA—EXTRAINTESTINAL/Toxoplasma gondii/AIDS *(continued)*			
Trypanosomiasis. Ref.: *Ln 362:1469, 2003.* **Note: Drugs for African trypanosomiasis may be obtained free from WHO or CDC. *See Table 13D, page 165*, for source information.**			
West African sleeping sickness (T. brucei gambiense)			
Early: Blood/lymphatic—CNS OK	**Pentamidine** 4 mg/kg IV/IM daily x 7-10 days	In US, free from CDC drug service: **Suramin*** 100 mg IV (test dose), then 1 gm IV on days 1, 3, 7, 14, & 21. Peds dose is 20 mg/kg.	Suramin effective but avoid if possible due to possible co-infection with O. volvulus in W. Africa.
Late: Encephalitis	Combination of IV **eflornithine**, 400 mg/kg/day divided q12h x 7 days, plus **nifurtimox**, 15 mg/kg/day po, divided q8h x 10 days (abbreviated NECT) now WHO standard of care *(Lancet 374:56, 2009; CID 56:195 2013)*	Melarsoprol 2.2 mg/kg/day IV x 10 days; toxic arsenical	now superseded by NECT
East African sleeping sickness (T. brucei rhodesiense)			
Early: Blood/lymphatic	**Suramin*** 100 mg IV (test dose), then 1 gm IV on days 1 3, 7, 14, & 21	Peds: Suramin* 2 mg/kg test dose, then 20 mg/kg IV on days 1, 3, 7, 14 & 21	Suramin & Melarsoprol: CDC Drug Service or WHO (at no charge) *(see Table 13D)*
Late: Encephalitis (prednisolone may prevent encephalitis) Pre-treatment with Suramin advised by some.	**Melarsoprol** 2.2 mg/kg/day IV x 10 days *(PLoS NTD 6:e1695, 2012)*	**Melarsoprol*** From 2–3.6 mg/kg per day IV over 3 days; repeat 3.6 mg/kg after 7 days & for 3rd time at 3.6 mg/kg 7 days after 2nd course	Early illness: patient waiting for Suramin, use pentamidine 4 mg/kg/day IV/IM x 1-2 doses. Does not enter CSF.
T. cruzi—**Chagas disease** or acute American trypanosomiasis *Ref: NEJM 373:456, 2015.* For chronic disease: no benefit in established cardiopathy *(NEJM 373:1295, 2015)*	*Adult (Age ≥12 years):* **Benznidazole*** 5-7 mg kg/day po in 2 doses (q12h) x 60 days *Pediatric (Age <12 years):* **Benznidazole*** 7.5 mg/kg/day po in 2 doses (q12h) x 60 days	**Nifurtimox*** 8–10 mg/kg per day po div. 4x/day after meals x 120 days Ages 11–16 yrs: 12.5–15 mg/kg per day div. qid po x 90 days Children <11yrs: 15–20 mg/kg per day div. qid po x 90 days.	Due to adverse effects may give Benznidazole 300 mg per day for 60 days, regardless of body weight OR give 300 mg per day but prolong treatment to complete the total dose corresponding to 5 mg/kg per day for 60 days. *N Engl J Med 373:456, 2015.* Immunosuppression for heart transplant can reactivate chronic Chagas disease. Can transmit by organ/transfusions. Do not use benznidazole in pregnancy.
NEMATODES—INTESTINAL (Roundworms). Eosinophilia? Think Strongyloides, toxocaria and filariasis: *CID 34:407, 2005; 42:1781 & 1655, 2006*-- See *Table 13C.*			
Anisakis simplex (**anisakiasis**) Anisakiasis differentiated from Anisakidosis *(CID 51:806, 2010)*. Other: A. physiatry, Pseudoterranova decipiens.	Physical removal: endoscope or surgery IgE antibody test vs *A. simplex* may help diagnosis. No antimicrobial therapy.	Anecdotal reports of possible treatment benefit from albendazole *(Ln 360:54, 2002; CID 41:1825, 2005)*	Anisakiasis acquired by eating raw fish: herring, salmon, mackerel, cod, squid. Similar illness due to Pseudoterranova species acquired from cod, halibut, red snapper.
Ascaris lumbricoides (**ascariasis**) *Ln 367:1521, 2006*	**Albendazole** 400 mg po daily x 3 days or **mebendazole** 100 mg po bid x 3 days	**Ivermectin** 150–200 mcg/kg po x 1 dose	Review of efficacy of single dose: *JAMA 299:1937, 2008.*
Capillaria philippinensis (**capillariasis**)	**Albendazole** 400 mg po bid x 10 days	**Mebendazole** 200 mg po bid x 20 days	Albendazole preferred.
Enterobius vermicularis (**pinworm**)	**Mebendazole**NUS 100 mg po x 1, repeat in 2 wks OR **Pyrantel pamoate** 11 mg/kg base (to max. dose of 1 gm) po x 1 dose; repeat in 2 wks	**Albendazole** 400 mg po x 1 dose, repeat in 2 wks.	*Side-effects in Table 13B, page 164.* Treat whole household.
Gongylonemiasis (adult worms in oral mucosa)	Surgical removal	**Albendazole** 400 mg/day po x 3 days	Ref: *CID 32:1378, 2001; J Helminth 80:425, 2006.*
Hookworm (Necator americanus and Ancylostoma duodenale)	**Albendazole** 400 mg po daily x 3 days	**Mebendazole**NUS 100 mg po bid x 3 days OR **Pyrantel pamoate** 11 mg/kg (to max. dose of 1 gm) po daily x 3 days	NOTE: Ivermectin not effective. Single dose therapy as used in public health programs has lower cure rates and 3-day albendazole superior to 3-day mebendazole, *PLoS One 6:e25003, 2011*
Strongyloides stercoralis (**strongyloidiasis**) *(Hyperinfection, See Comment)*	**Ivermectin** 200 mcg/kg per day po x 2 days	**Albendazole** 400 mg po bid x 7 days ; less effective	**For hyperinfections,** repeat at 15 days. For hyperinfection: veterinary ivermectin given subcutaneously or rectally *(CID 49:1411, 2009).*

* For source of drug, see *Table 13D, page 165.*

TABLE 13A (8)

INFECTING ORGANISM	SUGGESTED REGIMENS		COMMENTS
	PRIMARY	ALTERNATIVE	
NEMATODES—INTESTINAL (Roundworms) *(continued)*			
Trichostrongylus orientalis, T. colubriformis	**Pyrantel pamoate** 11 mg/kg (max. 1 gm) po x 1	**Albendazole** 400 mg po x 1 dose	**Mebendazole** 100 mg po bid x 3 days
Trichuris trichiura (**whipworm**) *NEJM 370:610, 2014; PLoS One 6:e25003, 2011*	**Mebendazole**[HDS] 100 mg po bid x 3 days	**Albendazole** 400 mg po qd x 3 days or **Ivermectin** 200 mcg/kg po qd x 3 days	Mebendazole clearly superior for trichuris *(PLoS One.6:e25003, 2011; N Engl J Med 370:610, 2014)*
NEMATODES—EXTRAINTESTINAL (Roundworms)			
Ancylostoma braziliense & caninum: causes **cutaneous larva migrans**	**Albendazole** 400 mg po bid x 3-7 days *(Ln ID 8:302, 2008).*	**Ivermectin** 200 mcg/kg po x 1 dose/day x 1–2 days (not in children wt < 15 kg)	Also called "creeping eruption", dog and cat hookworm. Ivermectin cure rate 81-100% (1 dose) to 97% (2–3 doses) *(CID 31:493, 2000).*
Angiostrongylus cantonensis (Angiostrongyliasis); causes eosinophilic meningitis	Mild/moderate disease: Analgesics, serial LPs (if necessary). Prednisone 60 mg/day x 14 days reduces headache & need for LPs.	Adding **Albendazole** 15 mg/kg/day to prednisone 60 mg/day both for 14 days may reduce duration of headaches and need for repeat LPs.	**Do not use Albendazole without prednisone,** see *TRSMH 102:990, 2008.* Gnathostoma and Baylisascaris also cause eosinophilic meningitis.
Baylisascariasis (Raccoon roundworm); eosinophilic meningitis	No drug proven efficacious. Try po **albendazole,** Peds: 25–50 mg/kg/day po; Adults: 400 mg po bid with corticosteroids. Treat for one month.		*Clin Microbiol Rev 18:703, 2005.* Other causes of eosinophilic meningitis: Gnathostoma & Angiostrongylus.
Dracunculus medinensis: **Guinea worm** *(Trans R Soc Trop Med Hyg 108:249, 2014)*	Slow extraction of pre-emergent worm over several days	No drugs effective. Oral analgesics, anti-inflammatory drugs, topical antiseptics/antibiotic ointments to alleviate symptoms and facilitate worm removal by gentle manual traction over several days.	
Filariasis: Determine if co-infection with either Loa loa or Onchocerca			
Lymphatic filariasis (**Elephantiasis**): Etiologies: Wuchereria bancrofti Brugia malayi, Brugia timori	*Mono-infection:* **Diethylcarbamazine[3](DEC)*** 6 mg/kg/day po in 3 divided doses x 12 days + **Doxy** 200 mg/day po x 6 wks	*Dual infection with Onchocerciasis:* Treat Onchocerciasis first: **Ivermectin** 150 mcg/kg po x 1 dose, wait 1 month, then start **DEC** as for mono-infection *Dual infection with Loa Loa:* DEC drug of choice for both but can cause severe encephalopathy if >5000 Loa Loa microfilaria/mL in blood. Refer to expert center for apheresis pre-DEC or prednisone + small doses of DEC. If <5000 microfilaria/mL, start regular dose of **DEC.**	Doxy x 6 wks may improve mild/moderate lymphedema independent of parasite infection *(CID 55:621, 2012).* **Note: DEC can cause irreversible eye damage if concomitant Onchocerciasis.**
Loiasis Loa loa, eye worm disease: **Look for dual infection with either Onchocerciasis or Lymphatic filariasis**			
	Mono-infection with <5000 L. loa microfilaria/mL: **DEC** 8-10 mg/kg/day po in 3 divided doses x 21 days *Mono-infection with >5000 L. loa microfilaria/mL:* Refer to expert center for apheresis prior to **DEC** therapy; alternatively: **Albendazole** 200 mg po bid x 21 days	*Dual infection with Lymphatic filariasis:* See Lymphatic filariasis, above *Dual infection with Onchocerciasis:* Treat Onchocerciasis first with **Ivermectin**, then treat L. loa with **DEC**	If >5000 L. loa microfilaria/mL in blood & given Ivermectin for Onchocerciasis, can facilitate entry of L. loa into CNS with severe encephalopathy.
Onchocerca volvulus (Onchocerciasis), river blindness: **Look for dual infection with either Loa loa or Lymphatic filariasis**			
	Mono-infection: **Ivermectin** 150 mcg/kg x 1 dose, then repeat every 3-6 months until asymptomatic + **Doxy** 200 mg/day x 6 wks. No accepted alternative therapy.	*Dual infection with Lymphatic filariasis:* See Lymphatic filariasis, above *Dual infection with L. loa:* Treat Onchocerciasis first with **Ivermectin**, then treat L loa with **DEC. If** >5000 L. Loa microfilaria/mL in blood. Refer to expert center for apheresis before starting DEC	Onchocerciasis and Loa loa are mildly co-endemic in West and Central Africa.

[3] May need antihistamine or corticosteroid for allergic reaction from disintegrating organisms

* For source of drug, see *Table 13D, page 165.*

TABLE 13A (9)

INFECTING ORGANISM	SUGGESTED REGIMENS		COMMENTS
	PRIMARY	ALTERNATIVE	
NEMATODES—EXTRAINTESTINAL (Roundworms)/Filariasis *(continued)*			
Body cavity			
Mansonella perstans	In randomized trial, doxy 200 mg po once daily x 6 weeks cleared microfilaria from blood in 67 of 69 patients *(NEJM 361:1448, 2009).*	**Albendazole** in high dose x 3 weeks.	Efficacy of doxy believed to be due to inhibition of endosymbiont wolbachia; Ivermectin has no activity. Ref: *Trans R Soc Trop Med Hyg 100:458, 2006.*
Mansonella streptocerca	**Ivermectin** 150 µg/kg x 1 dose.	May need antihistamine or corticosteroid for allergic reaction from disintegrating organisms. Chronic pruritic hypopigmented lesions that may be confused with leprosy. Can be asymptomatic.	
Mansonella ozzardi	**Ivermectin** 200 µ/kg x 1 dose may be effective. Limited data but no other option. *Am J Trop Med Hyg 90:1170, 2014*	Usually asymptomatic. Articular pain, pruritus, lymphadenopathy reported. May have allergic reaction from dying organisms.	
Dirofilariasis: **Heartworms**			
D. immitis, dog heartworm	No effective drugs; surgical removal only option		Can lodge in pulmonary artery → coin lesion. Eosinophilia rare.
D. tenuis (raccoon), D. ursi (bear), D. repens (dogs, cats)	No effective drugs	Worms migrate to conjunctivae, subcutaneous tissue, scrotum, breasts, extremities. D. repens emerging throughout Europe *Clin Microbiol Rev 25:507, 2012*	
Gnathostoma spinigerum			
Cutaneous larva migrans	**Albendazole** 400 mg po q24h or bid times 21 days	**Ivermectin** 200 µg/kg/day po x 2 days.	Other etiology of larva migrans: Ancyclostoma sp., *see page 158*
Eosinophilic meningitis	Supportive care; monitor for cerebral hemorrhage	Case reports of steroid use: both benefit and harm from Albendazole or ivermectin *(EID 17:1174, 2011).*	Other causes of eosinophilic meningitis: **Angiostrongylus** *(see page 158)* & **Baylisascaris** *(see page 158)*
Toxocariasis *(Ann Trop Med Parasit 103:3, 2010)*	**Rx directed at relief of symptoms as infection self-limited, e.g., steroids & antihistamines; use of anthelmintics controversial.**		
Visceral larval migrans	**Albendazole** 400 mg po bid x 5 days ± **Prednisone** 60 mg/day	**Mebendazole** 100–200 mg po bid times 5 days	Severe lung, heart or CNS disease may warrant steroids *(Clin Micro Rev 16:265, 2003).* Differential dx of larval migrans syndromes: Toxocara canis & catis, Ancylostoma spp., Gnathostoma spp., Spirometra spp.
Ocular larval migrans	First 4 wks of illness: (Oral **prednisone** 30–60 mg po q24h + subtenon **triamcinolone** 40 mg/wk) x 2 wks (Surgery is sometimes necessary)		No added benefit of anthelmintic drugs. Rx of little effect after 4 wks. Some use steroids *(Clin Micro Rev 16:265, 2003).*
Trichinella spiralis (**Trichinellosis**) — muscle infection *(Review: Clin Micro Rev 22:127, 2009).*	**Albendazole** 400 mg po bid x 8–14 days	**Mebendazole** 200–400 mg po tid x 3 days, then 400–500 mg po tid x 10 days	Use albendazole/mebendazole with caution during pregnancy. ↑ IgE, ↑ CPK, ESR 0, massive eosinophilia: >5000/µL.
	Concomitant **prednisone** 40–60 mg po q24h		
TREMATODES (Flukes) – Liver, Lung, Intestinal. All flukes have snail intermediate hosts; transmitted by ingestion of metacercariae on plants, fish or crustaceans.			
Liver flukes: Clonorchis sinensis, Metorchis conjunctus, Opisthorchis viverrini	**Praziquantel** 25 mg/kg po tid x 2 days	**Albendazole** 10 mg/kg per day po x 7 days	Same dose in children
Fasciola hepatica (sheep liver fluke), Fasciola gigantica	**Triclabendazole*** once, may repeat after 12-24 hrs. 10 mg/kg po x 1 dose. Single 20 mg/kg po dose effective in treatment failures.		
Intestinal flukes: Fasciola buski Heterophyes heterophyes; Metagonimus yokogawai. Nanophyetus salmincola	**Praziquantel** 25 mg/kg po tid x 1 days		Same dose in children

* For source of drug, see *Table 13D, page 165.*

TABLE 13A (10)

INFECTING ORGANISM	SUGGESTED REGIMENS		COMMENTS
	PRIMARY	ALTERNATIVE	
TREMATODES (Flukes) – Liver, Lung, Intestinal *(continued)*			
Lung fluke: Paragonimus sp.	**Praziquantel** 25 mg/kg po tid x 2 days	**Triclabendazole*** 10 mg/kg po x 2 doses over 12-24 hrs.	Same dose in children
Schistosoma haematobium; GU bilharziasis.	**Praziquantel** 40 mg/kg po on the same day (one dose of 40 mg/kg or two doses of 20 mg/kg)		Same dose in children.
Schistosoma intercalatum	**Praziquantel** 20 mg/kg po on the same day in 1 or 2 doses		Same dose in children
Schistosoma japonicum; Oriental schisto.	**Praziquantel** 60 mg/kg po on the same day (3 doses of 20 mg/kg)		Same dose in children. Cures 60–90% pts.
Schistosoma mansoni (intestinal bilharziasis)	**Praziquantel** 40 mg/kg po on the same day in (one dose of 40 mg/kg or two doses of 20 mg/kg)		Praziquantel: Same dose for children and adults. Cures 60–90% pts. No advantage to splitting dose in 2 Cochrane Database Syst Rev. *8:CD000053, 2014*
Schistosoma mekongi	**Praziquantel** 60 mg per kg po on the same day (3 doses of 20 mg/kg)		Same dose for children
Toxemic schisto; Katayama fever	**Praziquantel** 20 mg per kg po bid with short course of high dose prednisone. Repeat Praziquantel in 4-6 wks *(Clin Micro Rev 16:225, 2010).*		Reaction to onset of egg laying 4-6 wks after infection exposure in fresh water.
CESTODES (Tapeworms)			
Echinococcus granulosus (hydatid disease) *(LnID 12:871, 2012; Inf Dis Clin No Amer 26:421, 2012)*	**Liver cysts:** Meta-analysis supports percutaneous aspiration-injection-reaspiration (**PAIR**) + albendazole for uncomplicated single liver cysts. Before & after drainage: **albendazole** ≥60 kg, 400 mg po bid or <60 kg, 15 mg/kg per day div. bid, with meals. After 1-2 days puncture (P) & needle aspirate (A) cyst content. Instill (I) hypertonic saline (15–30%) or absolute alcohol, wait 20–30 min, then re-aspirate (R) with final irrigation. **Continue albendazole for at least 30 days.** Cure in 96% as comp to 90% pts with surgical resection. Albendazole ref: *Acta Tropica 114:1, 2010.*		
Echinococcus multilocularis (alveolar cyst disease) *(COID 16:437, 2003)*	**Albendazole** efficacy not clearly demonstrated, can try in dosages used for hydatid disease. Wide surgical resection only reliable rx; technique evolving. Post-surgical resection or if inoperable: Albendazole for several years *(Acta Tropic 114:1, 2010).*		
Intestinal tapeworms			
Diphyllobothrium latum (fish), Dipylidium caninum (dog), Taenia saginata (beef), & Taenia solium (pork)	**Praziquantel** 5–10 mg/kg po x 1 dose for children and adults.	**Niclosamide*** 2 gm po x 1 dose	Niclosamide from Expert Compounding Pharm, see *Table 13D.*
Hymenolepis diminuta (rats) and H. nana (humans)	**Praziquantel** 25 mg/kg po x 1 dose for children and adults.	**Niclosamide*** 2 gm po daily x 7 days	
Neurocysticercosis (NCC): Larval form of T. solium Ref.: *AJTMH 72:3, 2005*	**NOTE: Treat concomitant T. solium intestinal tapeworms, if** present, with **praziquantel** 5-10 mg/kg po x 1 dose after starting steroid.		
Parenchymal NCC 1-20 "Viable" or degenerating cysts by CT/MRI Meta-analysis: Treatment assoc with cyst resolution, ↓ seizures, and ↓ seizure recurrence. Ref: *Neurology 80:1424, 2013.*	**Albendazole** 15 mg/kg/d po + **Praziquantel** 50 mg/kg/d po + **dexamethasone** 0.1 mg/kg/d po. Start steroid 1 day before anti-parasitics. Treat for 10 days. May need seizure meds for 1 yr.	**Albendazole** alone 800 mg per day plus **Dexamethasone** 0.1 mg/kg per day ± Anti-seizure medication). *See Comment*	Ref: *LnID 14:687, 2014.* Steroids decrease serum levels of praziquantel so shouldn't use afone without albendazole. NIH reports methotrexate at ~ 20 mg/wk allows a reduction in steroid use *(CID 44:449, 2007).*
Dead calcified cysts	**No treatment indicated**		
Subarachnoid NCC	(**Albendazole** + **steroids** as above) + shunting for hydrocephalus prior to drug therapy. Ref: *Expert Rev Anti Infect Ther 9:123, 2011.*		
Intraventricular NCC	Neuroendoscopic removal is treatment of choice with or without obstruction. If surgery not possible, **albendazole + dexamethasone; observe closely for evidence of obstruction of flow of CSF.**		

* For source of drug, *see Table 13D, page 165.*

TABLE 13A (11)

INFECTING ORGANISM		SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
CESTODES (Tapeworms)/Neurocysticercosis (NCC) *(continued)*				
Sparganosis (Spirometra mansonoides) Larval cysts; source—frogs/snakes		Surgical resection. No antiparasitic therapy. Can inject alcohol into subcutaneous masses.		
ECTOPARASITES. Ref.: *CID 36:1355, 2003; Ln 363:889, 2004.* **NOTE: Due to potential neurotoxicity and risk of aplastic anemia, lindane not recommended.**				
DISEASE	**INFECTING ORGANISM**			
Head lice *NEJM 367:1687 & 1750, 2012; Med Lett 54:61, 2012.*	Pediculus humanus, var. capitis	**Permethrin** 1% lotion: Apply to shampooed dried hair for 10 min.; repeat in 9-10 days. **OR** **Malathion** 0.5% lotion (Ovide): Apply to dry hair for 8–12 hrs, then shampoo. 2 doses 7-9 days apart. **OR** **Spinosad** 0.9% suspension; wash off after 10 min (85% effective). Repeat in 7 days, if needed. Use nit comb initially & repeat in 7-10 days	**Ivermectin** 200-400 µg/kg po once; 3 doses at 7 day intervals effective in 95% *(JID 193:474, 2006)*. Topical ivermectin 0.5% lotion, 75% effective. **Malathion**: Repeat Rx at 1-2 20-min. applications 98% effective *(Ped Derm 21:670, 2004)*. In alcohol potentially flammable. **Benzyl alcohol**: 76% effective	**Permethrin:** success in 78%. Resistance increasing. No advantage to 5% permethrin. **Spinosad** is effective, but expensive. Wash hats, scarves, coats & bedding in hot water, then dry in hot dryer for 20+ minutes.
Pubic lice (crabs)	Phthirus pubis	**Pubic hair: Permethrin** OR **malathion** as for head lice. Shave pubic hair.	**Eyelids: Petroleum jelly** applied qid x 10 days OR **yellow oxide of mercury** 1% qid x 14 days	**Do not use lindane.** Treat sex partners of the last 30 days.
Body lice	Pediculus humanus, var. corporis	No drugs for the patient. Organism lives in & deposits eggs in seams of clothing. Discard clothing; if not possible, treat clothing with 1% malathion powder or 0.5% permethrin powder. Success with ivermectin in homeless shelter: 12 mg po on days 0, 7, & 14 *(JID 193:474, 2006)*		
Myiasis Due to larvae of flies		Usually cutaneous/subcutaneous nodule with central punctum. Treatment: Occlude punctum to prevent gas exchange with petrolatum, fingernail polish, makeup cream or bacon. When larva migrates, manually remove. Ref: *Clin Microbiol Rev 25:79, 2012.*		
Scabies	Sarcoptes scabiei			
Immunocompetent patients Refs: *MMWR 59(RR-12):89, 2010; NEJM 362:717, 2010.*		**Permethrin** 5% cream (ELIMITE) under nails (finger and toe). Apply entire skin from chin down to and including under fingernails and toenails. Leave on 8–14 hrs. Repeat in 1-2 wks. Safe for children age >2 mos.	**Ivermectin** 200 µg/kg po with food x 1, then second dose in 2 wks. **Less effective: Crotamiton** 10% cream, apply x 24 hr, rinse off, then reapply x 24 hr.	Trim fingernails. Reapply cream to hands after handwashing. Treat close contacts; wash and heat dry linens. Pruritus may persist times 2 wks after mites gone.
AIDS and HTLV-infected patients (CD4 <150 per mm^3), debilitated or developmentally disabled patients (**Norwegian scabies**—see *Comments*)		For Norwegian crusted scabies: **Permethrin** 5% cream daily x 7 days, then twice weekly until cured. Add **ivermectin** po (dose in Alternative)	**Ivermectin** 200 mcg/kg po on days 1, 2, 8, 9 & 15+ **Permethrin** cream. May need addt'l doses of Ivermectin on days 22 & 29.	Norwegian scabies in AIDS pts: Extensive, crusted. Can mimic psoriasis. Not pruritic. Highly contagious—isolate!

* For source of drug, see *Table 13D, page 165.*

TABLE 13B – DOSAGE AND SELECTED ADVERSE EFFECTS OF ANTIPARASITIC DRUGS

Doses vary with indication. For convenience, drugs divided by type of parasite; some drugs used for multiple types of parasites, e.g., albendazole.

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE	ADVERSE REACTIONS/COMMENTS
Antiprotozoan Drugs		
Intestinal Parasites		
Diloxanide furoate[NUS] (Furamide)	500 mg po tid x 10 days	Source: *See Table 13D, page 165.* Flatulence, N/V, diarrhea.
Iodoquinol (Yodoxin)	Adults: 650 mg po tid (or 30-40 mg/kg/day div. tid); children: 40 mg/kg per day div. tid.	Rarely causes nausea, abdominal cramps, rash, acne. **Contraindicated if iodine intolerance** (contains 64% bound iodine). Can cause iododerma (papular or pustular rash) and/or thyroid enlargement.
Metronidazole	Side-effects similar for all. *See metronidazole in Table 10B, page 116, & Table 10A, page 112.*	
Nitazoxanide (Alinia)	Adults: 500 mg po q12h. Children 4–11: 200 mg susp. po q12h. Take with food. Expensive.	Abdominal pain 7.8%, diarrhea 2.1%. Rev.: *CID 40:1173, 2005; Expert Opin Pharmacother 7:953, 2006.* Headaches; rarely yellow sclera (resolves after treatment).
Paromomycin (Humatin) Aminosidine IV in U.K.	Up to 750 mg po qid (250 mg tabs). Source: *See Table 13D.*	**Aminoglycoside similar to neomycin;** if absorbed due to concomitant inflammatory bowel disease can result in oto/nephrotoxicity. Doses >3 gm daily are associated with nausea, abdominal cramps, diarrhea.
Quinacrine[NUS] (Atabrine, Mepacrine)	100 mg po tid. No longer available in U.S.; *www.expertpharmacy.com; www.fagron.com*	**Contraindicated for pts with history of psychosis or psoriasis. Yellow staining of skin.** Dizziness, headache, vomiting, toxic psychosis (1.5%), hemolytic anemia, leukopenia, thrombocytopenia, urticaria, rash, fever, minor disulfiram-like reactions.
Tinidazole (Tindamax)	250-500 mg tabs, with food. Regimen varies with indication.	**Chemical structure similar to metronidazole but better tolerated.** Seizures/peripheral neuropathy reported. **Adverse effects:** Metallic taste 4–6%, nausea 3–5%, anorexia 2–3%.
Antiprotozoan Drugs: Non-Intestinal Protozoa		
Extraintestinal Parasites		
Antimony compounds[NUS] Stibogluconate sodium (Pentostam) from CDC or Meglumine antimonate (Glucantime)—French trade name	For IV use: vials with 100 mg antimony/mL. Dilute selected dose in 50 mL of D5W shortly before use. Infuse over at least 10 minutes.	**AEs in 1st 10 days:** headache, fatigue, elevated lipase/amylase, clinical pancreatitis. After 10 days: elevated AST/ALT/ALK/PHOS. **NOTE: Reversible T wave changes in 30-60%. Risk of QTc prolongation. Renal excretion; modify dose if renal insufficiency. Metabolized in liver; lower dose if hepatic insufficiency. Generic drug may have increased toxicity due to antimony complex formation.**
Artemether-Lumefantrine, po (Coartem, FDA-approved)	Tablets contain 20 mg Artemether and 120 mg Lumefantrine. Take with food. Can be crushed and mixed with a few teaspoons of water	**Can prolong QT_C:** avoid in patients with congenital long QT_C, family history of sudden death or long QT_C, or need for drugs known to prolong QT_C *(see list under fluoroquinolones, Table 10A, page 111).* Artemether induces CYP3A4 and both Artemether & Lumefantrine are metabolized by CYP3A4 *(see drug-drug interactions, Table 22A, page 235).* Adverse effects experienced by >30% of adults: headache, anorexia, dizziness, arthralgia and myalgia. Non-life threatening, but transfusion requiring, hemolytic anemia can occur up to 15 days post-therapy *(AnIM 163:498, 2015).*
Artesunate, IV Ref: *NEJM 358:1829, 2008*	Available from CDC Malaria Branch. 2.4 mg/kg IV at 0, 12, 24, & 48 hrs	**More effective than qulnine & safer than quinidine.** Contact CDC at 770-488-7758 or 770-488-7100 after hours. No dosage adjustment for hepatic or renal insufficiency. No known drug interactions.
Atovaquone (Mepron) Ref.: *AAC 46:1163, 2002*	Suspension: 1 tsp (750 mg) po bid 750 mg/5 mL.	No. pts stopping rx due to side-effects was 9%; rash 22%, GI 20%, headache 16%, insomnia 10%, fever 14%
Atovaquone and proguanil (Malarone) For prophylaxis of P. falciparum; little data on P. vivax. Generic available in US.	**Prophylaxis:** 1 tab po (250 mg + 100 mg) q24h with food **Treatment:** 4 tabs po (1000 mg + 400 mg) once daily with food x 3 days Adult tab: 250/100 mg; Peds tab 62.5/25 mg. Peds dosage: *prophylaxis footnote 1 page 153; treatment see comment, page 154.*	Adverse effects in rx trials: Adults—abd. pain 17%, N/V 12%, headache 10%, dizziness 5%. Rx stopped in 1%. Asymptomatic mild ↑ in Al T/AST. Children—cough, headache, anorexia, vomiting, abd. pain. *See drug interactions, Table 22.* Safe in G6PD-deficient pts. Can crush tabs for children and give with milk or other liquid nutrients. Renal insufficiency: contraindicated if CrCl < 30 mL per min.

NOTE: Drugs available from CDC Drug Service indicated by "CDC". Call (+1) (404) 639-3670 (or -2888 (Fax)). **See *Table 13D, page 165* for sources and contact information for hard-to-find antiparasitic drugs.**

TABLE 13B (2)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE	ADVERSE REACTIONS/COMMENTS
Antiprotozoan Drugs: Non-intestinal Protozoa/Extraintestinal Parasites *(continued)*		
Benznidazole (CDC Drug Service)	7.5 mg/kg per day po. 100 mg tabs. May use 300 mg per day for 60 days, regardless of body weight OR give 300 mg per day but prolong treatment to complete the total dose corresponding to 5 mg/kg per day for 60 days.	**Photosensitivity in 50% of pts.** GI: abdominal pain, nausea/vomiting/anorexia. CNS: disorientation, insomnia, twitching/seizures, paresthesias, polyneuritis. **Contraindicated in pregnancy**
Chloroquine phosphate (Aralen)	Dose varies—*see Malaria Prophylaxis and rx, pages 153-154.*	Minor: anorexia/nausea/vomiting, headache, dizziness, blurred vision, pruritus in dark-skinned pts. Major: protracted rx in rheumatoid arthritis can lead to retinopathy. Can exacerbate psoriasis. Can block response to rabies vaccine. **Contraindicated in pts with epilepsy.**
Dapsone See *Comment re methemoglobinemia*	100 mg po q24h	Usually toferated by pts with rash after TMP-SMX. **Dapsone is common etiology of acquired methemoglobinemia** *(NEJM 364:957, 2011)*. Metabolite of dapsone converts heme iron to +3 charge (no O2 transport) from normal +2. Normal blood level 1%; cyanosis at 10%; headache, fatigue, tachycardia, dizziness at 30-40%, acidosis & coma at 60%, death at 70-80%. Low G6PD is a risk factor. Treatment: methylene blue 1-2 mg/kg IV over 5 min x 1 dose.
Eflornithine (Ornidyl) (WHO or CDC drug service)	200 mg/kg IV (slowly) q12h x 7 days for African trypanosomiasis	Diarrhea in ½ pts, vomiting, abdominal pain, anemia/leukopenia in ½ pts, seizures, alopecia, jaundice, ↓ hearing. Contraindicated in pregnancy.
Fumagillin	Eyedrops + po. 20 mg po tid. Leiter's: 800-292-6772.	Adverse events: Neutropenia & thrombocytopenia
Mefloquine	One 250 mg tab/wk for **malaria prophylaxis**; lor rx. 1250 mg x 1 or 750 mg & then 500 mg in 6–8 hrs. In U.S.: 250 mg tab = 228 mg base; outside U.S., 275 mg tab = 250 mg base	Side-effects in roughly 3%. Minor: headache, irritability, insomnia, weakness, diarrhea. **Toxic psychosis, seizures can occur.** Do not use with quinine, quinidine, or halofantrine. Rare: Prolonged QT interval and toxic epidermal necrolysis *(Ln 349:101, 1997)*. **Not used for self-rx due to neuropsychiatric side-effects.**
Melarsoprol (Mel B, Arsobal) (CDC)	See Trypanosomiasis for adult dose. Peds dose: 0.36 mg/kg IV, then gradual ↑ to 3.6 mg/kg q1–5 days for totaf of 9–10 doses.	**Post-rx encephalopathy (2-10%) with 50% mortality overall, risk of death 2° to rx 8-14%.** Prednisolone 1 mg per kg per day po may ↓ encephalopathy. Other: Heart damage, albuminuria, abdominal pain, vomiting, peripheral neuropathy, Herxheimer-like reaction, pruritus.
Miltefosine (Impavido) *Med Lett 56:89, 2014* FDA approved in 2014, but no commercialization in US at present	50 mg po bid (wt 33-44 kg); 50 mg po tid (wt ≥45 kg). Treat for 28 days	Contact CDC for IND. **Pregnancy—No;** teratogenic. Side-effects vary: kala-azar pts, vomiting in up to 40%, diarrhea in 17%; "motion sickness", headache & increased creatinine. Metabolized by liver; virtually no urinary excretion.
Nifurtimox (Lampit) *(CDC)* (Manufactured in Germany by Bayer)	8–10 mg/kg per day po div. 4 x per day for 90-120 days	**Side-effects in 40–70% of pts.** GI: abdominal pain, nausea/vomiting. CNS: polyneuritis (1/3), disorientation, insomnia, twitching, seizures. Skin rash. Hemolysis with G6PD deficiency.
Pentamidine (NebuPent)	300 mg via aerosol q month. Also used IM.	Hypotension, hypocalcemia, hypoglycemia followed by hyperglycemia, pancreatitis. Neutropenia (15%), thrombocytopenia. Nephrotoxicity. Others: nausea/vomiting, ↑ liver tests, rash.
Primaquine phosphate	26.3 mg (=15 mg base). Adult dose is 30 mg of base po daily.	**In G6PD def. pts, can cause hemolytic anemia with hemoglobinuria, esp. African, Asian peoples.** Methemoglobinemia. Nausea/abdominal pain if pt. fasting. *(CID 39:1336, 2004)*. **Pregnancy: No.**
Pyrimethamine (Daraprim, Malocide) Also combined with sulfadoxine as **Fansidar** (25–500 mg)	100 mg po, then 25 mg/day. **Very expensive:** $79,000 for 100 tabs (25 mg) (Sep 2015, US price)	**Major problem is hematofogic:** megalobfastic anemia, ↓ WBC, ↓ platelets. Can give 5 mg folinic acid per day to ↓ bone marrow depression and not interfere with antitoxoplasmosis effect. If high-dose pyrimethamine, ↑ folinic acid to 10–50 mg/day. Pyrimethamine + sulfadiazine can cause mental changes due to carnitine deficiency *(AJM 95:112, 1993)*. Other: Rash, vomiting, diarrhea, xerostomia.
Quinidine gluconate Cardiotoxicity ref: *LnID 7:549, 2007*	Loading dose of 10 mg (equiv to 6.2 mg of quinidine base) / kg IV over 1–2 hr, then constant infusion of 0.02 mg of quinidine gluconate / kg per minute. May be available for compassionate use from Lilly.	**Adverse reactions of quinidine/quinine similar:** (1) IV bolus injection can cause fatal hypotension, (2) hyperinsulinemic hypoglycemia, esp. in pregnancy, (3) ↓ rate of infusion of IV quinidine if OT interval ↑ >25% of baseline, (4) reduce dose 30–50% after day 3 due to ↓ renal clearance and ↓ vol. of distribution.

NOTE: Drugs available from CDC Drug Service indicated by "CDC". Call (+1) (404) 639-3670 (or -2888 (Fax)). ***See Table 13D, page 165 for sources and contact information for hard-to-find antiparasitic drugs.***

TABLE 13B (3)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE	ADVERSE REACTIONS/COMMENTS
Antiprotozoan Drugs: Non-Intestinal Protozoa/Extraintestinal Parasites *(continued)*		
Quinine sulfate (Qualaquin)	324 mg tabs. No IV prep. in US. Oral rx of chloroquine-resistant falciparum malaria: 624 mg po tid x 3 days, then (tetracycline 250 mg po qid or doxy 100 mg bid) x 7 days	Cinchonism; tinnitus, headache, nausea, abdominal pain, blurred vision. Rarely: blood dyscrasias, drug fever, asthma, hypoglycemia. Transient blindness in <1% of 500 pts *(AnIM 136:339, 2002)*. **Contraindicated if prolonged QTc, myasthenia gravis, optic neuritis or G6PD deficiency.**
Spiramycin (Rovamycin)	1 gm po q8h *(see Comment)*.	GI and allergic reactions have occurred. Available at no cost after consultation with Palo Alto Medical Foundation Toxoplasma Serology Lab: 650-853-4828 or from U.S. FDA 301-796-1600.
Sulfadiazine	1–1.5 gm po q6h.	See *Table 10A, page 113, for sulfonamide side-effects*
Sulfadoxine & pyrimethamine combination (Fansidar)	Contains 500 mg sulfadoxine & 25 mg pyrimethamine	Long half-life of both drugs: Sulfadoxine 169 hrs, pyrimethamine 111 hrs allows weekly dosage. In African, used empirically in pregnancy for intermittent preventative treatment (ITPp) against malaria: dosing at 3 set times during pregnancy. Reduces material and fetal mortality if HIV+. *See Expert Rev Anti Infect Ther 8:589, 2010.* **Fatalities reported due to Stevens-Johnson syndrome and toxic epidermal necrolysis.** Renal excretion—caution if renal impairment.
DRUGS USED TO TREAT NEMATODES, TREMATODES, AND CESTODES		
Albendazole (Albenza)	Doses vary with indication. Take with food; fatty meal increases absorption.	**Pregnancy Cat. C;** give after negative pregnancy test. Abdominal pain, nausea/vomiting, alopecia, ↑ serum transaminase. Rare leukopenia.
Diethylcarbamazine *(CDC)*	Used to treat filariasis.	Headache, dizziness, nausea, fever. Host may experience inflammatory reaction to death of adult worms: fever, urticaria, asthma, GI upset **(Mazzotti reaction). Pregnancy—No.**
Ivermectin (Stromectol, Mectizan) (3 mg tab & topical 0.5% lotion for head lice). Take on empty stomach.	Strongyloidiasis dose: 200 µg/kg/day po x 2 days Onchocerciasis: 150 µg/kg x 1 po Scabies: 200 µg/kg po x 1; if AIDS, wait 14 days & repeat	Mild side-effects: fever, pruritus, rash. In rx of onchocerciasis, can see tender lymphadenopathy, headache, bone/joint pain. Host may experience inflammatory reaction to death of adult worms: fever, urticaria, asthma, GI upset **(Mazzotti reaction)**.
Mebendazole (Vermox) Not available in US, but widely available elsewhere.	Doses vary with indication.	Rarely causes abdominal pain, nausea, diarrhea. Contraindicated in pregnancy & children <2 yrs old.
Praziquantel (Biltricide)	Doses vary with parasite; *see Table 13A.*	Mild: dizziness/drowsiness, N/V, rash, fever. **Only contraindication is ocular cysticercosis**. Potential exacerbation of neurocysticercosis. Metab.-induced by anticonvulsants and steroids; can negate effect with cimetidine 400 mg po tid. Reduce dose if advanced liver disease.
Pyrantel pamoate (over-the-counter)	Oral suspension. Dose for all ages: 11 mg/kg (to max. of 1 gm) x 1 dose	Rare GI upset, headache, dizziness, rash
Suramin (Germanin) *(CDC)*	Drug powder mixed to 10% solution with 5 mL water and used within 30 min. First give test dose of 0.1 gm IV. Try to avoid during pregnancy.	Does not cross blood-brain barrier; no effect on CNS infection. Side-effects: vomiting, pruritus, urticaria, fever, paresthesias, albuminuria (discontinue drug if casts appear). Do not use if renal/liver disease present. Deaths from vascular collapse reported.
Triclabendazole (Egaten) (CDC)	Used for fasciola hepatica liver fluke infection: 10 mg/kg po x 1 dose. May repeat in 12-24 hrs. 250 mg tabs	AEs ≥10%: sweating and abdominal pain. AEs 1-10%: weakness, chest pain, fever, anorexia, nausea, vomiting. **Note: use with caution if G6PD def. or impaired liver function.**

NOTE: Drugs available from CDC Drug Service indicated by "CDC". Call (+1) (404) 639-3670 (or -2888 (Fax)). ***See Table 13D, page 165 for sources and contact information for hard-to-find antiparasitic drugs.***

TABLE 13C – PARASITES THAT CAUSE EOSINOPHILIA (EOSINOPHILIA IN TRAVELERS)

Frequent and Intense (>5000 eos/mcL)	Moderate to Marked Early Infections	During Larval Migration; Absent or Mild During Chronic Infections	Other
Strongyloides (absent in compromised hosts); Lymphatic Filariasis; Toxocaria (cutaneous larva migrans)	Ascaris; Hookworm; Clonorchis; Paragonimis	Opisthorchis	Schistosomiasis; Cysticercosis; Trichuris; Angiostrongylus; Non-lymphatic filariasis; Gnathostoma; Capillaria; Trichostrongylus

TABLE 13D – SOURCES FOR HARD-TO-FIND ANTIPARASITIC DRUGS

Source	Drugs Available	Contact Information
CDC Drug Service	Artesunate, Benznidazole, Diethylcarbamazine (DEC), Eflornithine, Melarsoprol, Nifurtimox, Sodium stibogluconate, Suramin, Triclabendazole	www.cdc.gov/laboratory/drugservice/index.html (+1) 404-639-3670
WHO	Drugs for treatment of African trypanosomiasis	simarrop@who.int; (+41) 794-682-726; (+41) 227-911-345 francoj@who.int; (+41) 796-198-535; (+41) 227-913-313
Compounding Pharmacies, Specialty Distributors, Others		
Expert Compounding Pharmacy	Quinacrine, Iodoquinol, niclosamide	www.expertpharmacy.org 1-800-247-9767; (+1) 818-988-7979
Fagron Compounding Pharmacy (formerly Gallipot)	Quinacrine, Iodoquinol, Paromomycin, Diloxanide	www.fagron.com 1-800-423-6967; (+1) 651-681-9517
Leiter's Pharmacy	Fumagillin	www.leiterrx.com 1-800-292-6772, +1-408-292-6772
Profounda, Inc.	Miltefosine	www.impavido.com; +1 407-270-7790
Victoria Apotheke Zurich will ship worldwide if sent physicians prescription.	Paromomycin (oral and topical), Triclabendazole. Other hard to find anti-parasitic drugs	www.pharmaworld.com (+41) 43-344-6060
Palo Alto Medical Foundation, Toxoplasma Serology Lab	Spiramycin (consultation required for release)	(+1) 650-853-4828; toxlab@pamf.org

TABLE 14A – ANTIVIRAL THERAPY*

For HIV, see *Table 14C*; for Hepatitis, *see Table 14E* and *Table 14F*. For Antiviral Activity Spectra, *see Table 4C, page 79*

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Adenovirus: Cause of RTIs including fatal pneumonia in children & young adults and 60% mortality in transplant pts *(CID 43:331, 2006)*. Frequent cause of cystitis in transplant patients. Adenovirus 14 associated with severe pneumonia in otherwise healthy young adults *(MMWR 56(45):1181, 2007)*. **Findings include:** fever, ↑ liver enzymes, leukopenia, thrombocytopenia, diarrhea, pneumonia, or hemorrhagic cystitis.	In severe cases of pneumonia or post HSCT[1]: **Cidofovir** • 5 mg/kg/wk x 2 wks, then q 2 wks + **probenecid** 1.25 gm/M^2 given *3* hrs before cidofovir and *3* & 9 hrs after each infusion • Or 1 mg/kg IV *3x*/wk. For adenovirus hemorrhagic cystitis *(CID 40:199, 2005; Transplantation. 2006; 81:1398)*: Intravesical **cidofovir** (5 mg/kg in 100 mL saline instilled into bladder).	Cidofovir successful in *3/8* immunosuppressed children *(CID 38:45, 2004) & 8 of 10 children with HSCT (CID 41; 1812, 2005)*. ↓ in virus load predicted response to cidofovir. Ribavirin has had mixed activity; appears restricted to group C serotypes. Vidarabine and Ganciclovir have in vitro activity against adenovirus; little to no clinical data. **Brincidofovir** (CMX001-Chimerix) oral cidofovir prodrug in Phase III. Adenovirus specific T-cell (Cytovir) infusions under development.*(Cytotherapy 16.4: S22, 2014)*
Bunyaviridae; Severe fever with thrombocytopenia syndrome virus (SFTSV) Possibly transmitted by *Haemaphysalis longicornis tick.*	No therapy recommended. Ribavirin ineffective. Clinical symptoms: Fever, weakness, myalgias, GI symptoms	Lab: Elevated LDH (> 1200) and CPK (> 800) associated with higher mortality rates. Initially thought to be an anaplasma infection, but serology showed a new virus.
Coronavirus—SARS-CoV Severe acute respiratory syndrome *(NEJM 348:1953, 1967, 2003)* **MERS-CoV:** Middle East respiratory syndrome *(LnID 14:1090, 2014)*	**SARS:** • Ribavirin—ineffective. • Interferon alfa ± steroids—small case series. • Pegylated IFN-α effective in monkeys. • Low dose steroids alone successful in one Beijing hospital. High dose steroids ↑ serious fungal infections. • Inhaled nitric oxide improved oxygenation & improved chest x-ray *(CID 39:1531, 2004)*. **MERS:** Increased 14 day survival with **Ribavirin** po + **PEG-IFN** 180 mcg/kg sc x *2* wks *(LnID 14:1090, 2014)*. Other therapies: *LnID 14:1136, 2014.*	**SARS: Transmission by close contact:** effective infection control practices (**mask [changed frequently]**, eye protection, gown, gloves) key to stopping transmission. **MERS:** Suspected reservoirs are camels and perhaps other animals. *Review: Clin Micro Rev. 28:465, 2015.*
Enterovirus—Meningitis: most common cause of aseptic meningitis. Rapid CSF PCR test is accurate; reduces costs and hospital stay for infants *(Peds 120:489, 2007)*	**No rx currently recommended;** however, **pleconaril** (VP *63843*) still under investigation.	No clinical benefit from Pleconaril in double-blind placebo-controlled study in 21 infants with enteroviral aseptic meningitis *(PIDJ 22:335, 2003)*. Some improvement among those with severe headache *(AAC 2006 50:2409-14)*. Severe respiratory illness with enterovirus D68 *(MMWR 63:798 & 901, 2014)*.
Hemorrhagic Fever Virus Infections: *Review: LnID 6:203, 2006.*		
Congo-Crimean Hemorrhagic Fever (HF) Tick-borne; symptoms include N/V, fever, headache, myalgias, & stupor (*1/3*). Signs: *conjunctival* injection, hepatomegaly, petechiae (*1/3*). Lab: ↓ platelets, ↓ WBC, ↑ ALT, AST, LDH & CPK (100%).	Oral **ribavirin, 30 mg/kg** as initial loading dose & 15 mg/kg q6h x 4 days & then 7.5 mg/kg q8h x 6 days (WHO recommendation) *(see Comment)*. Reviewed *Antiviral Res 78: 125, 2008.*	*3/3* healthcare workers in Pakistan had complete recovery *(Ln 346:472, 1995)* & 61/69 (89%) with confirmed CCHF rx with ribavirin survived in Iran *(CID 36:1613, 2003)*. Shorter time of hospitalization among ribavirin treated pts (7.7 vs. 10.3 days), but no difference in mortality or transfusion needs in study done in Turkey *(J Infection 52: 207-215, 2006)*. Suggested benefit from ribavirin & dexamethasone *(281 pts) (CID 57:1270, 2013)*.

[1] HSCT = Hematopoietic stem cell transplant

* *See page 2 for abbreviations.* *NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.*

TABLE 14A (2)

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Hemorrhagic Fever Virus Infections *(continued)*		
Ebola/Marburg HF (Central Africa) Largest ever documented outbreak of Ebola virus (EVD), West Africa, 2014. Diagnostic testing at U.S. CDC. Within a few days of symptom onset, diagnosis is most commonly made by antigen-capture enzyme linked immunosorbent assay (ELISA), IgM antibody ELISA, NAAT or viral culture. *Updated in http://emergency.cdc.gov/han/han00365.asp. See also: http://www.bt.cdc.gov/han/han00364.asp*	**No effective antiviral rx** *(J Virol 77: 9733, 2003).* Investigational antibody treatment "ZMapp" used as compassionate use in a few selected patients (Mapp Biopharmaceutical; http://mappbio.com/). ZMapp is a 3 mice monoclonal antibody preparation derived from mice exposed to small fragments of Ebola virus. Use of convalescent serum from pts who have recovered is approved for use in newly infected pts by the WHO *(BMJ 349:g5539, 2014).* GS-5734 (Gilead) active in animal models.	**Abrupt onset of symptoms typically 8-10 days after exposure (range 2-21 days).** Nonspecific symptoms, which may include fever, chills, myalgias, and malaise. Fever, anorexia, asthenia / weakness are the most common signs and symptoms. Patients may develop a diffuse erythematous maculopapular rash (days 5-7) (usually involving the face, neck, trunk, and arms) that can desquamate. EVD can **often be confused with** other more common infectious diseases such as malaria, typhoid fever, meningococcemia, and other bacterial infections (e.g., pneumonia). **Gastrointestinal symptoms:** severe watery diarrhea, nausea, vomiting and abdominal pain. **Other:** chest pain, shortness of breath, headache or confusion, may also develop. Patients often have conjunctival injection. Hiccups reported. Seizures may occur, and cerebral edema reported. Bleeding is not universally present but can manifest later in the course as petechiae, ecchymoses/bruising, or oozing from venipuncture sites and mucosal hemorrhage. Frank hemorrhage is less common. Pregnant women may experience spontaneous miscarriages.
With pulmonary syndrome: Hantavirus pulmonary syndrome, "sin nombre virus"	**No benefit from ribavirin demonstrated** *(CID 39:1307, 2004).* Early recognition of disease and supportive (usually ICU) care is key to successful outcome.	Acute onset of fever, headache, myalgias, non-productive cough, thrombocytopenia, increased PT and non-cardiogenic pulmonary edema with respiratory insufficiency following exposure to droppings of infected rodents.
With renal syndrome: Lassa, Venezuelan, Korean, HF, Sabia, Argentinian HF, Bolivian HF, Junin, Machupo (> 90% occur in China *CID 59:1040, 2014*)	Oral **ribavirin, 30 mg/kg** as initial loading dose & 15 mg/kg q6h x 4 days & then 7.5 mg/kg x 6 days (WHO recommendation) *(see Comment).*	Toxicity low, hemolysis reported but recovery when treatment stopped. No significant changes in WBC, platelets, hepatic or renal function. *See CID 36:1254, 2003,* for management of contacts.
Dengue and dengue hemorrhagic fever (DHF) *www.cdc.gov/ncidod/dvbid/dengue/dengue-hcp.htm* Think dengue in traveler to tropics or subtropics (incubation period usually 4-7 days) with fever, bleeding, thrombocytopenia, or hemoconcentration with shock. Dx by viral isolation or serology; serum to CDC (telephone 787-706-2399).	**No data on antiviral rx.** Fluid replacement with careful hemodynamic monitoring critical. Rx of **DHF** with colloids effective: 6% hydroxyethyl starch preferred in 1 study *(NEJM 353:9, 2005).* Review in *Semin Ped Infect Dis 16: 60-65, 2005.*	Of 77 cases dx at CDC (2001–2004), recent (2-wks) travel to Caribbean island 30%, Asia 17%, Central America 15%, S. America 15% *(MMWR 54:556, June 10, 2005).* 5 pts with severe **DHF** rx with dengue antibody-neg. gamma globulin 500 mg per kg q24h IV for 3–5 days; rapid ↑ in platelet counts *(CID 36:1623, 2003).* Diagnosis: ELISA detects IgM antibody. Has some cross-reactivity with West Nile Virus infection. Should only be used in pts with symptoms c/w Dengue Fever.
West Nile virus *(JAMA 310:308, 2013)* A flavivirus transmitted by mosquitoes, blood transfusions, transplanted organs & breast-feeding. Birds (>200 species) are main host with humans & horses incidental hosts. The US epidemic continues.	**No proven rx to date.** Reviewed in *Lancet Neurology 6: 171-181, 2007.*	Usually nonspecific febrile disease but 1/150 cases develops meningoencephalitis, aseptic meningitis or polio-like paralysis *(AnIM 104:545, 2004; JCI 113: 1102, 2004).* Long-term sequelae (neuromuscular weakness & psychiatric) common *(CID 43:723, 2006).* Diagnosis: increased IgM antibody in serum & CSF or CSF PCR (contact State Health Dept./CDC). Blood supply now tested in U.S. Increased serum lipase in 11/17 cases *(NEJM 352:420, 2005).*
Yellow fever	**No data on antiviral rx** **Guidelines for use of preventative vaccine:** *(http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6423a5.htm?s_cid=mm6423a5_w)*	Reemergence in Africa & S. Amer. due to urbanization of susceptible population *(Lancet Inf 5:604, 2005).* Vaccination Diagnosis: increased IgM antibody safe and effective in HIV patients, especially in those with suppressed VL and higher CD4 counts *(CID 48:659, 2009).* A purified whole-virus, inactivated, cell-culture–derived vaccine (XRX-001) using the 17D strain proven safe and resulted in neutralizing antibodies after 2 doses in a de-escalation, phase I study. *(N Engl J Med 2011 Apr 7; 364:1326)*
Chikungunya fever: brake bone fever A self-limited arbovirus illness spread by Aedes mosquito. High epidemic potential (Caribbean).	**No antiviral therapy.** Fluids, analgesics, anti-pyretics *(NEJM 371:885, 2014).*	Clinical presentation: high fever, severe myalgias & headache, macular papular rash with occ. thrombocytopenia. Rarely hemorrhagic complications. Dx mostly clinical; definitive diagnosis by PCR *(NEJM 372:1231, 2015).*
SFTSV (Severe fever with thrombocytopenia syndrome virus)	**See *Bunyaviridae*, page 166**	
Hepatitis Viral Infections	*See Table 14E (Hepatitis A & B), Table 14F (Hepatitis C)*	

* *See page 2 for abbreviations.* NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.

TABLE 14A (3)

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Herpesvirus Infections		
Cytomegalovirus (CMV) At risk pts: HIV/AIDS, cancer chemotherapy, post-transplant Ref: *Transplantation 96:333, 2013; Am J Transplant 13(Suppl 4):93, 2013*	**Primary prophylaxis** not generally recommended except in certain transplant populations *(see TABLE 15E)*. Preemptive therapy in pts with ↑ CMV DNA plasma VL & CD4 <100/mm^3. If used: **valganciclovir** 900 mg po q12h *(CID 32: 783, 2001)*. Authors rec. primary prophylaxis be dc if response to ART with ↑ CD4 >100 for 6 mos. *(MMWR 53:98, 2004)*.	Risk for developing CMV disease correlates with quantity of CMV DNA in plasma: each $\log_{10}$ ↑ associated with 3.1-fold ↑ in disease *(CID 28:758, 1999)*. Resistance demonstrated in 5% of transplant recipients receiving primary prophylaxis *(J Antimicrob Chemother 65:2628, 2010)*. Consensus guidelines: *Transplantation 96:333, 2013.*
CMV: Colitis, Esophagitis, Gastritis Symptoms relate to site of disease	*Mild:* **Valganciclovir** 900 mg po bod with food x 14-21 days *Severe:* **Ganciclovir** 5 mg/kg IV q12h x 14-21 days OR **Foscarnet** (60 mg/kg IV q8h or 90 mg/kg q12h) x 14-21 days *Post-treatment suppression:* **Valganciclovir** 900 mg po once daily until CD4 > 100 x 6 mos	Diagnosis: Elevated whole blood quantitative PCR & histopathology. Severe bouts of Inflammatory Bowel Disease (IBD) colitis may be complicated by CMV; Rx of CMV in this setting is recommended *(European J Clin Micro & Inf Dis 34:13, 2015)*. Rx of CMV in less severe bouts of IBD colitis is unclear.
CMV: Neurologic disease, Encephalitis Myelitis, polyradiculopathy, peripheral neuropathy Symptoms relate to site of disease	Treat as for colitis, esophagitis, gastritis above	Diagnosis: Elevated whole blood and/or CSF quantitative PCR Note: **Severe or fatal IRIS** has occurred in AIDS pts; suggest delay starting ART for 2 wks after initiation of CMV therapy
CMV: Pneumonia At risk: 1st 6 months post-transplant & 3 months post-stopping prophylaxis Require evidence of invasive disease. Diagnosis: prefer whole blood quantitative PCR and/or positive lung biopsy histopathology Ref: *Transplantation 96:333, 2013; Am J Transplant 13(Suppl 4):93, 2013*	*Viremic but no/mild symptoms:* **Valganciclovir** 900 mg po bid (Am J Transplant 7:2106, 2007) *Severe in lung transplant or AIDS pts:* **Ganciclovir** 5 mg/kg IV q12h (adjust for renal insufficiency). Treat until clinical resolution & neg blood PCR; min duration: 2 wks *If Ganciclovir-resistant:* **Foscarnet** (60 mg/kg q8h or 90 mg/kg q12h) IV (adjust for renal insufficiency). Try to reduce immunosuppression.	*Post-treatment suppression:* Valganciclovir 900 mg po once daily x 1-3 months if high risk of relapse. Suspect resistant CMV if treatment failure or relapse. Do genotype resistance testing *(CID 56:1018, 2013)*. Note: IVIG or CMV specific immunoglobulin did not improve overall or attributable mortality in retrospective study of 421 bone marrow transplant pts *(CID 61:31, 2015)*.
CMV: Retinitis Most common ocular complication of HIV/AIDS. Rare in pts on ART with CD4 >200. If not on ART, wait to start until after 2 wks of CMV therapy. Ref: aidsinfo.nih.gov/guidelines **CMV immune recovery retinitis:** new retinitis after starting ART. Do not stop ART or Valganciclovir. No steroids.	*Not sight-threatening:* **Valganciclovir** 900 mg po bid with food x 14-21 days, then 900 mg po once daily until CD4 >100 x 6 months Sight-threatening (see Comment): **Valganciclovir** + intravitreal **Ganciclovir** 2 mg (1-4 doses over 7-10 days).	Sight-threatening: <1500 microns from fovea or next to head of optic nerve. If can't use Valganciclovir, Ganciclovir 5 mg/kg IV q12h x 14-21 days, then 5 mg/kg IV once daily. If suspect Ganciclovir resistance: Foscarnet (60 gm/kg q8h or 90 mg/kg q12h) x 14-21 days. Ganciclovir ocular implants no longer available.
CMV in Transplant patients: See *Table 15E for discussion of prophylaxis.* CMV disease can manifest as CMV syndrome with or without end-organ disease. **Guidelines for CMV therapy** (*Transplantation. 2013; 96(4):333; and Am J Transplant. 2013; 13 Suppl 4:93.* **Ganciclovir** 5 mg/kg IV q12h OR **Valganciclovir** 900 mg po q12h *(Am J Transplant 7:2106, 2007)* are effective treatment options. Treatment duration should be individualized. Continue treatment until (1) CMV PCR or antigenemia has become undetectable, (2) clinical evidence of disease has resolved, and (3) at least 2-3 weeks of treatment *(Am J Transplant 13(Suppl 4):93, 2013; Blood 113:5711, 2009)*. Secondary prophylaxis (**Valganciclovir** 900 mg daily) should be considered for 1-3 month course in patients recently treated with high-dose immunosuppression such as lymphocyte depleting antibodies, those with severe CMV disease, or those with >1 episode of CMV disease. In HSCT recipients, secondary prophylaxis should be considered in similar cases balancing the risk of recurrent infection with drug toxicity		
CMV in pregnancy: Hyperimmune globulin 200 IU/kg maternal weight as single dose during pregnancy (early), administered IV reduced complications of CMV in infant at one year of life. *(CID 55: 497, 2012)*.		
CMV: Congenital/Neonatal Symptomatic	Valganciclovir 16 mg/kg po bid x 6 mos	Better outcome after 6 mos compared to 6 wks with no difference in AEs *(NEJM 372:933, 2015)*.

TABLE 14A (4)

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Herpesvirus Infections *(continued)*		
Epstein Barr Virus (EBV) — Mononucleosis *(Ln ID 3:131, 2003)*	**No treatment.** Corticosteroids for tonsillar obstruction, CNS complications, or threat of splenic rupture.	**Etiology of atypical lymphocytes:** EBV, CMV, Hep A, Hep B, Toxo, measles, mumps, drugs *(Int Pediatr 18:20, 2003).*
HHV-6—Implicated as cause of roseola (exanthem subitum) & other febrile diseases of childhood *(NEJM 352:768, 2005).* Fever & rash documented in transplant pts *(JID 179:311, 1999).* Reactivation in 47% of 110 U.S. hematopoietic stem cell transplant pts assoc. with delayed monocytes & platelet engraftment *(CID 40:932, 2005).* Recognized in assoc. with meningoencephalitis in immunocompetent adults. Diagnosis made by pos. PCR in CSF. ↓ viral copies in response to **ganciclovir** rx *(CID 40:890 & 894, 2005).* Foscarnet therapy improved thrombotic microangiopathy *(Am J Hematol 76:156, 2004).* Cidofovir is second line therapy *(Bone Marrow Transplantation (2008) 42, 227–240)*		
HHV-7—ubiquitous virus (>90% of the population is infected by age 3 yrs). No relationship to human disease. Infects CD4 lymphocytes via CD4 receptor; transmitted via saliva.		
HHV-8—The agent of Kaposi's sarcoma, Castleman's disease, & body cavity lymphoma. Associated with diabetes in sub-Saharan Africa *(JAMA 299:2770, 2008).*	**No antiviral treatment.** Effective anti-HIV therapy may help.	Localized lesions: radiotherapy, laser surgery or intralesional chemotherapy. Systemic: chemotherapy. Castleman's disease responded to ganciclovir *(Blood 103:1632, 2004)* & valganciclovir *(JID 2006).*
Herpes simplex virus (HSV Types 1 & 2)		
Bell's palsy H. simplex most implicated etiology. Other etiologic considerations: VZV, HHV-6, Lyme disease.	As soon as possible after onset of palsy: **Prednisone** 1 mg/kg po divided bid x 5 days then taper to 5 mg bid over the next 5 days (total of 10 days prednisone) Alternate: **Prednisone** (dose as above) + **Valacyclovir** 500 mg bid x 5 days	Prospective randomized double blind placebo controlled trial compared prednisolone vs acyclovir vs. (prednisolone + acyclovir) vs placebo. Best result with prednisolone: 85% recovery with placebo, 96% recovery with prednisolone, 93% with combination of acyclovir & prednisolone *(NEJM 357:1598 & 1653, 2007).* **Large meta-analysis confirms: Steroids alone, effective; antiviral drugs alone, not effective; steroids + antiviral drugs, no more effective than steroids alone** *(JAMA: 302: 985, 2009).*
Encephalitis (Excellent reviews: *CID 35: 254, 2002).* UK experience *(EID 9:234, 2003; Eur J Neurol 12:331, 2005 ; Antiviral Res: 71:141-148, 2006)* HSV-1 is most common cause of sporadic encephalitis. Survival & recovery from neurological sequelae are related to mental status at time of initiation of rx. **Early dx and rx imperative.** *NEJM 371:68, 2014.*	**Acyclovir** IV 10 mg/kg IV (infuse over 1 hr) q8h x 14–21 days. 20 mg/kg q8h in children <12 yrs. Dose calculation in obese patients uncertain. To lessen risk of nephrotoxicity with larger doses seems reasonable to infuse each dose over more than 1 hour. In morbid obesity, use actual body weight.	Mortality rate reduced from >70% to 19% with acyclovir rx. PCR analysis of CSF for HSV-1 DNA is 100% specific & 75–98% sensitive. 8/33 (25%) CSF samples drawn before day 3 were neg. by PCR; neg. PCR assoc. with ↓ protein & <10 WBC per mm^3 in CSF *(CID 36:1335, 2003).* All were + after 3 days. Relapse after successful rx reported in 7/27 (27%) children. Relapse was associated with a lower total dose of initial acyclovir rx (285 ± 82 mg per kg in relapse group vs. 462 ± 149 mg per kg, p <0.03) *(CID 30:185, 2000; Neuropediatrics 35:371, 2004).* Series in 106 adults *J Clin Virol 60:112, 2014*
Genital Herpes: *Sexually Transmitted Treatment Guidelines 2010: MMWR 59 (RR-12), 2010.*		
Primary (initial episode)	**Acyclovir** (Zovirax or generic) 400 mg po tid x 7–10 days OR	↓ by 2 days time to resolution of signs & symptoms, ↓ by 4 days time to healing of lesions, ↓ by 7 days duration of viral shedding. Does not prevent recurrences. For severe cases only: 5 mg per kg IV q8h times 5–7 days.
	Valacyclovir (Valtrex) 1000 mg po bid x 7-10 days OR	An ester of acyclovir, which is well absorbed, bioavailability 3–5 times greater than acyclovir.
	Famciclovir (Famvir) 250 mg po tid x 7–10 days	Metabolized to penciclovir, which is active component. Side effects and activity similar to acyclovir. **Famciclovir** 250 mg po tid **equal to acyclovir** 200 mg 5 times per day.
Episodic recurrences	**Acyclovir** 800 mg po tid **x 2 days** or 400 mg po tid **x 5 days** or **Famciclovir** 1000 mg bid **x 1 day** or 125 mg po bid x 5 days or **Valacyclovir** 500 mg po bid **x 3 days** or 1 gm po once daily **x 5 days** For HIV patients, see *Comment*	For episodic recurrences in HIV patients: **acyclovir** 400 mg po tid x 5-10 days or **famciclovir** 500 mg po bid x 5-10 days or **valacyclovir** 1 gm po bid x 5-10 days

* See *page 2 for abbreviations.* NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.

TABLE 14A (5)

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Herpesvirus Infections/ Herpes simplex virus (HSV Types 1 & 2) *(continued)*		
Chronic daily suppression	Suppressive therapy reduces the frequency of genital herpes recurrences by 70–80% among pts who have frequent recurrences (i.e., >6 recurrences per yr) & many report no symptomatic outbreaks. **Acyclovir** 400 mg po bid , **or famciclovir** 250 mg po bid, **or valacyclovir** 1 gm po q24h; pts with <9 recurrences per yr could use 500 mg po q24h and then use **Valacyclovir** 1 gm po q24h if breakthrough at 500 mg. For HIV patients, see *Comment*	For chronic suppression in HIV patients: (all regimens equally efficacious: *Cochrane Database System Rev 8:CD009036, 2014*) **acyclovir** 400-800 mg po bid or tid or **famciclovir** 500 mg po bid or **valacyclovir** 500 mg po bid
Genital, immunocompetent		
Gingivostomatitis, primary (children)	**Acyclovir** 15 mg/kg po 5x/day x 7 days	Efficacy in randomized double-blind placebo-controlled trial *(BMJ 314:1800, 1997)*.
Keratoconjunctivitis and recurrent epithelial keratitis	**Trifluridine** (Viroptic), 1 drop 1% solution q2h (max. 9 drops per day) for max. of 21 days *(see Table 1, page 13)*	In controlled trials, response % > idoxuridine. Suppressive rx with acyclovir (400 mg bid) reduced recurrences of ocular HSV from 32% to 19% *(NEJM 339:300, 1998)*.
Mollaret's recurrent "aseptic" meningitis (usually HSV-2) *(Ln 363:1772, 2004)*	No controlled trials of antiviral rx & resolves spontaneously. If therapy is to be given, **acyclovir** (15–30 mg/kg/day IV) or **valacyclovir** 1-2 gm po qid should be used.	Pos. PCR for HSV in CSF confirms dx *(EJCMID 23:560, 2004)*. Daily suppression rx might ↓ frequency of recurrence but no clinical trials. Oral Valacyclovir ref: *JAC 47:855, 2001.*
Mucocutaneous *(for genital see previous page)*		
Oral labial, "fever blisters":		
Normal host *See Ann Pharmacotherapy 38:705, 2004; JAC 53:703, 2004*	Start rx with prodrome symptoms (tingling/burning) before lesions show. **Oral: Valacyclovir** 2 gm po q12h x 1 day ↓ 1 day **Famciclovir**[2] 500 mg po bid x 7 days ↓ 2 days **Acyclovir**[NFDA] 400 mg po 5 x per day (q4h while awake) x 5 days) ↓ ½ day **Topical:** **Penciclovir** 1% cream q2h during day x 4 days ↓ 1 day **Acyclovir** 5% cream[3] 6x/day (q3h) x 7 days ↓ ½ day	Penciclovir *(AAC 46: 2848, 2002)*. Oral acyclovir 5% cream *(AAC 46:2238, 2002)*. Oral famciclovir *(JID 179:303, 1999)*. Topical fluocinonide (0.05% Lidex gel) q8h times 5 days in combination with famciclovir ↓ lesion size and pain when compared to famciclovir alone *(JID 181:1906, 2000)*. Acyclovir 5% cream + 1% hydrocortisone (Xerese) superior to acyclovir alone *(AAC 58:1273, 2014)*.
Herpes Whitlow	*See Table 1, page 27*	
Oral labial or genital: Immunocompromised (includes pts with AIDS) and critically ill pts in ICU setting/large necrotic ulcers in perineum or face. *(See Comment)* Primary HSV in pregnancy: increased risk of dissemination, including severe hepatitis, Risk greatest in 3rd trimester *(NEJM 370:2211, 2014).*	**Acyclovir** 5 mg per kg IV (infused over 1 hr) q8h times 7 days (250 mg per M²) or 400 mg po 5 times per day times 14–21 days *(see Comment if suspect acyclovir-resistant)* **OR** **Famciclovir:** In HIV infected, 500 mg po bid for 7 days for recurrent episodes of genital herpes **OR** **Valacyclovir**[NAI]: In HIV-infected, 500 mg po bid for 5–10 days for recurrent episodes of genital herpes or 500 mg po bid for chronic suppressive rx.	**Acyclovir-resistant HSV: IV foscarnet** 90 mg/kg IV q12h x 7 days. Suppressive therapy with famciclovir (500 mg po bid), valacyclovir (500 mg po bid) or acyclovir (400-800 mg po bid) reduces viral shedding and clinical recurrences.

[2] FDA approved only for HIV pts

[3] Approved for immunocompromised pts

* *See page 2 for abbreviations.* NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.

TABLE 14A (6)

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Herpesvirus Infections/ Herpes simplex virus (HSV Types 1 & 2)/ Mucocutaneous *(continued)*		
Pregnancy and genital H. simplex	Acyclovir safe even in first trimester. No proof that acyclovir at delivery reduces risk/severity of neonatal Herpes. In contrast, C-section in women with active lesions reduces risk of transmission. Ref: *Obstet Gyn 106:845, 2006.*	
Herpes simiae (Herpes B virus): **Monkey bite** *CID 35:1191, 2002*	**Postexposure prophylaxis: Valacyclovir** 1 gm po q8h times 14 days or acyclovir 800 mg po 5 times per day times 14 days. **Treatment of disease:** (1) CNS symptoms absent **Acyclovir** 12.5–15 mg per kg IV q8h or ganciclovir 5 mg per kg IV q12h. (2) CNS symptoms present: **Ganciclovir** 5 mg per kg IV q12h	Fatal human cases of myelitis and hemorrhagic encephalitis have been reported following bites, scratches, or eye inoculation of saliva from monkeys. Initial sx include fever, headache, myalgias and diffuse adenopathy, incubation period of 2–14 days *(EID 9:246, 2003)*. In vitro ACV and ganciclovir less active than other nucleosides (penciclovir or 5-ethyldeoxyuridine may be more active; clinical data needed) *(AAC 51:2028, 2007)*.
Varicella-Zoster Virus (VZV)		
Varicella: Vaccination has markedly ↓ incidence of varicella & morbidity *(MMWR 61:609, 2012)*. Guidelines for VZV vaccine *(MMWR 56(RR-4) 2007)*.		
Normal host (chickenpox) Child (2–12 years)	**In general, treatment not recommended.** Might use oral **acyclovir** for healthy persons at ↑ risk for moderate to severe varicella, i.e., >12 yrs of age; chronic cutaneous or pulmonary diseases; chronic salicylate rx (↑ risk of Reye syndrome), **acyclovir** dose: 20 mg/kg po qid x 5 days (start within 24 hrs of rash) or **valacyclovir** 20 mg/kg tid x 5 days.	Acyclovir slowed development and ↓ number of new lesions and ↓ duration of disease in children: 9 to 7.6 days *(PIDJ 21:739, 2002)*. Oral dose of acyclovir in children should not exceed 80 mg per kg per day or 3200 mg per day.
Adolescents, young adults	Start within 24 hrs of rash: **Valacyclovir** 1000 mg po tid x 5-7 days or **Famciclovir** 500 mg po tid (probably effective, but data lacking)	↓ duration of fever, time to healing, and symptoms.
Pneumonia or chickenpox in 3rd trimester of pregnancy	**Acyclovir** 800 mg po 5 times per day or 10 mg per kg IV q8h times 5 days. Risks and benefits to fetus and mother still unknown. Many experts recommend rx, especially in 3rd trimester. Some would add VZIG (varicella-zoster immune globulin).	Varicella pneumonia associated with 41% mortality in pregnancy Acyclovir ↓ incidence and severity *(JID 185:422, 2002)*. If varicella-susceptible mother exposed and respiratory symptoms develop within 10 days after exposure, start acyclovir
Immunocompromised host	**Acyclovir** 10–12 mg per kg (500 mg per M^2) IV (infused over 1 hr) q8h times 7 days	Disseminated 1° varicella infection reported during infliximab rx of rheumatoid arthritis *(J Rheum 31:2517, 2004)*. Continuous infusion of high-dose acyclovir (2 mg per kg per hr) successful in 1 pt with severe hemorrhagic varicella *(NEJM 336:732, 1997)*.
Prevention—Postexposure prophylaxis Varicella deaths still occur in unvaccinated persons *(MMWR 56 (RR-4) 1-40, 2007)*	**CDC Recommendations for Prevention:** Since <5% of cases of varicella but >50% of varicella-related deaths occur in adults >20 yrs of age, the CDC recommends a more aggressive approach in this age group: **1st, varicella-zoster immune globulin** (VZIG) (125 units/10 kg (22 lbs) body weight IM up to a max. of 625 units; minimum dose is 125 units) is recommended for postexposure prophylaxis in susceptible persons at greater risk for complications (immunocompromised such as HIV, malignancies, pregnancy, and steroid therapy) as soon as possible after exposure (<96 hrs). If varicella develops, initiate treatment quickly (<24 hrs of rash) with **acyclovir** as below. Some would rx presumptively with acyclovir in high-risk pts. **2nd,** susceptible adults should be vaccinated. Check antibody in adults with negative or uncertain history of varicella (10–30% will be AB-neg.) and vaccinate those who are Ab-neg. **3rd,** susceptible children should receive vaccination. Recommended routinely before age 12–18 mos. but OK at any age.	

* See page 2 for abbreviations. NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.

TABLE 14A (7)

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Herpes zoster (shingles) *(See NEJM 369:255, 2013)*		
Normal host ▪ Effective therapy most evident in pts >50 yrs. ▪ *(For treatment of post-herpetic neuralgia, see CID 36: 877, 2003; Ln 374:1252, 2009)* ▪ Vaccination↓ herpes zoster & post-herpetic neuralgia *(NEJM 352: 2271, 2005; JAMA 292:157, 2006)*. Reviewed *in J Am Acad Derm 58:361, 2008.* ▪ Analgesics for acute pain associated with Herpes zoster *(NEJM 369:255, 2013)*	**[NOTE: Trials showing benefit of therapy: only in pts treated within 3 days of onset of rash]** **Valacyclovir** 1000 mg po tid times 7 days (adjust dose for renal failure) *(See Table 17A)* **OR** **Famciclovir** 500 mg tid x 7 days. Adjust for renal failure *(see Table 17A)* **OR** **Acyclovir** 800 mg po 5 times per day times 7–10 days Add **Prednisone** in pts over 50 yrs old to decrease discomfort during acute phase of zoster. Does not decrease incidence of post-herpetic neuralgia. Dose: 30 mg po bid days 1–7, 15 mg bid days 8–14 and 7.5 mg bid days 15–21.	Increasing recognition of ↑risk of stroke during 6 mos after episode of Shingles. Oral antivirals during clinical H. zoster infection may have protective effect *(CID 58:1497, 1504, 2014)*. VZV found in wall of cerebral and temporal arteries of pts with giant cell arteritis *(Neurology 84:1948, 2015; JID 51:537, 2015).* Time to healing more rapid. Reduced incidence of post-herpetic neuralgia (PHN) vs placebo in pts >50 yrs of age. Famciclovir similar to acyclovir in reduction of acute pain and incidence of PHN *(J Micro Immunol Inf 37:75, 2004)*. A meta-analysis of 4 placebo-controlled trials (691 pts): acyclovir accelerated by approx. 2-fold pain resolution and reduced incidence of post-herpetic neuralgia at 3 & 6 mos *(CID 22:341, 1996)*; med. time to resolution of pain 41 days vs 101 days in those >50 yrs. In post-herpetic neuralgia, controlled trials demonstrated effectiveness of **gabapentin**, the **lidocaine patch** (5%) & **opioid analgesic** in controlling pain *(Drugs 64:937, 2004; J Clin Virol 29:248, 2004)*. **Nortriptyline** & **amitriptyline** are equally effective but nortriptyline is better tolerated *(CID 36:877, 2003)*. Role of antiviral drugs in rx of PHN unproven *(Neurol 64:21, 2005)* but 8 of 15 pt improved with IV acyclovir 10 mg/kg q 8 hrs x 14 days followed by oral valacyclovir 1 gm 3x a day for 1 month *(Arch Neur 63:940, 2006)*. Review: *NEJM 371:1526, 2014; Expert Opin Pharmacotherapy 15:61, 2014*
Immunocompromised host		
Not severe	**Acyclovir** 800 mg po 5 times per day times 7 days. (**Options**: **Famciclovir** 750 mg po q24h or 500 mg bid or 250 mg 3 times per day times 7 days **OR valacyclovir** 1000 mg po tid times 7 days, though both are not FDA-approved for this indication)	If progression, switch to IV. RA pts on TNF-alpha inhibitors at high risk for VZV. Zoster more severe, but less post-herpetic neuralgia *(JAMA 301:737, 2009).*
Severe: >1 dermatome, trigeminal nerve or disseminated	**Acyclovir** 10–12 mg per kg IV (infusion over 1 hr) q8h times 7–10 days. In older pts, ↓ to 7.5 mg per kg. If nephrotoxicity and pt improving, ↓ to 5 mg per kg q8h.	A common manifestation of immune reconstitution following HAART in HIV-infected children *(J All Clin Immun 113:742, 2004)*. Rx must be begun within 72 hrs. For Acyclovir-resistant VZV in HIV+ pts previously treated with acyclovir: **Foscarnet** (40 mg per kg IV q8h for 14–26 days).
Human T-cell Leukotrophic Virus-1 (HTLV-1) Causes illness in only 5% of infected persons. Two are associated with HTLV-1: Adult T-cell leukemia/lymphoma *(NEJM 367:552, 2012)* and HTLV-1-associated myelopathy (HAM), also known as tropical spastic paraparesis (TSP).	No proven therapy. Some nucleoside antiretroviral therapies used with limited success	Laboratory diagnosis is by blood and CSF. Anti-HTLV-1 antibodies are detected by ELISA antibody testing; Western Blot is used for confirmation (Focus Diagnostics or Quest Diagnostics). HTLV DNA can be detected by PCR in circulating CD4 cells. One tube multiplex qPCR highly specific / sensitive *(Retrovirology 11(Suppl): P105, 2014).*

* *See page 2 for abbreviations.* NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.

Influenza A & B and novel influenza viruses Refs: *http://www.cdc.gov/flu/professionals/antivirals/index.htm http://www.cdc.gov/flu/weekly/; NEJM 370:789, 2014.*
Vaccine Info *(http://www.cdc.gov/flu/professionals/acip/index.htm); Med Lett 56:97, 2014; MMWR 63:691, 2014*

- **Oseltamivir and zanamivir are recommended drugs.** Amantadine and rimantidine should not be used because of widespread resistance.
- Novel H1N1 (referred to as pandemic H1N1, pH1N1, H1N1pdm and formerly swine flu) emerged in 2009 and now is the dominant H1N1 strain worldwide. Old distinction from seasonal H1N1 is still sometimes used but not relevant
- Rapid influenza tests are can be falsely negative in 20-50%. PCR is gold standard test.
- Initiate therapy as close to the onset of symptoms as possible, and certainly within 48 hrs of onset of symptoms. Starting therapy after 48 hours of onset of symptoms is associated with reduced therapeutic benefit. However, starting therapy up to 5 days after onset in patients who are hospitalized is associated with improved survival *(Clin Infect Dis 55:1198, 2012)*.
- Empiric therapy should be started for all patients who are hospitalized, have severe or progressive influenza or are at higher risk of complications due to age or underlying medical conditions.
- Look for concomitant bacterial pneumonia.
- Other important influenza viruses causing human disease
  - **H3N2v influenza**: 159 cases of influenza A/H3N2v reported over the summer of 2012. Most of the cases of influenza A/H3N2v occurred in children under the age of 10 with direct contact with pigs. This variant is susceptible to the neuraminidase inhibitors, oseltamivir and zanamivir. *See MMWR 61:619, 2012*
  - **Avian influenza H5N1**: Re-emerged in Asia in 2003 and human cases detected in 15 countries mostly in Asia as well as Egypt, Nigeria and Djibouti. Circulation associated with massive poultry die off. Imported cases rare – one in Canada. As of January 2014, 648 confirmed cases and 384 deaths (59%). Human infection associated with close contact with poultry; very limited human to human transmission. Mortality associated with high viral load, disseminated virus and high cytokine activity *(Nature Medicine 12:1203-1207 2006)*. Sensitive to oseltamivir but oseltamivir resistance has emerged on therapy *(NEJM 353:267-272 2005)*. Use oseltamivir and consider IV zanamivir
  - **Avian influenza H7N9**: Emerged in Eastern China in March 2013 and 132 cases documented during Spring 2013 with 44 deaths (33%). Cases appeared again in early winter 2013-2014 and continue to increase. Infection associated with close contact with live bird markets; extremely limited human to human transmission to date. Mortality highest among older persons and those with medical conditions. Oseltamivir active against most but not all strains. No zanamivir resistance documented to date.

Virus/Disease	Susceptible to (Recommended Drug/Dosage):	Resistant to:	Alternatives/Side Effects/Comments
• **A/H1N1 (current seasonal resembles pandemic H1N1)** • Influenza B • Influenza A (A/H3N2, A/H3N2v*, A/H5N1, A/H7N9**)	**Oseltamivir** Adult: Oseltamivir 75 mg po bid x 5 days Pediatric (child age 1-12 years): Infant 2 wks-11 months: 3 mg/kg bid x 5 days ≤15 kg: 30 mg bid x 5 days >15 kg to 23 kg: 45 mg bid x 5 days >23 kg to 40 kg: 60 mg bid x 5 days >40 kg: 75 mg bid x 5 days or **Zanamivir** 2 inhalations (5 mg each) bid x 5 days or Peramivir 600 mg IV once daily x 5-10 days For IV Zanamivir, *see Comment*	Amantadine and rimantidine (100%) * A/H3N2v strain are susceptible ** A/H7N9 resistant to oseltamivir (rarely)	• **A/H1N1**: Higher dose (150 mg bid) **not** more effective for H1N1 • **Zanamivir** not recommended for children < 7 years or those with reactive airway disease • **IV zanamivir** is available under compassionate use IND and clinical trials for hospitalized influenza patients with suspected or known gastric stasis, gastric malabsorption, gastrointestinal bleeding, or for patients suspected or confirmed with oseltamivir-resistant influenza virus infection. For compassionate use, contact GlaxoSmithKline at (+1) 919-315-5215 or email: gskclinicalsupportHD@GSK.com. • **Influenza B:** One study suggested virologic benefit to higher dose oseltamivir for critically ill patients with influenza B. • **A/H5N1**: Given high mortality, consider obtaining investigational drug. Zanamivir retains activity against most oseltamivir resistant H5N1 • Association between corticosteroid rx & increased mortality *(JID 212:183, 2015)*. For now, avoid steroids unless indicated for another reason.

TABLE 14A (9)

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Measles Increasing reports of measles in unvaccinated children and adults *(MMWR 63:781, 2014; NEJM 371:358, 2014).*		
Children	No therapy or **vitamin A** 200,000 units po daily times 2 days	Vitamin A may ↓ severity of measles.
Adults	No rx or **ribavirin** IV: 20–35 mg per kg per day times 7 days	↓ severity of illness in adults *(CID 20:454, 1994).*
Metapneumovirus (HMPV) A paramyxovirus isolated from pts of all ages, with mild bronchiolitis/bronchospasm to pneumonia. Review: *Sem Resp Crit Care Med 32:447, 2011.*	**No proven antiviral therapy** (intravenous ribavirin used anecdotally with variable results) Investigational Agents Reviewed *(Clin Vaccine Immunol 22:8 & 858, 2015)*	Human metapneumovirus isolated from 6-21% of children with RTIs *(NEJM 350:443, 2004).* Dual infection with RSV assoc. with severe bronchiolitis *(JID 191:382, 2005).*
Monkey pox (orthopox virus) *(see LnID 4:17, 2004)* Outbreak from contact with ill prairie dogs. Source likely imported Gambian giant rats *(CID 58:260, 2014)*	**No proven antiviral therapy.** Cidofovir is active in vitro & in mouse model	Incubation period of 12 days, then fever, headache, cough, adenopathy, & a vesicular papular rash that pustulates, umbilicates, & crusts on the head, trunk, & extremities. Transmission in healthcare setting rare.
Norovirus (Norwalk-like virus, or NLV) Vast majority of outbreaks of non-bacterial gastroenteritis *(NEJM 368:1121, 2013).*	**No antiviral therapy.** Replete volume. Transmission by contaminated food, fecal-oral contact with contaminated surfaces, or fomites.	Sudden onset of nausea, vomiting, and/or watery diarrhea lasting 12–60 hours. Ethanol-based hand rubs effective *(J Hosp Inf 60:144, 2005).*
Papillomaviruses: Warts **External Genital Warts** Also look for warts in anal canal *(MMWR 64(3):1, 2015)*	**Patient applied:** **Podofilox** (0.5% solution or gel): apply 2x/day x 3 days, 4th day no therapy, repeat cycle 4x; OR **imiquimod** 5% cream: apply once daily hs 3x/wk for up to 16 wks. **Sinecatechins**: Apply to external genital warts only 3x/day until effect or adverse effect **Provider administered:** Cryotherapy with liquid nitrogen; repeat q1-2 wks; OR **Trichloroacetic acid** (TCA): repeat weekly as needed; OR surgical removal.	**Podofilox:** Inexpensive and safe (pregnancy safety not established). Mild irritation after treatment. **Imiquimod:** Mild to moderate redness & irritation. Topical imiquimod effective for treatment of vulvar intraepithelial neoplasms *(NEJM 358:1465, 2008).* Safety in pregnancy not established. **Sinecatechins**: Local irritation, redness, pain, and itching **Cryotherapy:** Blistering and skin necrosis common. **Podophyllin resin:** No longer recommended as other less toxic regimens available. **TCA:** Caustic. Can cause severe pain on adjacent normal skin. Neutralize with soap or sodium bicarbonate.
Warts on cervix	Need evaluation for evolving neoplasia	Gynecological consult advised.
Vaginal warts	Cryotherapy with liquid nitrogen or **TCA**	
Urethral warts	Cryotherapy with liquid nitrogen	
Anal warts	Cryotherapy with liquid nitrogen or **TCA** or surgical removal	Advise anoscopy to look for rectal warts.
Skin papillomas	**Topical α-lactalbumin. Oleic acid** (from human milk) applied 1x/day for 3 wks	↓ lesion size & recurrence vs placebo ($p < 0.001$) *(NEJM 350:2663, 2004).* Further studies warranted.

* *See page 2 for abbreviations.* NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.

TABLE 14A (10)

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Parvo B19 Virus (Erythrovirus B19). *Review: NEJM 350:586, 2004. Wide range of manifestation.* **Treatment options for common symptomatic infections:**		
Erythema infectiosum	Symptomatic treatment only	Diagnostic tools: IgM and Igb antibody titers. Perhaps better: blood parvovirus PCR. Dose of IVIG not standardized; suggest 400 mg/kg IV of commercial IVIG for 5 or 10 days or 1000 mg/kg IV for 3 days. Most dramatic anemias in pts with pre-existing hemolytic anemia. Bone marrow shows erythrocyte maturation arrest with giant pronormoblasts. *(Rev Med Virol 25:224, 2015)*
Arthritis/arthralgia	Nonsteroidal anti-inflammatory drugs (NSAID)	
Transient aplastic crisis	Transfusions and oxygen	
Fetal hydrops	Intrauterine blood transfusion	
Chronic infection with anemia	**IVIG** and transfusion *(CID 56:968, 2013)* For dose, see *Comment*	
Chronic infection without anemia	Perhaps **IVIG**	
Papovavirus/Polyomavirus		
Progressive multifocal leukoencephalopathy (PML) Serious demyelinating disease due to JC virus in immunocompromised pts.	No specific therapy for JC virus. Two general approaches: 1. In HIV pts: HAART. Cidofovir may be effective 2. Stop or decrease immunosuppressive therapy	Failure of treatment with interferon alfa-2b, cytarabine and topotecan. Immunosuppressive **natalizumab** temporarily removed from market due to reported association with PML. Mixed reports on **cidofovir.** Most likely effective in ART-experienced pts.
BK virus induced nephropathy in immunocompromised pts and hemorrhagic cystitis	Decrease immunosuppression if possible. Suggested antiviral therapy based on anecdotal data. If progressive renal dysfunction: 1. **Fluoroquinolone** first; 2. **IVIG** 500 mg/kg IV; 3. **Leflunomide** 100 mg po daily x 3 days, then 10-20 mg po daily; 4. **Cidofovir** only if refractory to all of the above *(see Table 14B for dose).*	Use PCR to monitor viral "load" in urine and/or plasma. Report of cidofovir as potentially effective for BK hemorrhagic cystitis *(CID 49:233, 2009).*
Rabies *(see Table 20B, page 233; diagnosis and management: www.cdc.gov/rabies)*		
Rabid dogs account for 50,000 cases per yr worldwide. Most cases in the U.S. are cryptic, 70% assoc. with 2 rare bat species *(EID 9:151, 2003).* An organ donor with early rabies infected 4 recipients (2 kidneys, liver & artery) all died avg. 13 days after transplant *(NEJM 352:1103, 2005).*	**Mortality 100% with only survivors those who receive rabies vaccine before the onset of illness/symptoms** *(CID 36:61, 2003).* A 15-year-old female who developed rabies 1 month post-bat bite survived after drug induction of coma (+ other rx) for 7 days; did not receive immunoprophylaxis *(NEJM 352:2508, 2005).*	Corticosteroids ↑ mortality rate and ↓ incubation time in mice. Therapies that have failed after symptoms develop include rabies vaccine, rabies immunoglobulin, rabies virus neutralizing antibody, ribavirin, alfa interferon, & ketamine. For post-exposure prophylaxis, see *Table 20B, page 233.*
Respiratory Syncytial Virus (RSV) Major cause of morbidity in neonates/infants. Diagnosis: airway swab for RSV PCR	*All ages:* Hydration, O2 as needed. If wheezing, trial of beta-agonist. *Corticosteroids:* children-no; adults-maybe *Nebulized Ribavirin:* for severe RSV in children, adults *(CID 57:1731, 2013).* *Nebulized Ribavirin + RSV immune globulin:* immunocompromised adults (HSCT) *(CID 56:258, 2013).*	In adults, RSV accounted for 10.6% of hospitalizations for pneumonia, 11.4% of AECB, 7.2% for asthma & 5.4% for CHF in pts >65 yrs of age *(NEJM 352:1749, 2005).* RSV caused 11% of clinically important respiratory illnesses in military recruits *(CID 41:311, 2005).*
Prevention of RSV in: (1) Children <24 mos. old with chronic lung disease of prematurity (formerly bronchopulmonary dysplasia) requiring supplemental O_2 or (2) Premature infants (<32 wks gestation) and <6 mos. old at start of RSV season or (3) Children with selected congenital heart diseases	**Palivizumab** (Synagis) 15 mg per kg IM q month Nov-Apr. *See Pediatrics 126:e16, 2010.*	Expense argues against its use, Guidance from the Academy of Pediatrics recommends use of Palivizumab only in newborn infants born at 29 weeks gestation (or earlier) and in special populations (e.g., those infants with significant heart disease). *(Pediatrics 2014;134:415–420)*

TABLE 14A (11)

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Respiratory Syncytial Virus (RSV) *(continued)*		
Rhinovirus (Colds) *See Ln 361:51, 2003* Found in 1/2 of children with community-acquired pneumonia; role in pathogenesis unclear *(CID 39:681, 2004).* High rate of rhinovirus identified in children with significant lower resp tract infections *(Ped Inf Dis 28:337, 2009)*	No antiviral rx indicated *(Ped Ann 34:53, 2005).* Symptomatic rx: • **Ipratropium bromide** nasal (2 sprays per nostril tid) • **Clemastine** 1.34 mg 1–2 tab po bid–tid (OTC). • Oral zinc preparations reduce duration of symptoms by ~ 1 day; does not reduce severity of symptoms *(JAMA 311:1440, 2014)* Avoid intranasal zinc products *(see Comment).*	Sx relief: ipratropium nasal spray ↓ rhinorrhea and sneezing vs placebo *(AnIM 125:89, 1996).* Clemastine (an antihistamine) ↓ sneezing, rhinorrhea but associated with dry nose, mouth & throat in 6–19% *(CID 22:656, 1996).* **Echinacea** didn't work *(CID 38:1367, 2004 & 40:807, 2005)* —put it to rest! Public health advisory advising that three over-the-counter cold remedy products containing **zinc** (e.g., Zicam) should not be used because of multiple reports of permanent anosmia *(www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm166996.htm).*
Rotavirus: Leading recognized cause of diarrhea-related illness among infants and children world-wide and kills ½ million children annually.	**No antiviral rx available;** oral hydration life-saving.	**Two live-attenuated vaccines highly effective (85 and 98%)** and safe in preventing rotavirus diarrhea and hospitalization *(NEJM 354; 1 & 23, 2006).* ACIP recommends either of the two vaccines, RV1 or RV5, for infants *(MMWR 58(RR02): 1, 2009).*
Smallpox *(NEJM 346:1300, 2002)*	Smallpox vaccine (if within 4 days of exposure) + cidofovir (dosage uncertain but likely similar to CMV (5 mg/kg IV once weekly for 2 weeks followed by once weekly dosing. Must be used with hydration and Probenecid; *contact CDC: 770-488-7100)*	
Contact vaccinia *(JAMA 288:1901, 2002)*	From vaccination: Progressive vaccinia—vaccinia immune globulin may be of benefit. To obtain immune globulin, contact CDC: 770-488-7100. *(CID 39:759, 776 & 819, 2004)*	
West Nile virus: *See page 167*		
Zika Virus: Mosquito (Aedes sp.) transmitted flavivirus CDC Interim Guidance: *MMWR 65:30, January 22, 2016.* Travel advisory for pregnant women.	No treatment available. Symptomatic support (avoid aspirin, NSAIDs until Dengue ruled out Most serious manifestation of infection is **congenital birth defect**(s): microcephaly and fetal demise	3-7 day incubation. Asymptomatic infection most often; when symptoms occur, usually consists of low grade fever, arthralgias, morbiliform rash, and / or conjunctival redness (non-purulent conjunctivitis). Duration of symptoms ranges from a few days to one week. Rare Guillain-Barré syndrome. Hospitalization very infrequent, fatalities are very rare.

TABLE 14B – ANTIVIRAL DRUGS (NON-HIV)

DRUG NAME(S) GENERIC (TRADE)	DOSAGE/ROUTE IN ADULTS*	COMMENTS/ADVERSE EFFECTS
CMV *(See SANFORD GUIDE TO HIV/AIDS THERAPY)*		
Cidofovir (Vistide)	5 mg per kg IV once weekly for 2 weeks, then once every other week. **Properly timed IV prehydration with normal saline & Probenecid must be used with each cidofovir infusion:** 2 gm po 3 hrs before each dose and further 1 gm doses 2 & 8 hrs after completion of the cidofovir infusion. Renal function (serum creatinine and urine protein) must be monitored prior to each dose *(see pkg insert for details)*. Contraindicated if creatinine >1.5 mg/dL, CrCl ≤55 mL/min or urine protein ≥100 mg/dL.	**Adverse effects: Nephrotoxicity;** dose-dependent proximal tubular injury (Fanconi-like syndrome): proteinuria, glycosuria, bicarbonaturia, phosphaturia, polyuria (nephrogenic diabetic insipidus, ↑ creatinine. Concomitant saline prehydration, probenecid, extended dosing intervals allow use but still highly nephrotoxic. Other major toxicities: neutropenia (give G-CSF as needed); eye: monthly intra-ocular pressure. Dc cidofovir if pressure decreases; 50% of uveitis occurs. **Black Box warning.** Renal impairment can occur after ≤2 doses. Contraindicated in pts receiving concomitant nephrotoxic agents. Monitor for ↓ WBC. In animals, carcinogenic, teratogenic, causes ↓ sperm and ↓ fertility. FDA indication only CMV retinitis in HIV pts. **Comment**: Dose must be reduced or discontinued if changes in renal function occur during rx. For ↑ of 0.3–0.4 mg per dL in serum creatinine, cidofovir dose must be ↓ from 5 to 3 mg per kg; discontinue cidofovir if ↑ of 0.5 mg per dL above baseline or 3 + proteinuria develops (for 2 + proteinuria, observe pts carefully and consider discontinuation).
Foscarnet (Foscavir)	Induction: 90 mg per kg IV, over 1.5-2 hours, q12h **OR** 60 mg per kg, over 1 hour, q8h Maintenance: 90 –120 mg per kg IV, over 2 hours, q24h Dosage adjustment with renal dysfunction *(see Table 17A)*.	Use infusion pump to control rate of administration. **Adverse effects**: **Major toxicity is renal impairment (1/3 of patients).** Can cause infusion-related ionized hypocalcemia: manifests as arrhythmia, tetany, paresthesia, changes in mental status. Slow infusion rate and avoid drugs that lower Ca++, e.g., pentamidine. –↑ creatinine, proteinuria, nephrogenic diabetes insipidus, ↓K+, ↓Ca++, ↓ Mg++. Adequate hydration may ↓ toxicity. Other: headache, mild (100%); fatigue (100%), nausea (80%), fever (25%). CNS: seizures. Hematol: ↓ WBC, ↓ Hgb. Hepatic: liver function tests ↑. Neuropathy. Penile and oral ulcers.
Ganciclovir (Cytovene)	IV: 5 mg per kg q12h times 14 days (induction) 5 mg per kg IV q24h or 6 mg per kg 5 times per wk (maintenance) Dosage adjust. with renal dysfunction *(see Table 17A)*	**Adverse effects**: **Black Box warnings:** cytopenias, carcinogenicity/teratogenicity & aspermia in animals. Absolute neutrophil count dropped below 500 per mm^3 in 15%, thrombocytopenia 21%, anemia 6%. Fever 48%. GI 50%: nausea, vomiting, diarrhea, abdominal pain 19%, rash 10%. Confusion, headache, psychiatric disturbances and seizures. Neutropenia may respond to granulocyte colony stimulating factor (G-CSF or GM-CSF). Severe myelosuppression may be ↑ with coadministration of zidovudine or azathioprine. 32% dc/interrupted rx, principally for neutropenia. Avoid extravasation.
Valganciclovir (Valcyte)	450 mg tablets; take with food. Oral solution: 50 mg/mL. Adult does 900 mg. Treatment (induction): 900 mg po q12h with food; Prophylaxis (maintenance): 900 mg po q24h. Dosage adjustment for renal dysfunction *(See Table 17A)*.	A prodrug of ganciclovir with better bioavailability than oral ganciclovir: 60% with food. Preg cat: C (may be teratogenic, contraceptive precaution for females). **Adverse effects:** Similar to ganciclovir. May cause dose limiting neutropenia, anemia, thrombocytopenia. Acute renal failure may occur. Diarrhea (16-41%), nausea (8-30%), vomiting (3-21%). **CMV retinitis** (sight-threatening lesions): 900 mg po q12h + intravitreal Ganciclovir: 900 mg po q12h x 14-21 days, then 900 mg po q24h for maintenance
Herpesvirus		
Acyclovir (Zovirax or generic)	Doses: *see Table 14A for various indications* 400 mg or 800 mg tab 200 mg cap Suspension 200 mg per 5 mL Ointment or cream 5% IV injection Dosage adjustment for renal dysfunction *(See Table 17A)*.	**po:** Generally well-tolerated with occ. diarrhea, vertigo, arthralgia. Less frequent rash, fatigue, insomnia, fever, menstrual abnormalities, acne, sore throat, muscle cramps, lymphadenopathy. **IV**: Phlebitis, caustic with vesicular lesions with IV infiltration. **IV or po**: Renal (5%): ↑ creatinine, hematuria. With high doses may crystallize in renal tubules → obstructive uropathy (rapid infusion, dehydration, renal insufficiency and ↑ dose ↑ risk). Adequate pre-hydration may prevent such nephrotoxicity. Hepatic: ↑ ALT, AST. Uncommon: neutropenia, rash, diaphoresis, hypotension, headache, nausea. **Neurotoxicity**: halfucination, death delusions, invofuntary movements. To avoid, fower dose if renal impairment *(AJM 128:692, 2015)*.

* See page 2 for abbreviations. *NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.*

TABLE 14B (2)

DRUG NAME(S) GENERIC (TRADE)	DOSAGE/ROUTE IN ADULTS*	COMMENTS/ADVERSE EFFECTS
Herpesvirus *(continued)*		
Famciclovir (Famvir)	125 mg, 250 mg, 500 mg tabs Dosage depends on indication; *(see label and Table 14A).*	Metabolized to penciclovir. **Adverse effects:** similar to acyclovir, included headache, nausea, diarrhea, and dizziness but incidence does not differ from placebo. May be taken without regard to meals. Dose should be reduced if CrCl <60 mL per min *(see package insert & Table 14A, page 169 & Table 17A, page 225).* May be taken with or without food.
Penciclovir (Denavir)	Topical 1% cream	Apply to area of recurrence of herpes labialis with start of sx, then q2h while awake times 4 days. Well tolerated.
Trifluridine (Viroptic)	Topical 1% solution: 1 drop q2h (max. 9 drops/day) until corneal re-epithelialization, then dose is ↓ for 7 more days (one drop q4h for at least 5 drops/day), not to exceed 21 days total rx.	Mild burning (5%), palpebral edema (3%), punctate keratopathy, stromal edema. For HSV keratoconjunctivitis or recurrent epithelial keratitis.
Valacyclovir (Valtrex)	500 mg, 1 gm tabs Dosage depends on indication and renal function *(see label, Table 14A & Table 17A)*	An ester pro-drug of acyclovir that is well-absorbed, bioavailability 3–5 times greater than acyclovir. **Adverse effects** similar to acyclovir. Thrombotic thrombocytopenic purpura/hemolytic uremic syndrome reported in pts with advanced HIV disease and transplant recipients participating in clinical trials at doses of 8 gm per day. Death delusion with high serum levels.
Valganciclovir (Valcyte)	450 mg tablets; take with food. Oral solution: 50 mg/mL. Adult does 900 mg. Treatment (induction): 900 mg po q12h with food; Prophylaxis (maintenance): 900 mg po q24h. Dosage adjustment for renal dystunction *(See Table 17A).*	A prodrug of ganciclovir with better bioavailability than oral ganciclovir. 60% with food. Preg cat: C (may be teratogenic, contraceptive precaution for females). **Adverse effects:** Similar to ganciclovir. May cause dose limiting neutropenia, anemia, thrombocytopenia. Acute renal failure may occur. Diarrhea (16-41%), nausea (8-30%), vomiting (3-21%). **CMV retinitis** (sight-threatening lesions): 900 mg po q12h + intravitreal Ganciclovir; 900 mg po q12h x 14-21 days, then 900 mg po q24h for maintenance
Hepatitis B		
Adefovir dipivoxil (Hepsera)	10 mg po q24h (with normal CrCl) 10 mg tab	It is an acyclic nucleotide anafog with activity against hepatitis B (HBV) at 0.2–2.5 mM (IC_{50}). *See Table 9* for Cmax & T½. Active against lamivudine-resistant HBV strains and in vitro vs. entecavir- resistant strains. To minimize resistance, use in combination with lamivudine for lamivudine-resistant virus; consider alternative therapy if viral load remains > 1,000 copies/mL with treatment. Primarily renal excretion—adjust dose. No food interactions. Generally few side effects, but **Black Box warning** regarding lactic acidosis/hepatic steatosis with nucleoside analogs. At 10 mg per day potential for delayed nephrotoxicity. Monitor renal function, esp. with pts with pre-existing or other risks for renal impairment. Pregnancy Category C. **Hepatitis may exacerbate when treatment discontinued;** Up to 25% of pts developed ALT ↑ 10 times normal within 12 wks; usually responds to re-treatment or self-limited, but hepatic decompensation has occurred. **Do not use adefovir in HIV infected patients**
Entecavir (Baraclude)	0.5 mg q24h. If refractory or resistant to lamivudine or telbivudine: 1 mg per day Tabs: 0.5 mg & 1 mg. Oral solution: 0.05 mg/mL. Administer on an empty stomach.	A nucleoside analog active against HBV including lamivudine-resistant mutants. Minimal adverse effects reported: headache, fatigue, dizziness, & nausea reported in 22% of pts. Alopecia, anaphylactoid reactions reported. Potential for lactic acidosis and exacerbation of hepB at discontinuation (**Black Box warning**). Do not use as single anti-retroviral agent in HIV co-infected pts; M134 mutation can emerge *(NEJM 356:2614, 2007).* Adjust dosage in renal impairment *(see Table 17A, page 224).*
Lamivudine (3TC) (Epivir-HBV)	**HBV** dose: 100 mg po q24h Dosage adjustment with renal dysfunction *(see label).* Tabs 100 mg and oral solution 5 mg/mL.	**Black Box warnings:** caution, dose is lower than HIV dose, so must exclude co-infection with HIV before using this formulation; lactic acidosis/hepatic steatosis; severe exacerbation of liver disease can occur on dc. YMDD-mutants resistant to lamivudine may emerge on treatment. **Adverse effects:** *See Table 14C.*
Telbivudine (Tyzeka)	**HBV:** 600 mg orally q24h, without regard to food. Dosage adjustment with renal dysfunction, Ccr < 50 mL/min *(see label).* 600 mg tabs, 100 mg per 5 mL solution.	An oral nucleoside analog approved for Rx of Hep B. It has ↑ rates of response and superior viral suppression than lamivudine *(NEJM 357:2576, 2007).* **Black Box warnings** regarding lactic acidosis/hepatic steatosis with nucleosides and potential for severe exacerbation of HepB on dc. Generally well-tolerated with ↓ mitochondrial toxicity vs other nucleosides and no dose limiting toxicity observed *(Medical Letter 49:11, 2007).* Myalgias, myopathy and rhabdomyolysis reported. Peripheral neuropathy. Genotypic resistance rate was 4.4% by one yr, ↑ to 21.5% by 2 yrs of rx of eAg+ pts. Selects for YMDD mutation like lamivudine. Combination with lamivudine was inferior to monotherapy *(Hepatology 45:507, 2007).*
Tenofovir (TDF/TAF)	*See page 193*	

* *See page 2 for abbreviations. NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.*

TABLE 14B (3)

DRUG NAME(S) GENERIC (TRADE)	DOSAGE/ROUTE IN ADULTS*	COMMENTS/ADVERSE EFFECTS
Hepatitis C		
Daclatasvir (Daklinza)	60 mg 1 tab po once daily (dose adjustment when used with CYP 3A4 inhibitors / inducers)	Contraindicated with strong CYP3A inducers, e.g., phenytoin, carbamazepine, Rifampin, St. John's wort. Most common AE: headache and fatigue. Bradycardia when administered in combination with Sofosbuvir and Amiodarone. **Co-administration with Amiodarone not recommended** If used, cardiac monitoring advised.
Interferon alfa is avalfable as alfa-2a (Roferon-A), **alfa-2b** (Intron-A)	For HCV combination therapy, usual Roferon-A and Intron-A doses are 3 million international units 3x weekly subQ.	Depending on agent, available in pre-filled syringes, vials of solution, or powder. **Black Box warnings:** can cause/aggravate psychiatric illness, autoimmune disorders, ischemic events, infection. Withdraw therapy if any of these suspected. **Adverse effects: Flu-like syndrome** (common, resolving 1st wk of rx: fever 98%, fatigue 89%, myalgia 73%, headache 71%. **GI:** anorexia 46%, diarrhea 29%. CNS: dizziness 21%. Hemorrhagic or ischemic stroke. Rash 18%, may progress to Stevens Johnson or exfoliative dermatitis. Alopecia (~ 15%), autoimmune thyroid disorders with ↓- or ↑- thyroidism. **Hematol:** ↓ WBC 49%, ↓ Hgb 27%, ↓ platelets 35%. Post-marketing reports of antibody-mediated pure red cell aplasia in patients receiving interferon/ribavirin with erythropoiesis-stimulating agents.
PEG interferon alfa-2b (PEG-Intron)	0.5–1.5 mcg/kg subQ q wk	
Pegylated-40k interferon alfa-2a (Pegasys)	180 mcg subQ q wk	Acute reversible hearing loss &/or tinnitus in up to 1/3 *(Ann Int Med 121:334, 1994)*. Optic neuropathy (retinal hemorrhage, cotton wool spots, ↓ in color vision) reported *(AIDS 18:1805, 2004)*. Doses may require adjustment (or dc) based on individual response or adverse events, and can vary by product, indication (eg, HCV or HBV) and mode of use (mono- or combination-rx). (Refer to labels of individual products and to ribavirin if used in combination for details of use.)
Ledipasvir + Sofosbuvir (Harvoni)	Combination formulation (Ledipasvir 90 mg + Sotosbuvir 400 mg) 1 tab po once daily	NS5A/NS5B inhibitor combination for Genotype 1 HCV. First agent for HCV treatment without Ribavirin or Interferon. No adjustment for mile/moderate renal or hepatic impairment. Most common AEs: fatigue (16%), headache (14%), nausea (7%), diarrhea (3%), insomnia (5%). Antacids and H2 blockers interfere with absorption of ledipasvir. The drug solubility decreases as pH increases. Recommended to separate administration of ledipasvir and antacid Rx by at least 4 hours.
Ribavirin (Rebetol, Copegus)	For use with an interferon for hepatitis C. Available as 200 mg caps and 40 mg/mL oral solution (Rebetol) or 200 mg and 400 mg tabs (Copegus) *(See Comments regarding dosage).*	**Black Box warnings**: ribavirin monotherapy of HCV is ineffective; hemolytic anemia may precipitate cardiac events; teratogenic/ embryocidal (**Preg Category X**). Drug may persist for 6 mos, avoid pregnancy for at least 6 mos after end of rx of women *or their partners.* Only approved for pts with Ccr > 50 mL/min. Do not use in pts with severe heart disease or hemoglobinopathies. ARDS reported *(Chest 124:406, 2003).* **Adverse effects:** hemolytic anemia (may require dose reduction or dc), dental/periodontal disorders, and all adverse effects of concomitant interferon used (see above). Postmarketing: retinal detachment, ↓ hearing, hypersensitivity reactions. See *Table 14A* for specific regimens, but dosing depends on: interferon used, weight, HCV genotype, and is modified (or dc) based on side effects (especially degree of hemolysis, with different criteria in those with/without cardiac disease). **Initial Rebetrol dose with Intron A (interferon alfa-2b) is wt-based:** 400 mg am & 600 mg pm for ≤ 75 kg, and 600 mg am & 600 mg pm for wt > 75 kg, but with Pegintron approved dose is 400 mg am & 400 mg pm with meals. Doses and duration of Copegus with peg-interferon alfa-2a are less in pts with genotype 2 or 3 (800 mg per day divided into 2 doses, for 24 wks) than with genotypes 1 or 4 (1000 mg per day divided into 2 doses for wt < 75 kg and 1200 mg per day divided into 2 doses for ≥ 75 kg for 48 wks); in HIV/HCV co-infected pts, dose is 800 mg per day regardless of genotype. *(See individual labels for details, including initial dosing and criteria for dose modification in those with/without cardiac disease.)*
Paritaprevir/ritonavir + Ombitasvir + Dasabuvir (PrQD)(Viekira Pak); **Paritaprevir/ritonavir + Ombitasvir**(Technivie)	Ombitasvir 12.5 mg, Paritaprevir 75 mg, and Ritonavir 50 mg co-packaged with tablets of Dasabuvir 250 mg (Viekira Pak); or without Dasabuvir (Technivie)	Do not co-administer with drugs that are highly dependent on CYP3A for clearance; strong inducers of CYP3A and CYP2C8; and strong inhibitors of CYP2C8. Do not use if known hypersensitivity to Ritonavir (e.g., toxic epidermal necrolysis, Stevens-Johnson syndrome). If used with Ribavirin: fatigue, nausea, pruritus, other skin reactions, insomnia and asthenia. When used without Ribavirin: nausea, pruritus and insomnia. **Warning: Hepatic decompensation and hepatic failure, including liver transplantation or fatal outcomes, have been reported mostly in patients with advanced cirrhosis.**
Simeprevir (Olysio)	150 mg 1 cap po once daily with food + both Ribavirin and Interferon	NS3/4A inhibitor. Need to screen patients with HCV genotype 1a for the Q80K polymorphism; if present consider alternative therapy. Contraindicated in pregnancy and in men whose female partners are pregnant (risk category C); concern is combination with ribavirin (risk category X). No dose adjustment required in patients with mild, moderate or severe renal impairment; no dose adjustment for mild hepatic impairment. Most common AEs (in combination with Ribavirin, Interferon): rash, pruritus, nausea. CYP3A inhibitors affect plasma concentration of Simeprevir.

* See *page 2 for abbreviations. NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.*

TABLE 14B (4)

DRUG NAME(S) GENERIC (TRADE)	DOSAGE/ROUTE IN ADULTS*	COMMENTS/ADVERSE EFFECTS
Hepatitis C *(continued)*		
Sofosbuvir (Solvadi)	400 mg 1 tab po once daily with food + both Pegylated Interferon and Ribavirin. For combination formulation, see Ledipasvir.	NS5B inhibitor for Genotypes 1, 2, 3, 4 HCV. Efficacy established in patients awaiting liver transplant and in patients with HIV-1/HCV co-infection. No adjustment needed for mild to moderate renal impairment. No dose adjustment for mild, moderate, or severe hepatic impairment. Most common AEs (in combination with interferon and ribavirin): fatigue, headache, nausea, insomnia, anemia. Rifampin and St. John's wort may alter concentrations of Sofosbuvir.
Influenza A		
Amantadine (Symmetrel) **or Rimantadine** (Flumadine) Influenza B intrinsically resistant.	**Amantadine** 100 mg caps, tabs; 50 mg/mL oral solution & syrup. Treatment or prophylaxis: 100 mg bid; or 100 mg daily if age ≥65 y; dose reductions with CrCl starting at ≤50 mL/min. **Rimantadine** 100 mg tabs, 50 mg/5 mL syrup. Treatment or prophylaxis: 100 mg bid, or 100 mg daily in elderly nursing home pts, or severe hepatic disease, or CrCl ≤10 mL/min. For children, rimantadine only approved for prophylaxis.	**Side-effects/toxicity: CNS** (can be mild: nervousness, anxiety, difficulty concentrating, and lightheadedness). Serious: delirium, hallucinations, and seizures—are associated with high plasma drug levels resulting from renal insufficiency, esp. in older pts, those with prior seizure disorders, or psychiatric disorders.
Influenza A and B—For both drugs, initiate within 48 hrs of symptom onset		
Zanamivir (Relenza) For pts ≥ 7 yrs of age (treatment) or ≥ 5 yrs (prophylaxis)	Powder is inhaled by specially designed inhalation device. Each blister contains 5 mg zanamivir. **Treatment:** oral inhalation of 2 blisters (10 mg) bid for 5 days. **Prophylaxis:** oral inhalation of 2 blisters (10 mg) once daily for 10 days (household outbreak) to 28 days (community outbreak).	Active by inhalation against neuraminidase of both influenza A and B and inhibits release of virus from epithelial cells of respiratory tract. Approx. 4–17% of inhaled dose absorbed into plasma. Excreted by kidney but with low absorption, dose reduction not necessary in renal impairment. Minimal side-effects: <3% cough, sinusitis, diarrhea, nausea and vomiting. **Reports of respiratory adverse events in pts with or without h/o airways disease, should be avoided in pts with underlying respiratory disease.** Allergic reactions and neuropsychiatric events have been reported. **Caution: do not reconstitute zanamivir powder for use in nebulizers or mechanical ventilators** (MedWatch report of death). **Zanamivir for IV** administration is available for compassionate use through an emergency IND application. Contact GSK *(919-315-5215)* for forms, then contact FDA *(301-796-1500 or 301-796-9900)*.
Oseltamivir (Tamiflu) For pts ≥ 1 yr (treatment or prophylaxis)	For adults: **Treatment,** 75 mg po bid for 5 days; 150 mg po bid has been used for morbidly obese patients but this dose is not FDA-approved. **Prophylaxis,** 75 mg po once daily for 10 days to 6 wks. *(See label for pediatric weight-based dosing.)* Adjust doses for CrCl ≤30 mL/min. 30 mg, 45 mg, 75 mg caps; powder for oral suspension.	Well absorbed (80% bioavailable) from GI tract as ethyl ester of active compound GS 4071. T½ 6–10 hrs; excreted unchanged by kidney. Adverse effects include diarrhea, nausea, vomiting, headache. Nausea ↓ with food. Rarely, severe skin reactions (toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme). **Delirium** & abnormal behavior reported *(CID 48:1003, 2009)*. No benefit from higher dose in non- critically ill; not recommended *(CID 57:1511, 2013)*.
Peramivir (Rapivab)	600 mg IV single dose (acute uncomplicated intluenza)	FDA indication is for single dose use in acute uncomplicated influenza. No approved dose for hospitalized patients but 200-400 mg IV daily for 5 days used in trial. Flu with H275Y oseltamivir resistance has moderate resistance to peramivir
Respiratory Syncytial Virus (RSV) monoclonal antibody		
Palivizumab (Synagis) Used for prevention of RSV infection in high-risk children	15 mg per kg IM q month throughout HSV season Single dose 100 mg vial	A monoclonal antibody directed against the surface F glycoprotein; **AEs:** uncommon, occ. ↑ ALT. Anaphylaxis <1/10^5 pts; acute hypersensitivity reaction <1/1000. Postmarketing reports: URI, otitis media, fever, ↓ plts, injection site reactions. Preferred over polyclonal immune globulin in high risk infants & children.
Warts Regimens are from drug labels specific for external genital and/or perianal condylomata acuminata only *(see specific labels for indications, regimens, age limits)*.		
Interferon alfa-2b (IntronA)	Injection of 1 million international units into base of lesion, thrice weekly on alternate days for up to 3 wks. Maximum 5 lesions per course.	Interferons may cause "flu-like" illness and other systemic effects. 88% had at least one adverse effect. **Black box warning:** alpha interferons may cause or aggravate neuropsychiatric, autoimmune, ischemic or infectious disorders.
Interferon alfa-N3 (Alferon N)	Injection of 0.05 mL into base of each wart, up to 0.5 mL total per session, twice weekly for up to 8 weeks.	Flu-like syndrome and hypersensitivity reactions. Contraindicated with allergy to mouse IgG, egg proteins, or neomycin.
Imiquimod (Aldara)	5% cream. Thin layer applied at bedtime, washing off after 6-10 hr, thrice weekly to maximum of 16 wks; 3.75% cream apply qd.	Erythema, itching & burning, erosions. Flu-like syndrome, increased susceptibility to sunburn (avoid UV).
Podofilox (Condylox)	0.5% gel or solution twice daily for 3 days, no therapy for 4 days; can use up to 4 such cycles.	Local reactions—pain, burning, inflammation in 50%. Can ulcerate. Limit surface area treated as per label.
Sinecatechins (Veregen)	15% ointment. Apply 0.5 cm strand to each wart three times per day until healing but not more than 16 weeks.	Application site reactions, which may result in ulcerations, phimosis, meatal stenosis, superinfection.

* See page 2 for abbreviations. *NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.*

TABLE 14C – ANTIRETROVIRAL THERAPY (ART) IN TREATMENT-NAÏVE ADULTS (HIV/AIDS)

A. **Overview**

- Antiretroviral therapy (ART) in treatment-naïve adult patients.
- Guidelines: www.aidsinfo.nih.gov and IAS-USA in *JAMA 312:410, 2014.*
- Design a regimen consisting of:
  - **Dual-nucleoside/-nucleotide reverse transcriptase inhibitor (NRTI component) PLUS either a:**
    - **Non-nucleoside reverse transcriptase inhibitor (NNRTI) OR**
    - **Protease Inhibitor (PI) OR**
    - **Strand-Transfer Integrase Inhibitor (STII)**
- Selection of components is influenced by many factors, including:
  - Results of viral resistance testing
  - Pregnancy (e.g., avoid Efavirenz—pregnancy risk category D)
  - HIV status (e.g., Nevirapine CONTRAINDICATED in women with CD4 >250 cells/μL and men with CD4 >400 cells/μL)
  - Potential drug interactions or adverse drug effects; special focus on tolerability (even low grade side effects can profoundly affect adherence)
  - Co-morbidities (e.g., lipid effects of PIs, liver or renal disease, cardiovascular disease risk, chemical dependency, psychiatric disease)
  - Convenience of dosing. Co-formulations increase convenience, but sometimes prescribing the two constituents individually is preferred, as when dose-adjustments are needed for renal disease.
  - HLA-B5701 testing required prior to using Abacavir (ABC)
  - Co-receptor tropism assay if considering Maraviroc (MVC)

B. **Preferred Regimens (Non-pregnancy)**

Single tablet Combinations	• **Atripla** (Tenofovir/Emtricitabine/Efavirenz) 1 tablet once daily qhs OR • **Genvoya** (Elvitegravir/Cobicistat/Emtricitabine/Tenofovir alafenamide [TAF]) 1 tablet once daily with food • **Stribild** (use only if **Genvoya** not available) (Elvitegravir/Cobicistat/Emtricitabine/Tenofovir) 1 tablet once daily OR • **Complera/Eviplera** (Emtricitabine/Tenofovir/Rilpivirine) 1 tablet once daily with food(avoid when VL > 100,000 cells/mL) OR • **Triumeq** (Abacavir/3TC/Dolutegravir) 1 tablet each once daily (see Warnings below)
NNRTI Multi-tablet regimens (Select one)	• **Truvada** (Tenofovir/Emtricitabine) + **Efavirenz** 1 tablet each once daily qhs OR • **Epzicom/Kivexa** (Abacavir/3TC) + **Efavirenz** 1 tablet each once daily qhs *(see Warnings below)* OR
Ritonavir-boosted PI Multi-tablet regimens (Select one)	• **Truvada** (Tenofovir/Emtricitabine) + **Atazanavir/r** 1 tablet each once daily OR • **Epzicom/Kivexa** (Abacavir/3TC) + **Atazanavir/r** 1 tablet each once daily (see Warnings below) OR • **Truvada** (Tenofovir/Emtricitabine) + **Darunavir/r** 1 tablet each once daily OR
INSTI Multi-tablet regimens	• **Truvada** (Tenofovir/Emtricitabine) + **Raltegravir** 1 tablet each once daily OR • **Truvada** (Tenofovir/Emtricitabine) + **Dolutegravir** 1 tablet each once daily OR • **Epzicom/Kivexa** (Abacavir/3TC) + **Dolutegravir** 1 tablet each once daily (see Warnings below) OR

- NNRTI = non-nucleoside reverse transcriptase inhibitor, PI = protease inhibitor, INSTI = Strand transfer integrase inhibitor, /r = ritonavir boosted
- Warnings:
  - Epzicom/Kivexa (Abacavir/3TC) containing regimens: Use only in patients who are HLA-B5701 negative. Use Abacavir with caution in those with HIV RNA < 100,000 c/mL at baseline (this does not apply when Dolutegravir is the anchor drug of the regimen)
  - DO NOT USE Nevirapine if CD4 count > 250 cells/μL for women or > 400 cells/μL for men. Can result in life-threatening hypersensitivity reaction
- Co-formulations increase convenience, but sometimes prescribing the two components individually is preferred, as when dose adjustments are needed for renal disease.
- Rilpivirine is best used for patients with viral load < 100,000.
- Raltegravir 800 mg once daily is not quite as effective as 400 mg bid.

TABLE 14C (2)

C. **Alternative Regimens (Non-pregnancy)**

NNRTI Multi-tablet regimens (Select one)	• **Epzicom/Kivexa** (Abacavir/3TC) + **Rilpivirine** 1 tablet each once daily (see Warnings) OR • **Epzicom/Kivexa** (Abacavir/3TC) + **Nevirapine** 1 tablet each once daily (see Warnings) OR • **Truvada** (Tenofovir/Emtricitabine) + **Nevirapine** 1 tablet each once daily (see Warnings) OR
Boosted PI Multi-tablet regimens (Select one) **/c = cobicistat** **/r = ritonavir**	• **Epzicom/Kivexa** (Abacavir/3TC) + **Atazanavir/c** 1 tablet each once daily (see Warnings) OR • **Truvada** (Tenofovir/Emtricitabine) + **Atazanavir/c** 1 tablet each once daily OR • **Truvada** (Tenofovir/Emtricitabine) + **Darunavir/c** 1 tablet each once daily OR • **Epzicom/Kivexa** (Abacavir/3TC) + **Darunavir/c** 1 tablet each once daily (see Warnings) OR • **Epzicom/Kivexa** (Abacavir/3TC) + **Darunavir/r** 1 tablet each once daily (see Warnings) OR • **Epzicom/Kivexa** (Abacavir/3TC) one tablet daily + **Kaletra** (Lopinavir/r) 4 tablets once daily (see Warnings) OR • **Truvada** (Tenofovir/Emtricitabine) 1 tablet once daily + **Kaletra** (Lopinavir/r) 4 tablets once daily
Nucleoside sparing (or limited) regimens	• **Darunavir/r** 1 tablet once daily with food + Raltegravir 400 mg bid OR • **Kaletra** (Lopinavir/r) 4 tablets once daily + Raltegravir 400 mg bid OR • **Kaletra** (Lopinavir/r) 4 tablets once daily + Lamivudine 1 tablet each once daily

- Nevirapine 400 mg (Viramune XR) is the preferred formulation.
- Nevirapine should be used with caution with Abacavir owing to possible overlap of idiosyncratic hypersensitivity.
- Etravirine and Rilpivirine are options for some patients who have NNRTI resistance mutations, e.g., K103N, at baseline. Expert consultation is recommended.
- Boosted PIs can be administered once or twice daily.
- Cobicistat is now available as a PI-boosting agent
- Non-boosted PIs are no longer recommended
- Maraviroc is no longer recommended for initial treatment but may be used in cases of resistant viruses and as second line therapy (or beyond)
- Kaletra can be given as 2 tablets twice daily (must be given twice daily if multiple PI mutations present)

D. **Pregnancy Regimens**

• Timing of initiation of therapy and drug choice must be individualized • Viral resistance testing should be performed • Long-term effects of agents is unknown • Certain drugs are hazardous or contraindicated (Didanosine, Stavudine, Efavirenz)	• **Combivir** (Zidovudine/Lamivudine) 1 tablet bid + **Nevirapine** 1 tablet bid (fed or fasting)] after 14-day lead-in period or 1 tablet each once daily OR • **Combivir** (Zidovudine/Lamivudine) 1 tablet bid + **Kaletra** 2 tablets bid (without regard to food)

TABLE 14C (3)

E. **Selected Characteristics of Antiretroviral Drugs** (*CPE = CSF penetration effectiveness: 1-4)

1. **Selected Characteristics of Nucleoside or Nucleotide Reverse Transcriptase Inhibitors (NRTIs)**

All agents have Black Box warning: Risk of lactic acidosis/hepatic steatosis. Also, risk of fat redistribution/accumulation. For combinations, *see warnings for component agents.*

*** CPE (CNS Penetration Effectiveness) value:** 1= Low Penetration; 2 - 3 = Intermediate Penetration; 4 = Highest Penetration into CNS *(AIDS 25:357, 2011)*

Generic/ Trade Name	Pharmaceutical Prep.	Usual Adult Dosage & Food Effect	% Absorbed, po	Serum T½, hrs	Intracellular T½, hrs	CPE*	Elimination	Major Adverse Events/Comments *(See Table 14D)*
Abacavir (ABC; Ziagen)	300 mg tabs or 20 mg/mL oral solution	300 mg po bid or 600 mg po q24h. Food OK	83	1.5	20	1	Liver metab., renal excretion of metabolites, 82%	**Hypersensitivity reaction:** fever, rash, N/V, malaise, diarrhea, abdominal pain, respiratory symptoms. (Severe reactions may be ↑ with 600 mg dose.) **Do not rechallenge!** Report to 800-270-0425. **Test HLA-B*5701 before use.** ***See Comment Table 14D.*** Studies raise concerns re ABC/3TC regimens in pts with VL ≥ 100,000 *(www.niaid.nih.gov/news/newsreleases/2008/actg5202bulletin.htm).* Controversy re increased CV events with use of ABC. Large meta-analysis shows no increased risk *(JAIDS 61, 441, 2012)*
Abacavir (ABC)/lamivudine (Epzicom or Kivexa)	Film coated tabs ABC 600 mg + 3TC 300 mg	1 tab once daily (not recommended)	*(See individual components)*					*(See for individual components)* **Black Box warning**— limited data for VL >100,000 copies/mL. Not recommended as initial therapy because of inferior virologic efficacy.
Abacavir (ABC)/lamivudine (3TC)/dolutegravir (DTV)(Triumeq)	Film coated tabs: ABC 600 mg + 3TC 300 mg + DTV 50 mg	1 tab po once daily						
Abacavir (ABC)/ lamivudine (3TC)/ zidovudine (AZT) (Trizivir)	Film-coated tabs: ABC 300 mg + 3TC 150 mg + ZDV 300 mg	1 tab po bid (not recommended for wt <40 kg or CrCl <50 mL/min or impaired hepatic function)						
Didanosine (ddI; Videx or Videx EC)	125, 200, 250, 400 enteric-coated caps; 100, 167, 250 mg powder for oral solution;	≥60 kg Usually 400 mg enteric-coated po q24h 0.5 hr before or 2 hrs after meal. Do not crush. <60 kg: 250 mg EC po q24h. Food ↓ levels. *See Comment*	30–40	1.6	25–40	2	Renal excretion, 50%	**Pancreatitis,** peripheral neuropathy, lactic acidosis & hepatic steatosis (rare but life-threatening, esp. combined with stavudine in pregnancy). Retinal, optic nerve changes. **The combination ddI + TDF is generally avoided, but if used,** reduce dose of ddI-EC from 400 mg to 250 mg EC q24h (or from 250 mg EC to 200 mg EC for adults <60 kg). **Monitor for ↑ toxicity & possible ↓ in efficacy of this combination; may result in ↓ CD4.**

TABLE 14C (4)

Generic/ Trade Name	Pharmaceutical Prep.	Usual Adult Dosage & Food Effect	% Absorbed, po	Serum T½, hrs	Intracellular T½, hrs	CPE*	Elimination	Major Adverse Events/Comments (See Table 14D)
E. **Selected Characteristics of Antiretroviral Drugs** (*CPE = CSF penetration effectiveness: 1-4)								
1. **Selected Characteristics of Nucleoside or Nucleotide Reverse Transcriptase Inhibitors (NRTIs)** *(continued)*								
Emtricitabine (FTC, Emtriva)	200 mg caps; 10 mg per mL oral solution.	200 mg po q24h. Food OK	93 (caps), 75 (oral sol'n)	Approx. 10	39	3	Renal excretion 86%	Well tolerated; headache, nausea, vomiting & diarrhea occasionally, skin rash rarely. Skin hyperpigmentation. Differs only slightly in structure from lamivudine (5-fluoro substitution). **Exacerbation of Hep B reported in pts after stopping FTC.** Monitor at least several months after stopping FTC in Hep B pts; some may need anti-HBV therapy.
Emtricitabine/ tenofovir disoproxil fumarate (Truvada)	Film-coated tabs: FTC 200 mg + TDF 300 mg	1 tab po q24h for CrCl ≥50 mL/min. Food OK	92/25	10/17	—	*(See individual components)*	Primarily renal/renal	*See Comments for individual agents* **Black Box warning—Exacerbation of HepB after stopping FTC;** but preferred therapy for those with Hep B/HIV co-infection.
Emtricitabine/ tenofovir/efavirenz (Atripla)	Film-coated tabs: FTC 200 mg + TDF 300 mg + efavirenz 600 mg	1 tab po q24h on an empty stomach, preferably at bedtime. Do not use if CrCl <50 mL/min	*(See individual components)*					Not recommended for pts <18 yrs. *(See warnings for individual components).* **Exacerbation of Hep B** reported in pts discontinuing component drugs; some need anti-HBV therapy (tenofovir preferred). **Pregnancy category D-** Efavirenz may cause fetal harm. Avoid in pregnancy or in women who may become pregnant.
Emtricitabine/ tenofovir/rilpivirine (Complera/ Eviplera)	Film-coated tabs: FTC 200 mg +TDF 300 mg + RPL 25 mg	1 tab po q24h with food	*(See individual components)*					*See individual components.* Preferred use in pts with HIV RNA level <100,000 c/mL. Should not be used with PPI agents.
Lamivudine (3TC; Epivir)	150, 300 mg tabs; 10 mg/mL oral solution	150 mg po bid or 300 mg po q24h. Food OK	86	5–7	18	2	Renal excretion, minimal metabolism	**Use HIV dose, not Hep B dose.** Usually well-tolerated. **Risk of exacerbation of Hep B after stopping 3TC.** Monitor at least several months after stopping 3TC in Hep B pts; some may need anti-HBV therapy.
Lamivudine/ abacavir (Epzicom)	Film-coated tabs: 3TC 300 mg + abacavir 600 mg	1 tab po q24h. Food OK Not recommended for CrCl <50 mL/min or impaired hepatic function	86/86	5–7/1.5	16/20	*(See individual components)*	Primarily renal/ metabolism	*See Comments for individual agents.* **Note abacavir hypersensitivity Black Box warnings** (severe reactions may be somewhat more frequent with 600 mg dose) and 3TC Hep B warnings. Test HLA-B*5701 before use.
Lamivudine/ zidovudine (Combivir)	Film-coated tabs: 3TC 150 mg + ZDV 300 mg	1 tab po bid Not recommended for CrCl <50 mL/min or impaired hepatic function Food OK	86/64	5-7/ 0.5-3	—	*(See individual components)*	Primarily renal/ metabolism with renal excretion of glucuronide	*See Comments for individual agents* **Black Box warning**—exacerbation of Hep B in pts stopping 3TC

TABLE 14C (5)

Generic/ Trade Name	Pharmaceutical Prep.	Usual Adult Dosage & Food Effect	% Absorbed, po	Serum T½, hrs	Intracellular T½, hrs	CPE*	Elimination	Major Adverse Events/Comments *(See Table 14D)*
E. Selected Characteristics of Antiretroviral Drugs (*CPE = CSF penetration effectiveness: 1-4)								
1. Selected Characteristics of Nucleoside or Nucleotide Reverse Transcriptase Inhibitors (NRTIs) *(continued)*								
Stavudine (d4T; Zerit)	15, 20, 30, 40 mg capsules; 1 mg per mL oral solution	≥60 kg: 40 mg po bid <60 kg: 30 mg po bid Food OK	86	1.2–1.6	3.5	2	Renal excretion, 40%	Not recommended by DHHS as initial therapy because of adverse reactions. **Highest incidence of lipoatrophy, hyperlipidemia, & lactic acidosis of all NRTIs.** Pancreatitis. Peripheral neuropathy. *(See didanosine comments.)*
Tenofovir disoproxil fumarate (TDF; Viread)—a nucleotide	300 mg tabs	CrCl ≥50 mL/min: 300 mg po q24h. Food OK; high-fat meal ↑ absorption	39 (with food) 25 (fasted)	17	>60	1	Renal excretion	Headache, N/V. **Cases of renal dysfunction reported:** check renal function before using (dose reductions necessary if CrCl <50 cc/min); avoid concomitant nephrotoxic agents. One study found ↑ renal function at 48 wk in pts receiving TDF with a PI (mostly lopinavir/ritonavir) than with a NNRTI *(JID 197:102, 2008)*. Avoid concomitant ddI.
Tenofovir alfenamide (TAF)	25 mg (10 mg when used with Cobi or RTV)	CrCl >30 ml/min Food OK; high-fat meal ↑ absorption						Atazanavir & lopinavir/ritonavir ↑ tenofovir concentrations: monitor for adverse effects. **Black Box warning—exacerbations of Hep B reported after stopping tenofovir.** Monitor liver enzymes if TDF stopped on HBV pts.
Zidovudine (ZDV, AZT; Retrovir)	100 mg caps, 300 mg tabs; 10 mg per mL IV solution; 10 mg/mL oral syrup	300 mg po q12h. Food OK	64	1.1	11	4	Metabolized to glucuronide & excreted in urine	Bone marrow suppression, GI intolerance, headache, insomnia, malaise, myopathy.
2. Selected Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)								
Delavirdine (Rescriptor)	100, 200 mg tabs	400 mg po three times daily. Food OK	85	5.8	3		Cytochrome P450 (3A inhibitor). 51% excreted in urine (<5% unchanged)	Rash severe enough to stop drug in 4.3%. ↑ AST/ALT, headaches. **Use of this agent is not recommended.**

TABLE 14C (6)

Generic/ Trade Name	Pharmaceutical Prep.	Usual Adult Dosage & Food Effect	% Absorbed, po	Serum T½, hrs	Intracellular T½, hrs	CPE	Elimination	Major Adverse Events/Comments *(See Table 14D)*
E. Selected Characteristics of Antiretroviral Drugs (*CPE = CSF penetration effectiveness: 1-4)								
2. Selected Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) *(continued)*								
Efavirenz (Sustiva) New Guidelines indicate is OK to use in pregnant women (WHO Guidelines) or continue EFV in women identified as pregnant (HHS Guidelines).	50, 100, 200 mg capsules; 600 mg tablet	600 mg po q24h at bedtime, without food. Food may ↑ serum conc., which can lead to ↑ in risk of adverse events.	42	40–55 *See Comment*	3		Cytochrome P450 2B6 (3A mixed inducer/ inhibitor). 14–34% excreted in urine as glucuronidated metabolites, 16–61% in feces	Severe rash in 1.7%. High frequency of CNS AEs: somnolence, dreams, confusion, agitation. Serious psychiatric symptoms. Certain CYP2B6 polymorphisms may predict exceptionally high plasma levels with standard doses *(CID 45:1230, 2007)*. False-pos. cannabinoid screen. Very long tissue T½. **If rx to be discontinued, stop efavirenz 1–2 wks before stopping companion drugs.** Otherwise, risk of developing efavirenz resistance, as after 1–2 days only efavirenz in blood &/or tissue. Some bridge this gap by adding a PI to the NRTI backbone after efavirenz is discontinued. *(CID 42:401, 2006)*
Etravirine (Intelence)	100 mg tabs 200 mg tabs	200 mg twice daily after a meal. May also be given as 400 mg once daily	Unknown (↓ systemic exposure if taken fasting)	41	2		Metabolized by CYP 3A4 (inducer) & 2C9, 2C19 (inhibitor). Fecal extraction.	For pts with HIV-1 resistant to NNRTIs & others. Active in vitro against most such isolates. Rash common, but rarely can be severe. Potential for multiple drug interactions. Generally, multiple mutations are required for high-level resistance. *See Table 14D, page 193 for specific mutations and effects.* Because of interactions, do not use with boosted atazanavir, boosted tipranavir, unboosted PIs, or other NNRTIs.
Nevirapine (Viramune) Viramune XR	200 mg tabs; 50 mg per 5 mL oral suspension; XR 400 mg tabs	200 mg po q24h x 14 days & then 200 mg po bid *(see comments & **Black Box warning**)* Food OK. **If using Viramune XR, Still need the lead in dosing of 200 mg q24h prior to using 400 mg/d**	>90	25–30	4		Cytochrome P450 (3A4, 2B6) inducer; 80% excreted in urine as glucuronidated metabolites, 10% in feces	**Black Box warning—fatal hepatotoxicity.** Women with CD4 >250 esp. vulnerable, inc. pregnant women. Avoid in this group unless benefits clearly > risks *(www.fda.gov/cderdrug/advisory/nevirapine.htm)*. Intensive monitoring for liver toxicity required. Men with CD4 >400 also at ↑ risk. Severe rash in 7%, **severe or life-threatening skin reactions** in 2%. Do not restart if any suspicion of such reactions. 2 wk dose escalation period may ↓ skin reactions. Because of long T½, consider continuing companion agents for several days if nevirapine is discontinued.

TABLE 14C (7)

Generic/ Trade Name	Pharmaceutical Prep.	Usual Adult Dosage & Food Effect	% Absorbed, po	Serum T½, hrs	Intracellular T½, hrs	CPE	Elimination	Major Adverse Events/Comments *(See Table 14D)*
E. **Selected Characteristics of Antiretroviral Drugs** (*CPE = CSF penetration effectiveness: 1-4)								
2. **Selected Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)** *(continued)*								
Rilpivirine (Edurant)	25 mg tabs	25 mg daily with food	absolute bio-availability unknown; 40% lower Cmax in fasted state	50	unknown		Metabolized by Cyp3A4 in liver; 25% excreted unchanged in feces.	QTc prolongation with doses higher than 50 mg per day. Common AEs: depression, insomnia, headache, and rash. Do not co-administer with carbamazepine, phenobarbitol, phenytoin, rifabutin, rifampin, rifapentine, proton pump inhibitors, or multiple doses of dexamethasone. A fixed dose combination of rilpivirine + TDF/FTC (Complera/Eviplera) is approved. **Needs stomach acid for absorption. Do not administer with PPI.**

3. **Selected Characteristics of Protease Inhibitors (PIs)**

All PIs: Glucose metabolism: new diabetes mellitus or deterioration of glucose control; fat redistribution; possible hemophilia bleeding; hypertriglyceridemia or hypercholesterolemia. Exercise caution re: potential drug interactions & contraindications. QTc prolongation has been reported in a few pts taking PIs; some PIs can block HERG channels in vitro *(Lancet 365:682, 2005)*.

Generic/ Trade Name	Pharmaceutical Prep.	Usual Adult Dosage & Food Effect	% Absorbed, po	Serum T½, hrs	CPE*	Elimination	Major Adverse Events/Comments *(See Table 14D)*
Atazanavir (Reyataz)	100, 150, 200, 300 mg capsules	400 mg po q24h with food. Ritonavir-boosted dose (atazanavir 300 mg po q24h + ritonavir 100 mg po q24h), with food, is recommended for ART-experienced pts. Use boosted dose when combined with either efavirenz 600 mg po q24h or TDF 300 mg po q24h. If used with buffered ddI, take with food 2 hrs pre or 1 hr post ddI.	Good oral bioavailability; food enhances bioavailability & ↓ pharmacokinetic variability. Absorption ↓ by antacids, H_2-blockers, proton pump inhibitors. Avoid unboosted drug with PPIs/H2-blockers. Boosted drug can be used with or >10 hr after H2-blockers or >12 hr after a PPI, if limited doses of the acid agents are used.	Approx. 7	2	Cytochrome P450 (3A4, 1A2 & 2C9 inhibitor) & UGT1A1 inhibitor, 13% excreted in urine (7% unchanged), 79% excreted in feces (20% unchanged)	Lower potential for ↑ lipids. Asymptomatic unconjugated hyperbilirubinemia common; jaundice especially likely in Gilbert's syndrome *(JID 192:1381, 2005)*. Headache, rash, GI symptoms. Prolongation of PR interval (1st degree AV block) reported. Caution in pre-existing conduction system disease. Efavirenz & tenofovir ↓ atazanavir exposure: use atazanavir/ritonavir regimen; also, atazanavir ↑ tenofovir concentrations—watch for adverse events. In rx-experienced pts taking TDF and needing H2 blockers, atazanavir 400 mg with ritonavir 100 mg can be given; do not use PPIs. Rare reports of renal stones.
Darunavir (Prezista)	400 mg, 600 mg, 800 mg tablets	[600 mg darunavir + 100 mg ritonavir] po bid, with food or **[800 mg darunavir (two 400 mg tabs or one 800 mg tab) + 100 mg ritonavir] po once daily with food (Preferred regimen in ART naïve pts)**	82% absorbed (taken with ritonavir). Food ↑ absorption.	Approx 15 hr (with ritonavir)	3	Metabolized by CYP3A and is a CYP3A inhibitor	Contains sulfa moiety. Rash, nausea, headaches seen. Coadmin of certain drugs cleared by CYP3A is contraindicated *(see label)*. Use with caution in pts with hepatic dysfunction. (FDA warning about occasional hepatic dysfunction early in the course of treatment). Monitor carefully, esp. first several months and with pre-existing liver disease. May cause hormonal contraception failure.

TABLE 14C (8)

	Generic/ Trade Name	Pharmaceutical Prep.	Usual Adult Dosage & Food Effect	% Absorbed, po	Serum T½, hrs	CPE*	Elimination	Major Adverse Events/Comments *(See Table 14D)*
E	**Selected Characteristics of Antiretroviral Drugs** (*CPE = CSF penetration effectiveness: 1-4)							
	3. **Selected Characteristics of Protease Inhibitors (PIs)** *(continued)*							
	Fosamprenavir (Lexiva)	700 mg tablet, 50 mg/mL oral suspension	1400 mg (two 700 mg tabs) po bid **OR** with ritonavir: [1400 mg fosamprenavir (2 tabs) + ritonavir 100 mg or 200 mg] po q24h **OR** [700 mg fosamprenavir (1 tab) + ritonavir 100 mg] po bid	Bioavailability not established. Food OK	7.7 Ampre-navir	3	Hydrolyzed to amprenavir, then acts as cytochrome P450 (3A4 substrate, inhibitor, inducer)	Amprenavir prodrug. Contains sulfa moiety. Potential for serious drug interactions *(see label)*. Rash, including Stevens-Johnson syndrome. Once daily regimens: (1) not recommended for PI-experienced pts, (2) additional ritonavir needed if given with efavirenz *(see label)*. Boosted twice daily regimen is recommended for PI-experienced pts. Potential for PI cross-resistance with darunavir.
	Indinavir (Crixivan)	100, 200, 400 mg capsules Store in original container with desiccant	Two 400 mg caps (800 mg) po q8h, without food or with light meal. Can take with enteric-coated Videx. *[If taken with ritonavir (e.g., 800 mg indinavir + 100 mg ritonavir po q12h), no food restrictions]*	65	1.2–2	4	Cytochrome P450 (3A4 inhibitor)	**Maintain hydration. Nephrolithiasis,** nausea, inconsequential ↑ of indirect bilirubin (jaundice in Gilbert syndrome), ↑ AST/ALT, headache, asthenia, blurred vision, metallic taste, hemolysis. ↑ urine WBC (>100/hpf) has been assoc. with nephritis/ medullary calcification, cortical atrophy.
	Lopinavir + ritonavir (Kaletra)	(200 mg lopinavir + 50 mg ritonavir), and (100 mg lopinavir + 25 mg ritonavir) tablets. Tabs do not need refrigeration. Oral solution: (80 mg lopinavir + 20 mg ritonavir) per mL. Refrigerate, but can be kept at room temp. (≤77°F) x 2 mos.	(400 mg lopinavir + 100 mg ritonavir)—2 tabs po bid. Higher dose may be needed in non-rx-naïve pts when used with efavirenz, nevirapine, or unboosted fosamprenavir. [Dose adjustment in concomitant drugs may be necessary; *see Table 22B.*	No food effect with tablets.	5–6	3	Cytochrome P450 (3A4 inhibitor)	Nausea/vomiting/diarrhea (worse when administered with zidovudine), ↑ AST/ ALT, pancreatitis. Oral solution 42% alcohol. Lopinavir + ritonavir can be taken as a single daily dose of 4 tabs (total 800 mg lopinavir + 200 mg ritonavir), except in treatment-experienced pts or those taking concomitant efavirenz, nevirapine, amprenavir, or nelfinavir. Possible PR and QT prolongation. Use with caution in those with cardiac conduction abnormalities or when used with drugs with similar effects.
	Nelfinavir (Viracept)	625, 250 mg tabs; 50 mg/gm oral powder	Two 625 mg tabs (1250 mg) po bid, with food	20–80 Food ↑ exposure & ↓ variability	3.5–5	1	Cytochrome P450 (3A4 inhibitor)	Diarrhea. Coadministration of drugs with life-threatening toxicities & which are cleared by CYP34A is contraindicated. Not recommended in initial regimens because of inferior efficacy; **prior concerns about EMS now resolved. Acceptable choice in pregnant women although it has inferior virologic efficacy than most other ARV anchor drugs.**

TABLE 14C (9)

Generic/ Trade Name	Pharmaceutical Prep.	Usual Adult Dosage & Food Effect	% Absorbed, po	Serum T½, hrs	CPE	Elimination	Major Adverse Events/Comments *(See Table 14D)*
E. **Selected Characteristics of Antiretroviral Drugs**							
3. **Selected Characteristics of Protease Inhibitors (PIs).** *(continued)*							
Ritonavir (Norvir)	100 mg capsules; 600 mg per 7.5 mL solution. Refrigerate caps but not solution. Room temperature for 1 mo. is OK.	Full dose not recommended *(see comments).* **With rare exceptions, used exclusively to enhance pharmacokinetics of other PIs, using lower ritonavir doses.**	Food ↑ absorption	3–5	1	Cytochrome P450. Potent 3A4 & 2 d6 inhibitor	Nausea/vomiting/diarrhea, extremity & circumoral paresthesias, hepatitis, pancreatitis, taste perversion, ↑ CPK & uric acid. **Black Box warning**—potentially fatal drug interactions. Many drug interactions— *see Table 22A–Table 22B.*
Saquinavir (Invirase—hard gel caps or tabs) + **ritonavir**	Saquinavir 200 mg caps, 500 mg film-coated tabs; ritonavir 100 mg caps	[2 tabs saquinavir (1000 mg) + 1 cap ritonavir (100 mg)] po bid with food	Erratic, 4 (saquinavir alone). Much more reliably absorbed when boosted with ritonavir.	1–2	1	Cytochrome P450 (3A4 inhibitor)	Nausea, diarrhea, headache, ↑ AST/ALT. Avoid rifampin with saquinavir + ritonavir: ↑ hepatitis risk. **Black Box warning**—Invirase to be used only with ritonavir. Possible QT prolongation. Use with caution in those with cardiac conduction abnormalities or when used with drugs with similar effects.
Tipranavir (Aptivus)	250 mg caps. Refrigerate unopened bottles. Use opened bottles within 2 mo. 100 mg/mL solution	[500 mg (two 250 mg caps) + ritonavir 200 mg] po bid with food.	Absorption low, ↑ with high fat meal, ↓ with Al^{+++} & Mg^{++} antacids.	5.5-6	1	Cytochrome 3A4 but with ritonavir, most of drug is eliminated in feces.	Contains sulfa moiety. **Black Box warning—reports of fatal/nonfatal intracranial hemorrhage, hepatitis, fatal hepatic failure.** Use cautiously in liver disease, esp. hepB, hepC; contraindicated in Child-Pugh class B-C. Monitor LFTs. Coadministration of certain drugs contraindicated *(see label).* **For highly ART-experienced pts or for multiple-PI resistant virus.** Do not use tipranavir and etravirine together owing to 76% reduction in etravirine levels.

4. **Selected Characteristics of Fusion Inhibitors**

Generic/ Trade Name	Pharmaceutical Prep.	Usual Adult Dosage	% Absorbed	Serum T½, hrs	CPE*	Elimination	Major Adverse Events/Comments *(See Table 14D)*
Enfuvirtide (T20, Fuzeon)	Single-use vials of 90 mg/mL when reconstituted. Vials should be stored at room temperature. Reconstituted vials can be refrigerated for 24 hrs only.	90 mg (1 mL) subcut. bid. Rotate injection sites, avoiding those currently inflamed.	84	3.8	1	Catabolism to its constituent amino acids with subsequent recycling of the amino acids in the body pool. Elimination pathway(s) have not been performed in humans. Does not alter the metabolism of CYP3A4, CYP2 d6, CYP1A2, CYP2C19 or CYP2E1 substrates.	Local reaction site reactions 98%, 4% discontinue; erythema/induration ~80–90%, nodules/cysts ~80%. **Hypersensitivity reactions reported** (fever, rash, chills, N/V, ↓ BP, &/or ↑ AST/ALT)—do not restart if occur. Including background regimens, peripheral neuropathy 8.9%, insomnia 11.3%, ↓ appetite 6.3%, myalgia 5%, lymphadenopathy 2.3%, eosinophilia ~10%. ↑ incidence of bacterial pneumonias.

TABLE 14C (10)

Generic/ Trade Name	Pharmaceutical Prep.	Usual Adult Dosage & Food Effect	% Absorbed	Serum T½, hrs	CPE	Elimination	Major Adverse Events/Comments *(See Table 14D)*
E. Selected Characteristics of Antiretroviral Drugs (*CPE = CSF penetration effectiveness: 1-4) *(continued)*							
5. Selected Characteristics of CCR-5 Co-receptor Antagonists							
Maraviroc (Selzentry)	150 mg, 300 mg film-coated tabs	Without regard to food: - 150 mg bid if concomitant meds include CYP3A inhibitors including PIs (except tipranavir/ritonavir) and delavirdine (with/without CYP3A inducers) - 300 mg bid without significantly interacting meds including NRTIs, tipranavir/ritonavir, neverapine - 600 mg bid if concomitant meds include CYP3A inducers, including efavirenz (without strong CYP3A inhibitors)	Est. 33% with 300 mg dosage	14-18	3	CYP3A and P-glycoprotein substrate. Metabolites (via CYP3A) excreted feces > urine	**Black Box Warning-Hepatotoxicity,** may be preceded by rash, ↑ eos or IgE. NB: no hepatoxicity was noted in MVC trials. Black box inserted owing to concern about potential CCR5 class effect. Data lacking in hepatic/renal insufficiency; ↑ concern with either could ↑ risk of ↓BP. Currently for treatment-experienced patients with multi-resistant strains. **Document CCR-5-tropic virus before use, as treatment failures assoc. with appearance of CXCR-4 or mixed-tropic virus.**
6. Selected Characteristics of Strand Transfer Integrase Inhibitors							
Raltegravir (Isentress)	400 mg film-coated tabs	400 mg po bid, without regard to food	Unknown	~ 9	3	Glucuronidation via UGT1A1, with excretion into feces and urine. (Therefore does NOT require ritonavir boosting)	For naïve patients and treatment experienced pts with multiply-resistant virus. Well-tolerated. Nausea, diarrhea, headache, fever similar to placebo. CK↑ & rhabdomyolysis reported: unclear relationship. Increased depression in those with a history of depression. Low genetic barrier to resistance. Increase in CPK, myositis, rhabdomyolysis have been reported. Rare Stevens Johnson Syndrome. Better oral absorption if chewed *(CID 57:480, 2013)*.
Elvitegravir/ cobicistat (Stribild)	150 mg - 150 mg	150 mg-150 mg once daily with or without food	< 10%	12.9 (Cobi), 3.5 (ELV)	Un-known	The majority of **elvitegravir** metabolism is mediated by CYP3A enzymes. Elvitegravir also undergoes glucuronidation via UGT1A1/3 enzymes. **Cobicistat** is metabolized by CYP3A and to a minor extent by CYP2D6	For both treatment naïve patients and treatment experienced pts with multiply-resistant virus. Generally well-tolerated. Use of cobicistat increases serum creatinine by ~ 0.1 mg/dl via inhibition of proximal tubular enzyme; this does not result in reduction in true GFR but will result in erroneous apparent reduction in eGFR by MDRD or Cockcroft Gault calculations. Usual AEs are similar to those observed with ritonavir (cobi) and tenofovir/FTC.

TABLE 14C (11)

Generic/ Trade Name	Pharmaceutical Prep.	Usual Adult Dosage & Food Effect	% Absorbed	Serum T½, hrs	CPE	Elimination	Major Adverse Events/Comments *(See Table 14D)*
6. **Selected Characteristics of Strand Transfer Integrase Inhibitors** *(continued)*							
Elvitegravir (Vitekta)(EVG)	85 mg, 150 mg tabs	• EVG85 mg once daily + ATV/r 300/100 mg po once daily • EVG85 mg once daily + LPV/r 400/100 mg po bid • EVG150 mg once daily + DRV/r 600/100 mg po bid • EVG150 mg once daily + FOS/r 700/100 mg po bid • EVG150 mg once daily + TPV/r 500/200 mg po bid	ND	8 /	No	Hepatobiliary, metabolized by CYP3A	Well tolerated, mild diarrhea
Dolutegravir (Tivicay)	50 mg	50 mg po once daily 50 mg po BID (if STII resistance present or if co-admin with EFV, FOS, TIP, or Rif	Unknown	14	4	Glucuronidation via UGT1A1 (therefore does not require ritonavir or cobicistat boosting)	Hypersensitivity (rare); Most common: insomnia (3%) headache (2%), N/V (1%), rash (<1%). Watch for IRIS; Watch for elevated LFTs in those with HCV

F. **Other Considerations in Selection of Therapy**

Caution: Initiation of ART may result in immune reconstitution syndrome with significant clinical consequences. See Table 11B, of Sanford Guide to HIV/AIDS Therapy *(AIDS Reader 16:199, 2006)*.

1. Resistance testing: Given current rates of resistance, resistance testing is recommended in all patients prior to initiation of therapy, including those with acute infection syndrome (may initiate therapy while waiting for test results and adjusting Rx once results return), at time of change of therapy owing to antiretroviral failure, when suboptimal virologic response is observed, and in pregnant women. **Resistance testing NOT recommended if pt is off ART for > 4 weeks or if HIV RNA is < 1000 c/mL.** *See Table 6F of SANFORD GUIDE TO HIV/AIDS THERAPY.*

2. Drug-induced disturbances of glucose & lipid metabolism *(see Table 14D)*
3. Drug-induced lactic acidosis & other FDA "box warnings" *(see Table 14D)*
4. Drug-drug interactions *(see Table 22B)*
5. Risk in pregnancy *(see Table 8)*
6. Use in women & children *(see Table 14C)*
7. Dosing in patients with renal or hepatic dysfunction *(see Table 17A & Table 17B)*

*** CPE (CNS Penetration Effectiveness) value:** 1 = Low Penetration; 2 - 3 = Intermediate Penetration; 4 = Highest Penetration into CNS *(AIDS 25:357, 2011)*

TABLE 14D – ANTIRETROVIRAL DRUGS & ADVERSE EFFECTS
(www.aidsinfo.nih.gov)

DRUG NAME(S): GENERIC (TRADE)	MOST COMMON ADVERSE EFFECTS	MOST SIGNIFICANT ADVERSE EFFECTS
Nucleoside Reverse Transcriptase Inhibitors (NRTI) Black Box warning for all nucleoside/nucleotide RTIs: lactic acidosis/hepatic steatosis, potentially fatal. Also carry Warnings that fat redistribution and immune reconstitution syndromes (including autoimmune syndromes with delayed onset) have been observed		
Abacavir (Ziagen)	Headache 7–13%, nausea 7–19%, diarrhea 7%, malaise 7-12%	**Black Box warning-Hypersensitivity reaction (HR)** in 8% with malaise, fever, GI upset, rash, lethargy & respiratory symptoms most commonly reported; myalgia, arthralgia, edema, paresthesia less common. **Discontinue immediately if HR suspected. Rechallenge contraindicated; may be life-threatening.** Severe HR may be more common with once-daily dosing. **HLA-B*5701 allele** predicts ↑ risk of HR in Caucasian pop.; excluding pts with B*5701 markedly ↓'d HR incidence *(NEJM 358:568, 2008; CID 46:1111-1118, 2008)*. DHHS guidelines recommend testing for B*5701 and use of abacavir-containing regimens only if HLA-B*5701 negative; Vigilance essential in all groups. Possible increased risk of MI with use of abacavir had been suggested *(JID 201:318, 2010)*. Other studies found no increased risk of MI *(CID 52: 929, 2011)*. A meta-analysis of randomized trials by FDA also did not show increased risk of MI *(www.fda.gov/drugs/drugsafety/ucm245164.htm)*. Nevertheless, care is advised to optimize potentially modifiable risk factors when abacavir is used.
Didanosine (ddI) (Videx)	Diarrhea 28%, nausea 6%, rash 9%, headache 7%, fever 12%, hyperuricemia 2%	**Pancreatitis 1–9%. Black Box warning—Cases of fatal & nonfatal pancreatitis** have occurred in pts receiving ddI, especially when used in combination with d4T or d4T + hydroxyurea. Fatal lactic acidosis in pregnancy with ddI + d4T. Peripheral neuropathy in 20%, 12% required dose reduction. ↑ toxicity if used with ribavirin. Use with TDF generally avoided (but would require dose reduction of ddI) because of ↑ toxicity and possible ↓ efficacy; may result in ↓ CD4. Rarely, retinal changes or optic neuropathy. Diabetes mellitus and rhabdomyolysis reported in post-marketing surveillance. Possible increased risk of MI under study *(www.fda.gov/CDER; JID 201:318, 2010)*. Non-cirrhotic portal hypertension with ascites, varices, splenomegaly reported in post-marketing surveillance. *See also Clin Infect Dis 49:626, 2009; Amer J Gastroenterol 104:1707, 2009.*
Emtricitabine (FTC) (Emtriva)	Well tolerated. Headache, diarrhea, nausea, rash, skin hyperpigmentation	Potential for lactic acidosis (as with other NRTIs). Also **in Black Box—severe exacerbation of hepatitis B on stopping drug reported—monitor clinical/labs for several months after stopping in pts with hepB.** Anti-HBV rx may be warranted if FTC stopped.
Lamivudine (3TC) (Epivir)	Well tolerated. Headache 35%, nausea 33%, diarrhea 18%, abdominal pain 9%, insomnia 11% (all in combination with ZDV). Pancreatitis more common in pediatrics.	**Black Box warning**. Make sure to use HIV dosage, not Hep B dosage. **Exacerbation of hepatitis B on stopping drug. Patients with hepB who stop lamivudine require close clinical/lab monitoring for several months.** Anti-HBV rx may be warranted if 3TC stopped.
Stavudine (d4T) (Zerit)	Diarrhea, nausea, vomiting, headache	**Peripheral neuropathy** 15–20%. Pancreatitis 1%. Appears to produce lactic acidosis, hepatic steatosis and lipoatrophy/lipodystrophy more commonly than other NRTIs. **Black Box warning—Fatal & nonfatal pancreatitis with d4T + ddI.** Use with TDF generally avoided (but would require dose reduction of ddI) because of ↑ toxicity and possible ↓ efficacy; may result in ↓ CD4. Rarely, retinal changes or optic neuropathy. Diabetes mellitus and rhabdomyolysis reported in post-marketing surveillance. **Fatal lactic acidosis/steatosis in pregnant women receiving d4T + ddI.** Fatal and non-fatal lactic acidosis and severe hepatic steatosis can occur in others receiving d4T. Use with particular caution in patients with risk factors for liver disease, but lactic acidosis can occur even in those without known risk factors. Possible ↑ toxicity if used with ribavirin. Motor weakness in the setting of lactic acidosis mimicking the clinical presentation of Guillain-Barré syndrome (including respiratory failure) (rare).
Zidovudine (ZDV, AZT) (Retrovir)	Nausea 50%, anorexia 20%, vomiting 17%, **headache 62%.** Also reported: asthenia, insomnia, myalgias, nail pigmentation. Macrocytosis expected with all dosage regimens.	**Black Box warning—hematologic toxicity, myopathy. Anemia** (<8 gm, 1%), granulocytopenia (<750, 1.8%). Anemia may respond to epoetin alfa if endogenous serum erythropoietin levels are ≤500 milliUnits/mL. Possible ↑ toxicity if used with ribavirin. Co-administration with Ribavirin not advised. Hepatic decompensation may occur in HIV/HCV co-infected patients receiving zidovudine with interferon alfa ± ribavirin.

TABLE 14D (2)

DRUG NAME(S): GENERIC (TRADE)	MOST COMMON ADVERSE EFFECTS	MOST SIGNIFICANT ADVERSE EFFECTS
Nucleotide Reverse Transcriptase Inhibitor (NtRTI) Black Box warning for all nucleoside/nucleotide RTIs: lactic acidosis/hepatic steatosis, potentially fatal. Also carry Warnings that fat redistribution and immune reconstitution syndromes (including autoimmune syndromes with delayed onset) have been observed *(continued)*		
Tenofovir disoproxil fumarate (TDF) (Viread); Tenofovir alafenamide (TAF)	Diarrhea 11%, nausea 8%, vomiting 5%, flatulence 4% (generally well toferated)	**Black Box Warning—Severe exacerbations of hepatitis B reported in pts who stop tenofovir.** Monitor carefully if drug is stopped, anti-HBV rx may be warranted if TDF stopped. Reports of renal injury from TDF, including Fanconi syndrome *(CID 37:e174, 2003; J AIDS 35:269,204; CID 42:283, 2006)*. Fanconi syndrome and diabetes insipidus reported with TDF + ddI *(AIDS Reader 19:114, 2009)*. Modest decline in renal function appears greater with TDF than with NRTIs (CID 51:296, 2010) or TAF and may be greater in those receiving TDF with a PI instead of an NNRTI *(JID 197:102, 2008, AIDS 26:567, 2012)*. In a VA study that followed >10,000 HIV-infected individuals, TDF exposure was significantly associated with increased risk of proteinuria, a more rapid decline in renal function and chronic kidney disease *(AIDS 26:867, 2012)*. Monitor Ccr, serum phosphate and urinalysis, especially carefully in those with pre existing renal dysfunction or nephrotoxic medications. TDF, but not TAF, also appears to be associated with increased risk of bone loss. In a substudy of an ACTG comparative treatment trial, those randomized to TDF + FTC experienced greater decreases in spine and hip bone mineral density (BMD) at 96 weeks compared with those treated with ABC-3TC *(JID 203:1791, 2011)*. Consider monitoring BMD in those with history of pathologic fractures, or who have risks for osteoporosis or bone loss.
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI). Labels caution that fat redistribution and immune reconstitution can occur with ART.		
Delavirdine (Rescriptor)	Nausea, diarrhea, vomiting, headache	**Skin rash** has occurred in 18%; can continue or restart drug in most cases. Stevens-Johnson syndrome & erythema multiforme have been reported rarely. ↑ in liver enzymes in <5% of patients.
Efavirenz (Sustiva)	**CNS side effects 52%;** symptoms include dizziness, insomnia, somnolence, impaired concentration, psychiatric sx, & abnormal dreams; symptoms are worse after 1st or 2nd dose & improve over 2–4 weeks; discontinuation rate 2.6%. Rash 26% (vs. 17% in comparators); often improves with oral antihistamines; discontinuation rate 1.7%. Can cause false-positive urine test results for cannabinoid with CEDIA DAU multi-level THC assay. Metabolite can cause false-positive urine screening test for benzodiazepines *(CID 48:1787, 2009)*.	**Caution:** CNS effects may impair driving and other hazardous activities. Serious neuropsychiatric symptoms reported, including severe depression (2.4%) & suicidal ideation (0.7%). Elevation in liver enzymes. Fulminant hepatic failure has been reported *(see FDA label)*. **Teratogenicity reported in primates; pregnancy category D—may cause fetal harm, avoid in pregnant women or those who might become pregnant.** NOTE: No single method of contraception is 100% reliable. Barrier + 2nd method of contraception advised, continued 12 weeks after stopping efavirenz. Contraindicated with certain drugs metabolized by CYP3A4. Slow metabolism in those homozygous for the CYP-2B6 G516T allele can result in exaggerated toxicity and intolerance. This allele much more common in blacks and women *(CID 42:408, 2006)*. Stevens-Jonson syndrome and erythema multiforme reported in post-marketing surveillance.
Etravirine (Intelence)	Rash 9%, generally mild to moderate and spontaneously resolving; 2% dc clinical trials for rash. More common in women. Nausea 5%.	Severe rash (erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson syndrome) has been reported. Hypersensitivity reactions can occur with rash, constitutional symptoms and organ dysfunction, including hepatic failure *(see FDA label)*. Potential for CYP450-mediated drug interactions. Rhabdomyolysis has been reported in post-marketing surveillance.
Nevirapine (Viramune)	**Rash 37%**: usually occurs during 1st 6 wks of therapy. Follow recommendations for 14-day lead-in period to ↓ risk of rash *(see Table 14C)*. Women experience 7-fold ↑ in risk of severe rash *(CID 32:124, 2001)*. 50% resolve within 2 wks of dc drug & 80% by 1 month. 6.7% discontinuation rate.	**Black Box warning—Severe life-threatening skin reactions reported:** Stevens-Johnson syndrome, toxic epidermal necrolysis, & hypersensitivity reaction or drug rash with eosinophilia & systemic symptoms (DRESS) *(ArIM 161:2501, 2001)*. For severe rashes, dc drug immediately & do not restart. In a clinical trial, the use of prednisone ↑ the risk of rash. **Black Box warning—Life-threatening hepatotoxicity reported,** 2/3 during the first 12 wks of rx. Overall 1% develops hepatitis. Pts with pre-existing ↑ in ALT or AST &/or history of chronic Hep B or C ↑ susceptible *(Hepatol 35:182, 2002)*. Women with CD4 >250, including pregnant women, at ↑ risk. Avoid in this group unless no other option. Men with CD4 >400 also at ↑ risk. Monitor pts intensively (clinical & LFTs), esp. during the first 12 wks of rx. If clinical hepatotoxicity, severe skin or hypersensitivity reactions occur, dc drug & never rechallenge.

TABLE 14D (3)

DRUG NAME(S): GENERIC (TRADE)	MOST COMMON ADVERSE EFFECTS	MOST SIGNIFICANT ADVERSE EFFECTS
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI) *(continued)*		
Rilpivirine (Edurant)	Headache (3%), rash (3%; led to discontinuation in 0.1%), insomnia (3%), depressive disorders (4%). Psychiatric disorders led to discontinuation in 1%. Increased liver enzymes observed.	Drugs that induce CYP3A or increase gastric pH may decrease plasma concentration of rilpivirine and co-administration with rilpivirine should be avoided. Among these are certain anticonvulsants, rifamycins, PPIs, dexamethasone and St. John's wort. At supra-therapeutic doses, rilpivirine can increase QTc interval; use with caution with other drugs known to increase QTc. May cause depressive disorder, including suicide attempts or suicidal ideation. Overall, appears to cause fewer neuropsychiatric side effects than efavirenz *(JAIDS 60:33, 2012)*.
Protease Inhibitors (PI) Diarrhea is common AE (**crofelemer** 125 mg bid may help, but expensive). Abnormalities in glucose metabolism, dyslipidemias, fat redistribution syndromes are potential problems. Pts taking PI may be at increased risk for developing osteopenia/osteoporosis. Spontaneous bleeding episodes have been reported in HIV+ pts with hemophilia being treated with PI. Rheumatoid complications have been reported *(An Rheum Dis 61:82, 2002)*. Potential for QTc prolongation *(Lancet 365:682, 2005)*. **Caution for all PIs** Coadministration with drugs dependent on CYP3A or other enzymes for elimination & for which ↑ levels can cause serious toxicity may be contraindicated. ART may result in immune reconstitution syndromes, which may include early or late presentations of autoimmune syndromes. Increased premature births among women receiving ritonavir-boosted PIs as compared with those receiving other antiretroviral therapy, even after accounting for other potential risk factors *(CID 54: 1348, 2012)*.		
Atazanavir (Reyataz)	Asymptomatic unconjugated hyperbilirubinemia in up to 60% of pts, jaundice in 7–9% [especially with Gilbert syndrome *(JID 192: 1381, 2005)*]. Moderate to severe events: Diarrhea 1–3%, nausea 6–14%, abdominal pain 4%, headache 6%, rash 20%.	Prolongation of PR interval (1st degree AV block in 5-6%) reported; rarely 2° AV block. QTc increase and torsades reported *(CID 44:e67, 2007)*. Acute interstitial nephritis *(Am J Kid Dis 44:E81, 2004)* and urolithiasis (atazanavir stones) reported *(AIDS 20:2131, 2006; NEJM 355:2158, 2006)*. Potential ↑ transanimases in pts co-infected with HBV or HCV. Severe skin eruptions (Stevens-Johnson syndrome, erythema multiforme, and toxic eruptions, or DRESS syndrome) have been reported.
Darunavir (Prezista)	With background regimens, headache 15%, nausea 18%, diarrhea 20%, ↑ amylase 17%. Rash in 10% of treated; 0.5% discontinuation.	Hepatitis in 0.5%, some with fatal outcome. Use caution in pts with HBV or HCV co-infections or other hepatic dysfunction. Monitor for clinical symptoms and LFTs. Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme. Contains sulfa moiety. Potential for major drug interactions. May cause failure of hormonal contraceptives.
Fosamprenavir (Lexiva)	Skin rash ~ 20% (moderate or worse in 3–8%), nausea, headache, diarrhea.	Rarely Stevens-Johnson syndrome, hemolytic anemia. Pro-drug of amprenavir. Contains sulfa moiety. Angioedema and nephrolithiasis reported in post-marketing experience. Potential increased risk of MI *(see FDA label)*. Angioedema, oral paresthesias, myocardial infarction and nephrolithiasis reported in post-marketing experience. Elevated LFTs seen with higher than recommended doses; increased risk in those with pre-existing liver abnormalities. Acute hemolytic anemia reported with amprenavir.
Indinavir (Crixivan)	↑ in indirect bilirubin 10–15% (~2.5 mg/dl, with overt jaundice especially likely in those with Gilbert syndrome *(JID 192: 1381, 2005)*. Nausea 12%, vomiting 4%, diarrhea 5%. Metallic taste. Paronychia and ingrown toenails reported *(CID 32:140, 2001)*.	**Kidney stones.** Due to indinavir crystals in collecting system. Nephrolithiasis in 12% of adults, higher in pediatrics. Minimize risk with good hydration (at least 48 oz. water/day) *(AAC 42:332, 1998)*. Tubulointerstitial nephritis/renal cortical atrophy reported in association with asymptomatic ↑ urine WBC. Severe hepatitis reported in 3 cases *(Ln 349:924, 1997)*. Hemolytic anemia reported.
Lopinavir/Ritonavir (Kaletra)	GI: **diarrhea** 14–24%, nausea 2–16%. More diarrhea with q24h dosing	Lipid abnormalities in up to 20–40%. Possible increased risk of MI with cumulative exposure *(JID 201:318, 2010)*. ↑ PR interval, 2° or 3° heart block described. Post-marketing reports of ↑ QTc and torsades: avoid use in congenital QTc prolongation or in other circumstances that prolong QTc or increase susceptibility to torsades. Hepatitis, with hepatic decompensation; caution especially in those with pre-existing liver disease. Pancreatitis. Inflammatory edema of legs *(AIDS 16:673, 2002)*. Stevens-Johnson syndrome & erythema multiforme reported. Note high drug concentration in oral solution. Toxic potential of oral solution (contains ethanol and propylene glycol) in neonates.
Nelfinavir (Viracept)	Mild to moderate **diarrhea** 20%. Oat bran tabs, calcium, or oral anti-diarrheal agents (e.g., loperamide, diphenoxylate/atropine sulfate) can be used to manage diarrhea.	Potential for drug interactions. Powder contains phenylalanine.

TABLE 14D (4)

DRUG NAME(S): GENERIC (TRADE)	MOST COMMON ADVERSE EFFECTS	MOST SIGNIFICANT ADVERSE EFFECTS
Protease inhibitors (PI) *(continued)*		
Ritonavir (Norvir) (Currently, primary use is to enhance levels of other anti-retrovirals, because of ↑ toxicity/ interactions with full-dose ritonavir)	GI: bitter aftertaste ↓ by taking with chocolate milk, Ensure, or Advera; nausea 23%, ↓ by initial dose esc (titration) regimen; vomiting 13%; diarrhea 15%. Circumoral paresthesias 5–6%. Dose >100 mg bid assoc. with ↑ GI side effects & ↑ in lipid abnormalities.	**Black Box** warning relates to many important drug-drug interactions—inhibits P450 CYP3A & CYP2 D6 system—may be life-threatening *(see Table 22A)*. Several cases of iatrogenic Cushing's syndrome reported with concomitant use of ritonavir and corticosteroids, including dosing of the latter by inhalation, epidural injection or a single IM injection. Rarely Stevens-Johnson syndrome, toxic epidermal necrolysis anaphylaxis. Primary A-V block (and higher) and pancreatitis have been reported. Hepatic reactions, including fatalities. Monitor LFTs carefully during therapy, especially in those with pre-existing liver disease, including HBV and HCV.
Saquinavir (Invirase: hard cap, tablet)	**Diarrhea,** abdominal discomfort, nausea, headache	**Warning—Use Invirase only with ritonavir.** Avoid garlic capsules (may reduce SQV levels) and use cautiously with proton-pump inhibitors (increased SQV levels significant. Use of saquinavir/ritonavir can prolong QTc interval or may rarely cause 2° or 3° heart block; torsades reported. Contraindicated in patients with prolonged QTc or those taking drugs or who have other conditions (e.g., low K+ or Mg++) that pose a risk with prolonged QTc *(http://www.fda.gov/drugs/DrugSafety/ucm230096.htm, accessed May 25, 2011)*. Contraindicated in patients with complete AV block, or those at risk, who do not have pacemaker. Hepatic toxicity encountered in patients with pre-existing liver disease or in individuals receiving concomitant rifampin. Rarely, Stevens Johnson syndrome.
Tipranavir (Aptivus)	Nausea & vomiting, diarrhea, abdominal pain. Rash in 8-14%, more common in women, & 33% in women taking ethinyl estradiol. Major lipid effects.	**Black Box Warning—associated with hepatitis & fatal hepatic failure.** Risk of hepatotoxicity increased in hepB or hepC co-infection. Possible photosensitivity skin reactions. Contraindicated in Child-Pugh Class B or C hepatic impairment. **Associated with fatal/nonfatal intracranial hemorrhage (can inhibit platelet aggregation).** Caution in those with bleeding risks. Potential for major drug interactions. Contains sulfa moiety and vitamin E.
Fusion Inhibitor		
Enfuvirtide (T20, Fuzeon)	Local injection site reactions (98% at least 1 local ISR, 4% dc because of ISR) (pain & discomfort, induration, erythema, nodules & cysts, pruritus, & ecchymosis). Diarrhea 32%, nausea 23%, fatigue 20%.	↑ Rate of bacterial pneumonia (3.2 pneumonia events/100 pt yrs), **hypersensitivity reactions** ≤1% (rash, fever, nausea & vomiting, chills, rigors, hypotension, & ↑ serum liver transaminases); can occur with reexposure. Cutaneous amyloid deposits containing enfuvirtide peptide reported in skin plaques persisting after discontinuation of drug *(J Cutan Pathol 39:220, 2012)*.
CCR5 Co-receptor Antagonists		
Maraviroc (Selzentry)	With ARV background: Cough 13%, fever 12%, rash 10%, abdominal pain 8%. Also, dizziness, myalgia, arthralgias. ↑ Risk of URI, HSV infection.	**Black box warning-Hepatotoxicity.** May be preceded by allergic features (rash, ↑eosinophils or ↑IgE levels). Use with caution in pt with HepB or C. Cardiac ischemia/infarction in 1.3%. May cause ↓BP, orthostatic syncope, especially in patients with renal dysfunction. Significant interactions with CYP3A inducers/inhibitors. Long-term risk of malignancy unknown. Stevens-Johnson syndrome reported post-marketing. Generally favorable safety profile during trial of ART-naïve individuals *(JID 201:* 803, 2010).
Integrase Inhibitors		
Raltegravir (Isentress)	Diarrhea, headache, insomnia, nausea. LFT ↑ may be more common in pts co-infected with HBV or HCV.	Hypersensitivity reactions can occur. Rash, Stevens-Johnson syndrome, toxic epidermal necrolysis reported. Hepatic failure reported. ↑CK, myopathy and rhabdomyolysis reported *(AIDS 22:1382, 2008)*. ↑ of preexisting depression reported in 4 pts; all could continue raltegravir after adjustment of psych. meds *(AIDS 22:1890, 2008)*. Chewable tablets contain phenylalanine.
Elvitegravir+ Cobicistat (Stribild), Elvitegravir (Vitekta)	Nausea and diarrhea are the two most common AEs. Increased serum creatinine 0.1-0.15 mg/dL due to inhibition of prox. tubular enzymes by cobicistat with no decrease in GFR.	**Same Black Box warnings as ritonavir and tenofovir (TDF and TAF)**. Rare lactic acidosis syndrome. Owing to renal toxicity, should not initiate Rx when pre-Rx eGFR is < 70 cc/min. Follow serial serum creatinine and urinary protein and glucose. Discontinue drug if serum Cr rises > 0.4 mg/dl above baseline value.
Dolutegravir (Tivicay)	Insomnia and headache (2-4%)	Rash, liver injury reported. Increased ALT/AST in 203%. Competition with creatinine for tubular secretion increased serum creatinine by a mean of 0.1 mg/dL with no change in GFR.

TABLE 14E – HEPATITIS A & HBV TREATMENT

For HBV Activity Spectra, see *Table 4C, page 79*

Hepatitis A Virus (HAV)

1. **Drug/Dosage:** No therapy recommended. If within 2 wks of exposure, prophylactic IVIG 0.02 mL per kg IM times 1 protective. Hep A vaccine equally effective as IVIG in randomized trial and is emerging as preferred Rx *(NEJM 357:1685, 2007)*.

2. **HAV Superinfection:** 40% of pts with chronic Hepatitis C virus (HCV) infection who developed superinfection with HAV developed fulminant hepatic failure *(NEJM 338:286, 1998)*. Similar data in pts with chronic Hepatitis B virus (HBV) infection that suffer acute HAV *(Ann Trop Med Parasitol 93:745, 1999)*. **Hence, need to vaccinate all HBV and HCV pts with HAV vaccine.**

HBV Treatment.

	ALT	HBV DNA	HBe Ag	Recommendation
Immune-Tolerant Phase	Normal	> 1x106 IU/ml	Positive	**Monitor:** ALT levels be tested at least every 6 months for adults with immunetolerant CHB to monitor for potential transition to immune-active or -inactive CHB. **NB: For those over 40 years of age + liver fibrosis, TREAT as Immune Active (below)**
HBeAg+ Immune Active Phase	Elevated	> 20,000 IU/ml	Positive	**TREAT (Duration of therapy+):** Tenofovir (indefinitely; esp. if fibrosis) OR Entecavir (indefinitely; esp. if fibrosis) OR Peg-IFN++ (48 weeks of Rx)
Inactive CHB Phase	Normal	< 2,000 IU/ml	Negative	**Monitor:** ALT levels at least once / year
HBeAg-neg Immune Reactivation Phase	Elevated	> 2,000 IU/ml	Negative	**TREAT (Duration of therapy+):** Tenofovir (indefinitely; esp. if fibrosis) OR Entecavir (indefinitely; esp. if fibrosis) OR Peg-IFN++ (48 weeks of Rx)

\+ Duration of therapy largely unknown; most experts favor indefinite Rx, esp. among those with moderate to advanced fibrosis or inflammation (liver biopsy)

++ Peg-INF contraindicated in patients with decompensated cirrhosis, autoimmune disease, uncontrolled psychiatric disease, cytopenias, severe cardiac disease, and uncontrolled seizures

For details of therapy, especially in special populations (e.g., pregnant women, children) see updated AASLD Guidelines *(Hepatology, 2015 Nov 13. doi: 10.1002/hep.2)*

HBV Treatment Regimens. Single drug therapy is usually sufficient; combination therapy for HIV co-infection.

	Drug/Dose	Comments
Preferred Regimens	**Pegylated-Interferon-alpha 2a** 180 µg sc once weekly OR **Entecavir** 0.5 mg po once daily OR **Tenofovir** 300 mg po once daily OR **Tenofovir alfenamide** 25 mg po once daily	PEG-IFN: Treat for 48 weeks Entecavir: Do not use Entecavir if Lamivudine resistance present. Entecavir/Tenofovir: Treat for at least 24-48 weeks after seroconversion from HBeAg to anti-HBe (if no mod-adv fibrosis present). Indefinite chronic therapy for HBeAg negative patients. Renal impairment dose adjustments necessary.
Alternative Regimens	**Lamivudine** 100 mg po once daily OR **Telbivudine** 600 mg po once daily OR **Emtricitabine** 200 mg po once daily (investigational) OR **Adefovir** 10 mg po once daily	These alternative agents are rarely used except in combination. When used, restrict to short term therapy owing to high rates of development of resistance. Not recommended as first-line therapy. Use of Adefovir has mostly been replaced by Tenofovir.
Preferred Regimen for HIV-HBV Co-infected Patient	**Truvada** (Tenofovir 300 mg + Emtricitabine 200 mg) po once daily + another anti-HIV drug	ALL patients if possible as part of a fully suppressive anti-HIV/anti-HBV regimen. Continue therapy indefinitely.

TABLE 14F – HCV TREATMENT REGIMENS AND RESPONSE

For HCV Activity Spectra, *see Table 4C, page 79*

1. **Indications for Treatment.** Treatment is indicated for all patients with chronic HCV. Rx should be initiated urgently for those with more advanced fibrosis (F3 / F4) and those with underlying co-morbid conditions due to HCV. Type and duration of Rx is based on genotype. Pegylated interferon (Peg-IFN) is no longer a recommended regimen; all DAA regimens with or without ribavirin are the preferred choice.

2. **Definitions of Response to Therapy.**

End of Treatment Response (ETR)	Undetectable at end of treatment.
Relapse	Undetectable at end of therapy (ETR) but rebound (detectable) virus within 12 weeks after therapy stopped.
Sustained Virologic Response (SVR)	CURE! Still undetectable at end of therapy and beyond 12 weeks after therapy is stopped.

3. **HCV Treatment Regimens**

- Biopsy is a "gold standard" for staging HCV infection and is helpful in some settings to determine the ideal timing of HCV treatment. When biopsy not obtained, "non-invasive" tests are often employed to assess the relative probability of advanced fibrosis or cirrhosis. Fibroscan (elastography) is now approved in the US and most of the world as a means of assessing liver fibrosis. Elastography values of > 10 kPa (Kilopascals) correlates with significant fibrosis (F3 or F4 disease).

- Resistance tests: Genotypic resistance assays are available that can determine polymorphisms associated with reduction in susceptibility to some DAAs (Direct Acting Agents, e.g., protease inhibitors). **However, resistance tests are recommended only for those who have failed treatment with a prior NS5A or protease inhibitor regimen.**

- **Patients with decompensated cirrhosis should only be treated by hepatologists owing to the risk of rapid clinical deterioration while receiving treatment for HCV.**

- **IMPORTANT NOTE REGARDING TREATMENT DECISION-MAKING:** Newer drugs are in development and options for Rx are changing rapidly (i.e., several times per year). Monitor updates at *webedition.sanfordguide.com* or *hcvguidelines.org*.

INITIAL TREATMENT FOR PATIENTS WITH CHRONIC HCV

For retreatment and special populations (e.g., decompensated cirrhotics) see *www.hcvguidelines.org*.

Drug	Abbreviation	Formulation/Dose
Daclatasvir	DCL	60 mg tablet once daily (dose adjustment needed for CYP3A4 inhibitors or inducers)
Dasabuvir	DBV	250 mg tablet po twice daily
Paritaprevir + Ritonavir + Ombitasvir	PTV/r/OBV	Fixed dose combination tablet (Paritaprevir 150 mg + Ritonavir 100 mg + Ombitasvir 25 mg) po once daily
Pegylated Interferon (alfa 2a)	PEG-IFN	180 mcg sc per week
Ribavirin	RBV	Weight based dosing: 1000 mg (< 75 kg) or 1200 mg (> 75 kg)) po twice daily
Simeprevir	SMV	150 mg tablet po once daily
Sofosbuvir	SOF	400 mg tablet po once daily
Sofosbuvir + Ledipasvir	SOF/LDV	Fixed dose combination tablet (Sofosbuvir 400 mg + Ledipasvir 90 mg) po once daily

TABLE 14F (2)

Genotype	Recommended	Alternative	Not Recommended
1a	• **(Harvoni) SOF/LDV** x 12 weeks OR • **DCL / SOF** x 12 weeks (24 wks +/- RBV if cirrhosis) OR • **(Viekira Pak) PTV/r/OBV + DBV + RBV X 12** weeks OR • **SOF/SMV ± RBV** x 12 weeks	None	• SOF + RBV x 24 weeks • SOF + PEG-IFN/RBV x 12 weeks • SMV + PEG-IFN/RBV X 24 or 48 weeks (RGT) TVR + PEG-IFN/RBV x 24 or 48 weeks (RGT) • BOC + PEG-IFN/RBV x 28 or 48 weeks (RGT) • PEG-IFN/RBV x 48 weeks • Monotherapy with PEG-IFN, RBV, or a DAA Do not treat with PEG-IFN or combination DAA regimens. See www.hcvguidelines.org
1b	• **(Harvoni) SOF/LDV** x 12 weeks * OR • **DCL / SOF** x 12 weeks (24 wks +/- RBV if cirrhosis) OR • **(Viekira Pak) PTV/r/OBV + DBV ± RBV** (cirrhosis) X 12 weeks OR • **SOF + SMV** x 12 weeks	None	
2	• **SOF + RBV** x 12-16 weeks (if cirrhosis: extend course) OR • **DCL / SOF** x 12 weeks	None	• PEG-IFN/RBV x 24 weeks • Monotherapy with PEG-IFN, RBV or a DAA • Any regimen with TVR, BOC or SMV
3	• **DCL / SOF** x 12 weeks (24 wks +/- RBV if cirrhosis) OR • **SOF + RBV** x 24 weeks	**SOF + PEG-IFN/RBV** x 12 weeks	• PEG-IFN/RBV x 24 -48 weeks • Monotherapy with PEG-IFN, RBV or a DAA • Any regimen with TVR, BOC or SMV
4	• **(Technivie) PTV/r/OBV + RBV** x 12 weeks OR • **SOF + RBV** x 24 weeks OR • **(Harvoni) SOF/LDV** x 12 weeks	• **SOF + PEG-IFN/RBV** x 12 weeks • **SOF/SMV +/- RBV** x 12 weeks	• SMV x 12 weeks + PEG-IFN/RBV x 24-48 weeks • SMV x 12 weeks + PEG-IFN/RBV x 24-48 weeks • Monotherapy with PEG-IFN, RBV, or a DAA • Any regimen with TVR or BOC
5	**SOF + PEG-IFN + RBV** x 12 weeks	**PEG-IFN + RBV** x 48 weeks	• Monotherapy with PEG-IFN, RBV, or a DAA • Any regimen with TVR or BOC
6	**(Harvoni) SOF/LDV** x 12 weeks	**SOF + PEG-IFN + RBV** x 12 weeks	

* 8 weeks of therapy can be used in selected patients (see www.hcvguidelines.org); not applicable to those with HIV-HCV coinfection

The regimens will change. For updates go to: webedition.sanfordguide.com and www.hcvguidelines.org

TABLE 15A – ANTIMICROBIAL PROPHYLAXIS FOR SELECTED BACTERIAL INFECTIONS*

CLASS OF ETIOLOGIC AGENT/DISEASE/CONDITION	PROPHYLAXIS AGENT/DOSE/ROUTE/DURATION	COMMENTS
Group B streptococcal disease (GBS), neonatal: Approaches to management [CDC Guidelines, *MMWR 59 (RR-10):1, 2010*]:		
Pregnant women—Intrapartum antimicrobial prophylaxis procedures: 1. Screen all pregnant women with vaginal & rectal swab for GBS at 35–37 wks gestation (unless other indications for prophylaxis exist: GBS bacteriuria during this pregnancy or previously delivered infant with invasive GBS disease; even then cultures may be useful for susceptibility testing). Use transport medium; GBS survive at room temp. up to 96 hrs. **Rx during labor if swab culture positive.** 2. Rx during labor if previously delivered infant with invasive GBS infection, or if any GBS bacteriuria during this pregnancy. 3. Rx if GBS status unknown but if any of the following are present: (a) delivery at <37 wks gestation [see *MMWR 59 (RR-10): 1, 2010* algorithms for preterm labor and preterm premature rupture of membranes]; or (b) duration of ruptured membranes ≥18 hrs; or (c) intrapartum temp. ≥100.4°F (≥38.0°C). If amnionitis suspected, broad-spectrum antibiotic coverage should include an agent active vs. group B streptococci. 4. Rx if positive intra-partum NAAT for GBS. 5. Rx not indicated if: negative vaginal/rectal cultures at 35-37 wks gestation or C-section performed before onset of labor with intact amniotic membranes (use standard surgical prophylaxis).		**Regimens for prophylaxis against early-onset group B streptococcal disease in neonate used during labor:** **Penicillin G** 5 million Units IV (initial dose) then 2.5 to 3 million Units IV q4h until delivery Alternative: **Ampicillin** 2 gm IV (initial dose) then 1 gm IV q4h until delivery Penicillin-allergic patients: • Patient not at high risk for anaphylaxis: **Cefazolin** 2 gm IV (initial dose) then 1 gm IV q8h until delivery • Patient at high risk for anaphylaxis from β lactams: □ If organism is both clindamycin- and erythromycin-susceptible, **or** is erythromycin-resistant, but clindamycin-susceptible confirmed by D-zone test (or equivalent) showing lack of inducible resistance: **Clindamycin** 900 mg IV q8h until delivery □ If susceptibility of organism unknown, lack of inducible resistance to clindamycin has not been excluded, or patient is allergic to clindamycin: **Vancomycin** 1 gm IV q12h until delivery
Neonate of mother given prophylaxis	*See detailed algorithm in MMWR 59 (RR-10):1, 2010.*	
Preterm, premature rupture of the membranes: Grp B strep-negative women Cochrane Database Rev *12:CD00:1058, 2013;* *Obstet Gyn 124:515:2014;* *Am J Ob-Gyn 207:475. 2012.*	(**AMP** 2 gm IV q6h + **Erythro** 250 mg IV q6h) x 48 hrs, then (**Amox** 250 mg po q8h + **Erythro base** 333 mg po q8h) x 5 days	
Post-splenectomy bacteremia. Usually encapsulated bacteria: pneumococci, meningococci, H. flu type B; bacteremia: Enterobacter, S. aureus, Capnocytophaga, P. aeruginosa. Also at risk for fatal malaria, severe babesiosis	Protein conjugate pneumococcal (followed by polysaccharide vaccine at least 8 wks later in those age 2 yrs or older) H. influenza type B and meningococcal vaccine (CID 58:309, 2014); persons age 10 yrs or older should also receive meningococcal B vaccine *(MMWR 64:608, 2015)*. Daily Prophylaxis in asplenic child (daily until age 5 yrs or minimum of 1 yr rx): **Amox** 125 mg po bid (age 2mo-3yr); **Amox** 250 mg po bid (age >3yr-5 yr). If allergic, e.g. rash only: **Cephalexin** 250 mg po bid. If IgE-mediated reaction, no good choice. Fever in Children & Adults: **AM-CL** 875/125 po bid (adult), 90 mg/kg po div bid (child); Alternative: (**Levo** 750 mg po or **Moxl** 400 mg po) once daily. Seek immediate medical care. Some recommend **Amox** 2 gm po before sinus or airway procedures.	

TABLE 15A (2)

CLASS OF ETIOLOGIC AGENT/DISEASE/CONDITION	PROPHYLAXIS AGENT/DOSE/ROUTE/DURATION	COMMENTS
Sexual Exposure		
Sexual assault survivor [likely agents and risks, see *CDC Guidelines at MMWR 64(RR-3):1, 2015].* For review of overall care: *NEJM 365:834, 2011.*	[**Ceftriaxone** 250 mg IM + **Azithro** 1 gm po once + (**Metro** 2 gm po once or **Tinidazole** 2 gm po once)]. Can delay Metro/Tinidazole if alcohol was recently ingested.	• Obtain expert individualized advice re: forensic exam and specimens, pregnancy (incl. emergency contraception), physical trauma, psychological support • Test for chlamydia and gonococci at sites of penetration or attempted penetration by NAATs. Obtain molecular tests for trichomonas and check vaginal secretions for BV and candidiasis. • Serological evaluation for syphilis, HIV, HBV, HCV • Initiate post-exposure protocols for HBV vaccine, HIV post-exposure prophylaxis as appropriate • HPV vaccine recommended for females 9-26 or males 9-21, if not already immunized • Follow-up in 1 week to review results, repeat negative tests in 1-2 weeks to detect infections not detected previously, repeat syphilis testing 4-6 weeks and 3 months, repeat HIV testing 6 weeks and 3-6 months. • Check for anogenital warts at 1-2 months. Notes: If ceftriaxone not available, can use cefixime 400 mg po once in its place for prevention of gonorrhea, but the latter is less effective for pharyngeal infection and against strains with reduced susceptibility to cephalosporins. For non-pregnant individuals who cannot receive cephalosporins, treatment with (Gemi 320 mg po once + azithro 2 gm po once) or (gent 240 mg IM once + azithro 2 gm po once) can be substituted for ceftriaxone/ azithro.
Contact with specific sexually transmitted diseases	See comprehensive guidelines for specific pathogens in *MMWR 59 (RR-10): 1, 2010.*	
Syphilis exposure		Presumptive rx for exposure within 3 mos., as tests may be negative. *See Table 1, page 24.* If exposure occurred > 90 days prior, establish dx or treat empirically *(MMWR 59 (RR-12): 1, 2010).*
Sickle-cell disease. Likely agent: S. pneumoniae *(see post-splenectomy, above)* Ref.: *2009 Red Book Online, Amer Acad Pediatrics*	Children <5 yrs: **Penicillin V** 125 mg po bid ≥5 yrs: **Penicillin V** 250 mg po bid. (Alternative in children: Amoxicillin 20 mg per kg per day)	Start prophylaxis by 2 mos. *(Pediatrics 106:367, 2000);* continue until at least age 5. When to d/c must be individualized. Age-appropriate vaccines, including pneumococcal, Hib, influenza, meningococcal. Treating infections, consider possibility of penicillin non-susceptible pneumococci.

TABLE 15B – ANTIBIOTIC PROPHYLAXIS TO PREVENT SURGICAL INFECTIONS IN ADULTS*

2013 Guidelines: Am J Health Syst Pharm 70:195, 2013

General Comments:

- To be optimally effective, antibiotics must be started within 60 minutes of the surgical incision. Vancomycin and FQs may require 1-2 hr infusion time, so start dose 2 hrs before the surgical incision.
- Most applications employ a single preoperative dose or continuation for less than 24 hrs.
- For procedures lasting > 2 half-lives of prophylactic agent, intraoperative supplementary dose(s) may be required.
- Dose adjustments may be desirable in pts with BMI ~ 30.
- Prophylaxis does carry risk: e.g., C. difficile colitis, allergic reactions
- Active S. aureus screening, decolonization & customized antimicrobial prophylaxis demonstrated efficacious in decreasing infections after hip, knee & cardiac surgery *(JAMA 313:2131 & 2162, 2015).*
- In general, recommendations are consistent with those of the Surgical Care Improvement Project (SCIP)

Use of Vancomycin:

- For many common prophylaxis indications, vancomycin is considered an alternative to β-lactams in pts allergic to or intolerant of the latter.
- Vancomycin use may be justifiable in centers where rates of post-operative infection with methicillin-resistant staphylococci are high or in pts at high risk for these.
- Unlike β-lactams in common use, vancomycin has no activity against gram-negative organisms. **When gram-negative bacteria are a concern following specific procedures, it may be necessary or desirable to add a second agent with appropriate in vitro activity.** This can be done using cefazolin with vancomycin in the non-allergic pt, or in pts intolerant of β-lactams using vancomycin with another gram-negative agent (e.g., aminoglycoside, fluoroquinolone, possibly aztreonam, if pt not allergic; local resistance patterns and pt factors would influence choice).
- Infusion of vancomycin, especially too rapidly, may result in hypotension or other manifestations of histamine release (red person syndrome). Does not indicate an allergy to vancomycin.

TABLE 15B (2)

TYPE OF SURGERY	PROPHYLAXIS	COMMENTS
Cardiovascular Surgery Antibiotic prophylaxis in cardiovascular surgery has been proven beneficial in the following procedures: • Reconstruction of abdominal aorta • Procedures on the leg that involve a groin incision • Any vascular procedure that inserts prosthesis/foreign body • Lower extremity amputation for ischemia • Cardiac surgery • Permanent Pacemakers *(Circulation 121:458, 2010)* • Heart transplant • Implanted cardiac defibrillators	**Cefazolin** 1–2 gm (Wt <120 kg) or 3 gm (Wt >120 kg) IV as a single dose or q8h for 1–2 days or **cefuroxime** 1.5 gm IV as a single dose or q12h for total of 6 gm or **vancomycin** 1 gm IV as single dose or q12h for 1–2 days. For pts weighing > 90 kg, use vanco 1.5 gm IV as a single dose or q12h for 1-2 days. Re-dose cefazolin q4h if CrCl>30 mL/min or q8h if CrCl ≤30 mL/min Consider **intranasal mupirocin** evening before, day of surgery & bid for 5 days post-op in pts with pos. nasal culture for S. aureus. Mupirocin resistance has been encountered.	**Timing & duration:** Single infusion just before surgery as effective as multiple doses. No prophylaxis needed for cardiac catheterization. For prosthetic heart valves, customary to stop prophylaxis either after removal of retrosternal drainage catheters or just a 2nd dose after coming off bypass. **Vancomycin** may be preferable in hospitals with ↑ freq of MRSA, in high-risk pts, those colonized with MRSA or for Pen-allergic pts. Clindamycin 900 mg IV is another alternative for Pen-allergic or Vanco-allergic pt. Implanted devices ref: *JAC 70:325, 2015.*
Gastric, Biliary and Colonic Surgery **Gastroduodenal/Biliary** Gastroduodenal, includes percutaneous endoscopic gastrostomy (high risk only), pancreaticoduodenectomy (Whipple procedure)	**Cefazolin** (1-2 gm IV) or **cefoxitin** (1-2 gm IV) or **cefotetan** (1-2 gm IV) or **ceftriaxone** (2 gm IV) as a single dose (some give additional doses q12h for 2–3 days). *See Comment*	Gastroduodenal (PEG placement): High-risk is marked obesity, obstruction, ↓ gastric acid or ↓ motility. Re-dose cefazolin q4h and cefoxitin q2h if CrCl >30 mL/min; q8h and q4h, respectively, if CrCl ≤30 ml/min
Biliary, includes laparoscopic cholecystectomy	Low risk, laparoscopic: No prophylaxis Open cholecystectomy: **cefazolin, cefoxitin, cefotetan, ampicillin-sulbactam**	Biliary high-risk or open procedure: age >70, acute cholecystitis, non-functioning gallbladder, obstructive jaundice or common duct stones. With cholangitis, treat as infection, not prophylaxis.
Endoscopic retrograde cholangiopancreatography	No rx without obstruction. If obstruction: **Ciprofloxacin** 500–750 mg po or 400 mg IV 2 hrs prior to procedure or **PIP-TZ** 4.5 gm IV 1 hr prior to procedure	Most studies show that **achieving adequate drainage** will prevent post-procedural cholangitis or sepsis and no further benefit from prophylactic antibiotics; greatest benefit likely when complete drainage cannot be achieved. *See Gastroint Endosc 67:791, 2008; Gut 58:868, 2009.*
Colorectal Recommend combination of: • Mechanical bowel prep • PO antibiotic (See Comment) • IV antibiotic	**Parenteral regimens** (emergency or elective): [**Cefazolin** 1-2 gm IV + **metronidazole** 0.5 gm IV] *(see Comment)* or **cefoxitin** or **cefotetan** 1-2 gm IV (if available) or **Ceftriaxone** 2 gm IV + **Metro** 0.5 gm IV or **ERTA** 1 gm IV Beta-lactam allergy, see *Comment*	**Oral regimens: Neomycin** + **erythromycin.** Pre-op day: (1) 10 am 4L polyethylene glycol electrolyte solution (Colyte, GoLYTELY) po over 2 hr. (2) Clear liquid diet only. (3) 1 pm, 2 pm & 11 pm, neomycin 1 gm + erythro base 1 gm po. (4) NPO after midnight. Alternative regimens have been less well studied; GoLYTELY 1–6 pm, then neomycin 2 gm po + metronidazole 2 gm po at 7 pm & 11 pm. Oral regimen as effective as parenteral; parenteral in addition to oral not required but often used *(Am J Surg 189:395, 2005).* Study found **Ertapenem** more effective than cefotetan, but associated with non-significant ↑ risk of C. difficile *(NEJM 355:2640, 2006).* **Beta lactam allergy: Clindamycin** 900 mg IV + (**Gentamicin** 5 mg/kg or **Aztreonam** 2 gm IV or **Ciprofloxacin** 400 mg IV)
Ruptured viscus: *See Peritoneum/Peritonitis, Secondary, Table 1, page 47.*		

TABLE 15B (3)

TYPE OF SURGERY	PROPHYLAXIS	COMMENTS
Head and Neck Surgery		
	Cefazolin 2 gm IV (Single dose) (some add **metronidazole** 500 mg IV) **OR** **Clindamycin** 600-900 mg IV (single dose) ± **gentamicin** 5 mg/kg IV (single dose) *(See Table 10D for weight-based dose calculation).*	Antimicrobial prophylaxis in head & neck surg appears efficacious only for procedures involving oral/ pharyngeal mucosa (e.g., laryngeal or pharyngeal tumor) but even with prophylaxis, wound infection rate can be high. **Clean, uncontaminated head & neck surg does not require prophylaxis.** Re-dose cefazolin q4h if CrCl>30 mL/min or q8h if CrCl ≤30 mL/min
Neurosurgical Procedures		
Clean, non-implant; e.g., elective craniotomy	**Cefazolin** 1-2 gm IV once. Alternative: **vanco** 1 gm IV once; for pts weighing > 90 kg, use vanco 1.5 gm IV as single dose.	Clindamycin 900 mg IV is alternative for vanco-allergic or beta-lactam allergic pt. Re-dose cefazolin q4h if CrCl>30 mL/min or q8h if CrCl ≤30 mL/min
Clean, contaminated (cross sinuses, or naso/oropharynx)	**Clindamycin** 900 mg IV (single dose)	British recommend amoxicillin-clavulanate 1.2 gm IV[NUS] or (cefuroxime 1.5 gm IV + metronidazole 0.5 gm IV)
CSF shunt surgery, intrathecal pumps:	**Cefazolin** 1-2 gm (Wt <120 kg) or 3 gm (Wt > 120 kg) IV once. Alternative: **vanco** 1 gm IV once; for pts weighing > 90 kg, use vanco 1.5 gm IV as single dose OR **Clindamycin** 900 mg IV.	Randomized study in a hospital with high prevalence of infection due to methicillin-resistant staphylococci showed vancomycin was more effective than cefazolin in preventing CSF shunt infections *(J Hosp Infect 69:337, 2008).* Re-dose cefazolin q4h if CrCl>30 mL/min or q8h if CrCl ≤30 mL/min
Obstetric/Gynecologic Surgery		
Vaginal or abdominal hysterectomy	**Cefazolin** 1–2 gm or **cefoxitin** 1–2 gm or **cefotetan** 1–2 gm or **ampicillin-sulbactam** 3 gm IV 30 min. before surgery.	Alternative: (**Clindamycin** 900 mg IV or **Vancomycin** 1 gm IV) + (**Gentamicin** 5 mg/kg x 1 dose or **Aztreonam** 2 gm IV or **Ciprofloxacin** 400 mg IV) OR (**Metronidazole** 500 mg IV + **Ciprofloxacin** 400 mg IV)
Cesarean section for premature rupture of membranes or active labor	**Cefazolin** 1-2 gm IV *(See Comments).* Alternative: **Clindamycin** 900 mg IV + (**Gentamicin** 5 mg/kg IV or **Tobramycin** 5 mg/kg IV) x 1 dose	Prophylaxis decreases risk of endometritis and wound infection. Traditional approach had been to administer antibiotics after cord is clamped to avoid exposing infant to antibiotic. However, studies suggest that administering prophylaxis before the skin incision results in fewer surgical site infections *(Obstet Gynecol 115:187, 2010; Amer J Obstet Gynecol 199:301.e1 and 310:e1, 2008)* and endometritis *(Amer J Obstet Gynecol 196:455.e1, 2007).*
Surgical Abortion (1st trimester)	1st trimester: **Doxycycline** 300 mg po: 100 mg 1 hr before procedure + 200 mg post-procedure.	Meta-analysis showed benefit of antibiotic prophylaxis in all risk groups.
Orthopedic Surgery		
Hip arthroplasty, spinal fusion	Same as cardiac surgery	Customarily stopped after "Hemovac" removed. 2013 Guidelines recommend stopping prophylaxis within 24 hrs of surgery *(Am J Health Syst Pharm 70:195, 2013).*
Total joint replacement (other than hip)	**Cefazolin** 1–2 gm IV pre-op (± 2nd dose) or **vancomycin** 1 gm IV. For pts weighing > 90 kg, use vanco 1.5 gm IV as single dose or **Clindamycin** 900 mg IV.	2013 Guidelines recommends stopping prophylaxis within 24 hrs of surgery *(Am J Health Syst Pharm 70:195, 2013).* Usual to administer before tourniquet inflation. Intranasal mupirocin if colonized with S. aureus.
Open reduction of closed fracture with internal fixation	**Ceftriaxone** 2 gm IV once	3.6% (ceftriaxone) vs 8.3% (for placebo) infection found in Dutch trauma trial *(Ln 347:1133, 1996).* Several alternative antimicrobials can ↓ risk of infection *(Cochrane Database Syst Rev 2010: CD 000244).*

TABLE 15B (4)

TYPE OF SURGERY	PROPHYLAXIS	COMMENTS
Orthop. Surgery, (cont'd) Prophylaxis to protect prosthetic joints from hematogenous infection related to distant procedures (patients with plates, pins and screws only are not considered to be at risk)	• A prospective, case-control study concluded that antibiotic prophyfaxis for dental procedures did not decrease the risk of hip or knee prosthesis infection *(Clin Infect Dis 50:8, 2010).* • An expert panel of the American Dental Association concluded that, in general, prophylactic antibiotics are not recommended prior to dental procedures to prevent prosthetic joint infection *(J Amer Dental Assoc 146: 11, 2015).* • Individual circumstances should be considered; when there is planned manipulation of tissues thought to be actively infected, antimicrobial therapy for the infection is likely to be appropriate.	
Peritoneal Dialysis Catheter Placement	**Vancomycin** single 1 gm IV dose 12 hrs prior to procedure	Effectively reduced peritonitis during 14 days post-placement in 22 f pts: vanco 1%, cefazolin 7%, placebo 12% (p=0.02) *(Am J Kidney Dis 36:1014, 2000).*
Urologic Surgery/Procedures • *See Best Practice Policy Statement* of Amer. Urological Assoc. (AUA) *(J Urol 179:1379, 2008)* and 2013 Guidelines *(Am J Health Syst Pharm 70:195, 2013).* • Selection of agents targeting urinary pathogens may require modification based on local resistance patterns; ↑ TMP-SMX and/or fluoroquinolone (FQ) resistance among enteric gram-negative bacteria is a concern.		
Cystoscopy	• Prophylaxis generally not necessary if urine is sterile (however, AUA recommends FQ or TMP-SMX for those with several potentially adverse host factors (e.g., advanced age, immunocompromised state, anatomic abnormalities, etc.) • Treat patients with UTI prior to procedure using an antimicrobial active against pathogen isolated	
Cystoscopy with manipulation	**Ciprofloxacin** 500 mg po (**TMP-SMX** 1 DS tablet po may be an alternative in populations with low rates of resistance)	Procedures mentioned include ureteroscopy, biopsy, fulguration, TURP, etc. Treat UTI with targeted therapy before procedure if possible.
Transrectal prostate biopsy	**Ciprofloxacin** 500 mg po 12 hrs prior to biopsy and repeated 12 hrs after 1st dose. *See Comment.*	Bacteremia 7% with **CIP** vs 37% with **gentamicin** *(JAC 39:115, 1997).* **Levofloxacin** 500 mg 30-60 min before procedure was effective in low risk pts; additional doses were given for ↑ risk *(J Urol 168:1021, 2002).* Serious bacteremias due to FQ-resistant organisms have been encountered in patients receiving FQ prophylaxis. Screening stool cultures pre-procedure for colonization with FQ-resistant organisms is increasingly utilized to inform choice of prophylaxis *(Clin Infect Dis 60: 979, 2015).* One study showed non-significant decrease in risk of infection with culture-directed antimicrobiaf prophylaxis *(Urology 146: 11, 2015).* Pre-operative prophylaxis should be determined on an institutional basis based on susceptibility profiles of prevailing organisms. Although 2nd or 3rd generation Cephalosporins or addition of single-dose gentamicin has been suggested, infections due to ESBL-producing and gent-resistant organisms have been encountered *(Urol 74:332, 2009).*
Other Breast surgery, herniorrhaphy	**Cefazolin** 1-2 gm IV x 1 dose or **Ampicillin-sulbactam** 3 gm IV x 1 dose or **Clindamycin** 900 mg IV x 1 dose or **Vancomycin** 1 gm IV x 1 dose (1.5 gm if wt > 90 kg)	*Am J Health Syst Pharm 70:195, 2013.*

TABLE 15C – ANTIMICROBIAL PROPHYLAXIS FOR THE PREVENTION OF BACTERIAL ENDOCARDITIS IN PATIENTS WITH UNDERLYING CARDIAC CONDITIONS*

In 2007, the American Heart Association guidelines for the prevention of bacterial endocarditis were updated. The resulting document *(Circulation 2007; 116:1736-1754 and http://circ.ahajournals.org/cgi/reprint/116/15/1736)*, which was also endorsed by the Infectious Diseases Society of America, represents a significant departure from earlier recommendations.

- Antibiotic prophylaxis for dental procedures is now directed at individuals who are likely to suffer the most devastating consequences should they develop endocarditis. Prophylaxis to prevent endocarditis is no longer specified for gastrointestinal or genitourinary procedures. The following is adapted from and reflects the new AHA recommendations. *See original publication for explanation and precise details.*

SELECTION OF PATIENTS FOR ENDOCARDITIS PROPHYLAXIS

FOR PATIENTS WITH ANY OF THESE HIGH-RISK CARDIAC CONDITIONS ASSOCIATED WITH ENDOCARDITIS:	WHO UNDERGO DENTAL PROCEDURES INVOLVING:	WHO UNDERGO INVASIVE RESPIRATORY PROCEDURES INVOLVING:	WHO UNDERGO INVASIVE PROCEDURES OF THE GI OR GU TRACTS:	WHO UNDERGO PROCEDURES INVOLVING INFECTED SKIN AND SOFT TISSUES:
Prosthetic heart valves Previous infective endocarditis Congenital heart disease with any of the following: • Completely repaired cardiac defect using prosthetic material (Only for 1st 6 months) • Partially corrected but with residual defect near prosthetic material • Uncorrected cyanotic congenital heart disease • Surgically constructed shunts and conduits Valvulopathy following heart transplant	Any manipulation of gingival tissue, dental periapical regions, or perforating the oral mucosa. **PROPHYLAXIS RECOMMENDED‡** *(see Dental Procedures Regimens table below)* (Prophylaxis is *not* recommended for routine anesthetic injections (unless through infected area), dental x-rays, shedding of primary teeth, adjustment of orthodontic appliances or placement of orthodontic brackets or removable appliances.)	Incision of respiratory tract mucosa **CONSIDER PROPHYLAXIS** *(see Dental Procedures Regimens table)* Or For treatment of established infection **PROPHYLAXIS RECOMMENDED** *(see Dental Procedures Regimens table for oral flora, but include anti-staphylococcal coverage when S. aureus is of concern)*	PROPHYLAXIS is no longer recommended solely to prevent endocarditis, **but the following approach is reasonable:** For patients with enterococcal UTIs • treat before elective GU procedures • include enterococcal coverage in perioperative regimen for non-elective procedures† For patients with existing GU or GI infections or those who receive perioperative antibiotics to prevent surgical site infections or sepsis • it is reasonable to include agents with anti-enterococcal activity in perioperative coverage†.	Include coverage against staphylococci and β-hemolytic streptococci in treatment regimens

† Agents with anti-enterococcal activity include penicillin, ampicillin, amoxicillin, vancomycin and others. Check susceptibility if available. *(See Table 5 for highly resistant organisms.)*
‡ 2008 AHA/ACC focused update of guidelines on valvular heart disease use term "is reasonable" to reflect level of evidence *(Circulation 118:887, 2008)*.

PROPHYLACTIC REGIMENS FOR DENTAL PROCEDURES

SITUATION	AGENT	REGIMEN[1]
Usual oral prophylaxis	Amoxicillin	Adults 2 gm, children 50 mg per kg; orally, 1 hour before procedure
Unable to take oral medications	Ampicillin[2]	Adults 2 gm, children 50 mg per kg; IV or IM, within 30 min before procedure.
Allergic to penicillins	Cephalexin[3] OR	Adults 2 gm, children 50 mg per kg; orally, 1 hour before procedure
	Clindamycin OR	Adults 600 mg, children 20 mg per kg; orally, 1 hour before procedure
	Azithromycin or clarithromycin	Adults 500 mg, children 15 mg per kg; orally, 1 hour before procedure
Allergic to penicillins and unable to take oral medications	Cefazolin[3] OR	Adults 1 gm, children 50 mg per kg; IV or IM, within 30 min before procedure
	Clindamycin	Adults 600 mg, children 20 mg per kg; IV or IM, within 30 min before procedure

[1] Children's dose should not exceed adult dose. AHA document lists all doses as 30-60 min before procedure.
[2] AHA lists cefazolin or ceftriaxone (at appropriate doses) as alternatives here.
[3] Cephalosporins should not be used in individuals with immediate-type hypersensitivity reaction (urticaria, angioedema, or anaphylaxis) to penicillins or other β-lactams. AHA proposes ceftriaxone as potential alternative to cefazolin; and other 1st or 2nd generation cephalosporin in equivalent doses as potential alternatives to cephalexin.

TABLE 15O – MANAGEMENT OF EXPOSURE TO HIV-1 AND HEPATITIS B ANO C*

OCCUPATIONAL EXPOSURE TO BLOOO, PENILE/VAGINAL SECRETIONS OR OTHER POTENTIALLY INFECTIOUS BOOY FLUIDS OR TISSUES WITH RISK OF TRANSMISSION OF HEPATITIS B/C ANO/OR HIV-1 (E.G., NEEOLESTICK INJURY)

Free consultation for occupational exposures, call (PEPline) 1-888-448-4911. *[Information also available at www.aidsinfo.nih.gov]*

General steps In management:

1. Wash clean wounds/flush mucous membranes immediately (use of caustic agents or squeezing the wound is discouraged; data lacking regarding antiseptics).
2. Assess risk by doing the following: (a) Characterize exposure; (b) Determine/evaluate source of exposure by medical history, risk behavior, & testing for hepatitis B/C, HIV; (c) Evaluate and test exposed individual for hepatitis B/C & HIV.

Hepatitis B Occupational Exposure Prophylaxis *(MMWR 62(RR-10):1-19, 2013)*

Exposed Person Vaccine Status	Exposure Source		
	HBs Ag+	HBs Ag–	Status Unknown or Unavailable for Testing†
Unvaccinated	Give HBIG 0.06 mL per kg IM & initiate HB vaccine	Initiate HB vaccine	Initiate HB vaccine
Vaccinated (antibody status unknown)	Do anti-HBs on exposed person: If titer ≥10 milli-International units per mL, no rx If titer <10 milli-International units per mL, give HBIG + 1 dose HB vaccine**	No rx necessary	Do anti-HBs on exposed person: If titer ≥10 milli-International units per mL, no rx § If titer <10 milli-International units per mL, give 1 dose of HB vaccine**

§ Persons previously infected with HBV are immune to reinfection and do not require postexposure prophylaxis.

For known vaccine series responder (titer ≥10 milli-International units per mL), monitoring of levels or booster doses not currently recommended. Known non-responder (<10 milli-International units per mL) to 1° series HB vaccine & exposed to either HBsAg+ source or suspected high-risk source—rx with HBIG & re-initiate vaccine series **or** give 2 doses HBIG 1 month apart. For non-responders after a 2nd vaccine series, 2 doses HBIG 1 month apart is preferred approach to new exposure.

If known high risk source, treat as if source were HBsAG positive
** Follow-up to assess vaccine response or address completion of vaccine series.

Hepatitis B Non-Occupational Exposure & Reactivation of Latent Hepatitis B

Non-Occupational Exposure *(MMWR 59(RR-10):1, 2010)*

- Exposure to blood or sexual secretion of HBsAg-positive person
  - o Percutaneous (bite, needlestick)
  - o Sexual assault
- Initiate immunoprophylaxis within 24 hrs or sexual exposure & no more than 7 days after parenteral exposure
- Use Guidelines for occupational exposure for use of HBIG and HBV vaccine

TABLE 15D (2)

Hepatitis B Non-Occupational Exposure & Reactivation of Latent Hepatitis B *(continued)*

Reactivation of Latent HBV *(Eur J Cancer 49:3486, 2013; Seminar of Liver Dis 33:167, 2013; Crit Rev Oncol-Hematol 87:12, 2013)*

- Patients requiring administration of anti-CD 20 monoclonal antibodies as part of treatment selected malignancies, rheumatoid arthritis and vasculitis are at risk for reactivation of latent HBV
- Two FDA-approved anti-CD 20 drugs: ofatumumab (Arzerra) & rituximab (Rituxan)
- Prior to starting anti-CD 20 drug, test for latent HBV with test for HBsAg and Anti IgG HB core antibody
- If pt has latent HBV & anti-CD 20 treatment is necessary, treatment should include an effective anti-HBV drug

Hepatitis C Exposure

Determine antibody to hepatitis C for both exposed person &, if possible, exposure source. If source + or unknown and exposed person negative, follow-up HCV testing for HCV RNA (detectable in blood in 1-3 weeks) and HCV antibody (90% who seroconvert will do so by 3 months) is advised. **No recommended prophylaxis;** immune serum globulin not effective. Monitor for early infection, as therapy may ↓ risk of progression to chronic hepatitis. Persons who remain viremic 8-12 weeks after exposure should be treated with a course of pegylated interferon *(Gastro 130:632, 2006 and Hpt 43:923, 2006). See Table 14F.* Case-control study suggested risk factors for occupational HCV transmission include percutaneous exposure to needle that had been in artery or vein, deep injury, male sex of HCW, & was more likely when source VL >6 log10 copies/mL.

HIV: Occupational exposure management *[Adapted from CDC recommendations, Infect Control Hosp Epi 34: 875, 2014*

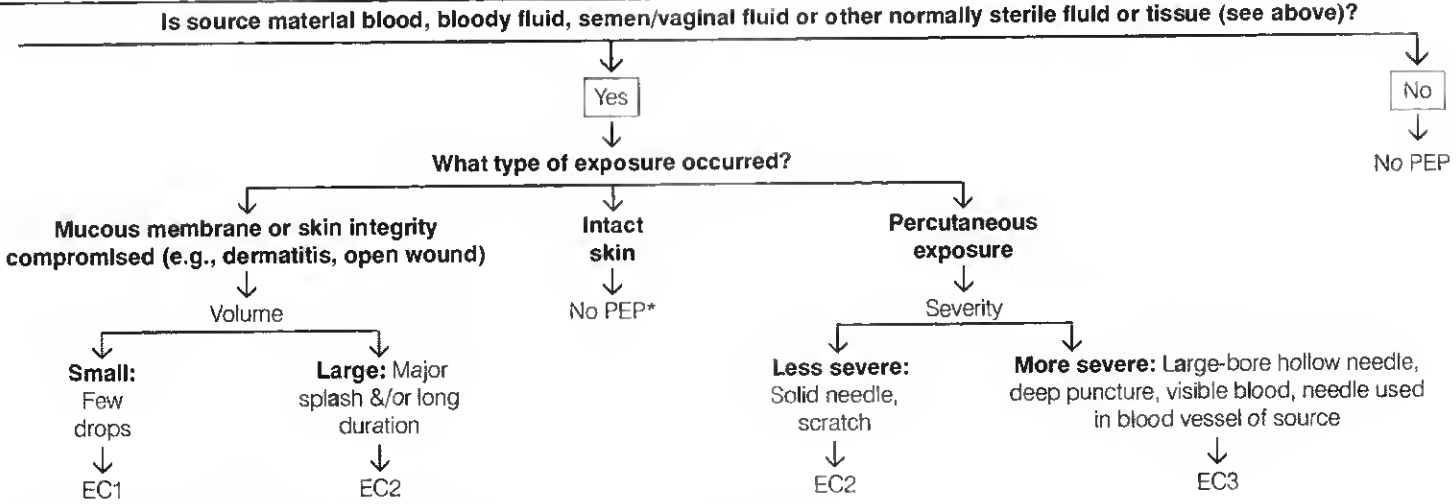
- The decision to initiate postexposure prophylaxis (PEP) for HIV is a clinical judgment that should be made in concert with the exposed healthcare worker (HCW). It is based on:
  1. Likelihood of the source patient having HIV infection: ↑ with history of high-risk activity—injection drug use, sexual activity with known HIV+ person, unprotected sex with multiple partners (either hetero- or homosexual), receipt of blood products 1978–1985. ↑ with clinical signs suggestive of advanced HIV (unexplained wasting, night sweats, thrush, seborrheic dermatitis, etc.).
  2. Type of exposure (approx. 1 in 300–400 needlesticks from infected source will transmit HIV).
  3. Limited data regarding efficacy of PEP *(Cochrane Database Syst Rev. Jan 24; (1):CD002835, 2007).*
  4. Significant adverse effects of PEP drugs & potential for drug interactions.

  Substances considered potentially infectious include: blood, tissues, semen, vaginal secretions, CSF, synovial, pleural, peritoneal, pericardial and amniotic fluids; and other visibly bloody fluids. Fluids normally considered low risk for transmission, unless visibly bloody, include: urine, vomitus, stool, sweat, saliva, nasal secretions, tears and sputum.
- If source person is **known positive for HIV** or **likely to be infected** and **status of exposure warrants PEP,** antiretroviral drugs should be started **immediately.** If source person is HIV antibody negative, drugs can be stopped **unless source is suspected of having acute HIV infection.** The HCW should be re-tested at **3–4 weeks, 3 & 6 months whether PEP is used or not** (the vast majority of seroconversions will occur by 3 months; delayed conversions after 6 months are exceedingly rare). Tests for HIV RNA should not be used for dx of HIV infection in HCW because of false-positives (esp. at low titers) & these tests are only approved for established HIV infection [a possible exception is if pt develops signs of acute HIV (mononucleosis-like) syndrome within the 1st 4–6 wks of exposure when antibody tests might still be negative.]
- PEP for HIV is usually given for **4 wks** and monitoring of adverse effects recommended: baseline **complete blood count, renal and hepatic panel** to be **repeated at 2 weeks.** 50–75% of HCW on PEP demonstrates mild side-effects (nausea, diarrhea, myalgias, headache, etc.) but in up to ½ severe enough to discontinue PEP. Consultation with infectious diseases/ HIV specialist valuable when questions regarding PEP arise. **Seek expert help in special situations, such as pregnancy, renal impairment, treatment-experienced source.**

TABLE 15D (3)

3 Steps to HIV Postexposure Prophylaxis (PEP) After Occupational Exposure: *[Latest CDC recommendations available at www.aidsinfo.nih.gov]*

Step 1: Determine the exposure code (EC)



** Exceptions can be considered when there has been prolonged, high-volume contact.*

Step 2: Determine the HIV Status Code (HIV SC)

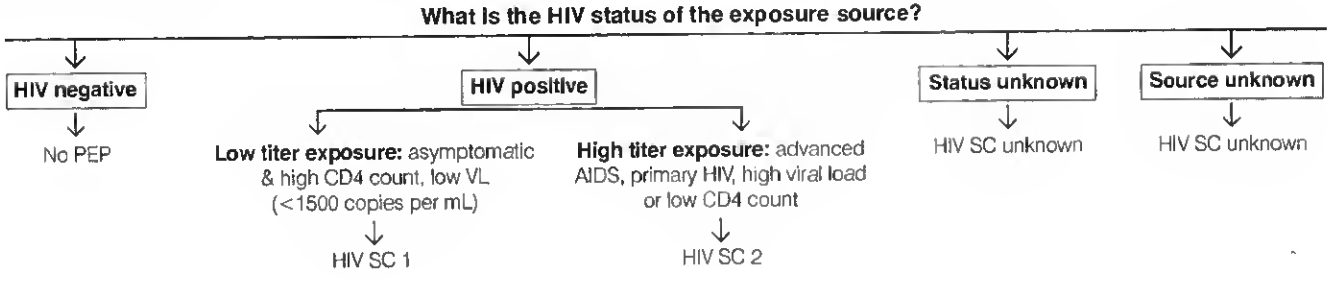


TABLE 15D (4)

3 Steps to HIV Postexposure Prophylaxis (PEP) After Occupational Exposure *(continued)*

Step 3: Determine Postexposure Prophylaxis (PEP) Recommendation

EC	HIV SC	PEP
1	1	Consider basic regimen[a]
1	2	Recommend basic regimen[a,b]
2	1	Recommend basic regimen[b]
2	2	Recommend expanded regimen
3	1 or 2	Recommend expanded regimen
1, 2, 3	Unknown	If exposure setting suggests risks of HIV exposure, consider basic regimen[c]

[a] Based on estimates of ↓ risk of infection after mucous membrane exposure in occupational setting compared with needlestick.
[b] Or, consider expanded regimen[†].
[c] In high risk circumstances, consider expanded regimen[†] on case-by-case basis.

Around the clock, urgent expert consultation available from: National Clinicians' Postexposure Prophylaxis Hotline (PEPline) at 1-888-448-4911 (1-888-HIV-4911) and on-line at *http://www.ucsf.edu/hivcntr*

Regimens: (Treat for 4 weeks; monitor for drug side-effects every 2 weeks)

Basic regimen: ZDV + 3TC, or **FTC + TDF,** or as an alternative **d4T + 3TC.**

Expanded regimen: Basic regimen + one of the following: lopinavir/ritonavir *(preferred)*, or *(as alternatives)* atazanavir/ritonavir or fosamprenavir/ritonavir. Efavirenz can be considered (except in pregnancy or potential for pregnancy—**Pregnancy Category D**), but CNS symptoms might be problematic. [**Do not use nevirapine;** serious adverse reactions including hepatic necrosis reported in healthcare workers.]

Other regimens can be designed. If possible, use antiretroviral drugs for which resistance is unlikely based on susceptibility data or treatment history of source pt (if known). Seek expert consultation if ART-experienced source or in pregnancy or potential for pregnancy.

NOTE: Some authorities feel that an expanded regimen should be employed whenever PEP is indicated. Expanded regimens are likely to be advantageous with ↑ numbers of ART-experienced source pts or when there is doubt about exact extent of exposures in decision algorithm. Mathematical model suggests that under some conditions, completion of full course basic regimen is better than prematurely discontinued expanded regimen. However, while expanded PEP regimens have ↑ adverse effects, there is not necessarily ↑ discontinuation.

POSTEXPOSURE PROPHYLAXIS FOR NON-OCCUPATIONAL EXPOSURES TO HIV-1
[Adapted from CDC recommendations, MMWR 54 (RR2), 2005, available at www.cdc.gov/mmwr/indrr_2005.html]

Because the risk of transmission of HIV via sexual contact or sharing needles by injection drug users may reach or exceed that of occupational needlestick exposure, it is reasonable to consider PEP in persons who have had a non-occupational exposure to blood or other potentially infected fluids (e.g., genital/rectal secretions, breast milk) from an HIV+ source. Risk of HIV acquisition per exposure varies with the act (for needle sharing and receptive anal intercourse, ≥0.5%; approximately 10-fold lower with insertive vaginal or anal intercourse, 0.05–0.07%). Overt or occult traumatic lesions may ↑ risk in survivors of sexual assault.

For pts at risk of HIV acquisition through non-occupational exposure to HIV + source material having occurred ≤72 hours before evaluation, DHHS recommendation is to treat for 28 days with an antiretroviral **expanded regimen,** using preferred regimens [efavirenz *(not in pregnancy or pregnancy risk—Pregnancy Category D)* + (3TC or FTC) + (ZDV or TDF)] **or** [lopinavir/ritonavir + (3TC or FTC) + ZDV] or one of several alternative regimens *[see Table 14C & MMWR 54(RR-2):1, 2005]*. Failures of prophylaxis have been reported, and may be associated with longer interval from exposure to start of PEP; this supports prompt initiation of PEP if it is to be used.

Areas of uncertainty: (1) expanded regimens are not proven to be superior to 2-drug regimens, (2) while PEP not recommended for exposures >72 hours before evaluation, it may possibly be effective in some cases, (3) when HIV status of source patient is unknown, decision to treat and regimen selection must be individualized based on assessment of specific circumstances.

Evaluate for exposures to Hep B, Hep C *(see Occupational PEP above)*, and bacterial sexually-transmitted diseases *(see Table 15A)* and treat as indicated. DHHS recommendations for sexual exposures to HepB and bacterial pathogens are available in *MMWR 55(RR-11), 2006*. Persons who are unvaccinated or who have not responded to full HepB vaccine series should receive hepB immune globulin preferably within 24-hours of percutaneous or mucosal exposure to blood or body fluids of an HBsAg-positive person, along with hepB vaccine, with follow-up to complete vaccine series. Unvaccinated or not-fully-vaccinated persons exposed to a source with unknown HepBsAg-status should receive vaccine and complete vaccine series. See *MMWR 55(RR-11), 2006* for details and recommendations in other circumstances.

TABLE 15E – PREVENTION OF SELECTED OPPORTUNISTIC INFECTIONS IN HUMAN HEMATOPOIETIC CELL TRANSPLANTATION (HCT) OR SOLID ORGAN TRANSPLANTATION (SOT) IN ADULTS WITH NORMAL RENAL FUNCTION.

General comments: Medical centers performing transplants will have detailed protocols for the prevention of opportunistic infections which are appropriate to the infections encountered, patients represented and resources available at those sites. Regimens continue to evolve and protocols adopted by an institution may differ from those at other centers. Care of transplant patients should be guided by physicians with expertise in this area.

References:

For HCT: Expert guidelines endorsed by the IDSA, updating earlier guidelines *(MMWR 49 (RR-10):1, 2000)* in: *Biol Blood Marrow Transpl 15:1143, 2009*. These guidelines provide recommendations for prevention of additional infections not discussed in this table and provide more detailed information on the infections included here.
For SOT: Recommendations of an expert panel of The Transplantation Society for management of CMV in solid organ transplant recipients in: *Transplantation 89:779, 2010*. Timeline of infections following SOT in: *Amer J Transpl 9 (Suppl 4):S3, 2009*.

OPPORTUNISTIC INFECTION	TYPE OF TRANSPLANT	PROPHYLACTIC REGIMENS
CMV (Recipient + **or** Donor +/Recipient –) Ganciclovir resistance: risk, detection, management *(CID 56:1018, 2013)*	SOT	**Prophylaxis: Valganciclovir** 900 mg po q24h Alternatives include **Ganciclovir** 1000 mg po 3 x/day, **Ganciclovir** 5 mg/kg IV 1 x/day, **Valacyclovir** 2 gm po 4 x/day *(kidney only, see comment)*, CMV IVIG or IVIG. **Also consider preemptive therapy** (monitor weekly for CMV viremia by PCR (or antigenemia) for 3-6 months post transplant. If viremia detected, start Valganciclovir 900 mg po bid or Ganciclovir 5 mg/kg IV q12h until clearance of viremia, but for not less than 2 weeks followed by secondary prophylaxis or preemptive approach. Prophylaxis vs pre-emptive rx compared: *CID 58:785, 2014*. CMV hyper IVIG is as adjunct to prophylaxis in high-risk lung, heart/lung, heart, or pancreas organ transplant recipients. Dosing: 150 mg/kg within 72 hrs of transplant and at 2, 4, 6 and 8 weeks; then 100 mg/kg at weeks 12 and 16.
	HCT	Preemptive Strategy: Monitor weekly for CMV viremia by PCR (or antigenemia) for 3-6 months post transplant with consideration for more prolonged monitoring in patients at risk for late-onset CMV disease (chronic GVHD, requiring systemic treatment, patients receiving high-dose steroids, T-cell depleted or cord blood transplant recipients, and CD4 < 100 cells/mL). Start treatment with identification of CMV viremia or antigenemia as above. Consider prophylaxis (beginning post-engraftment) with **Valganciclovir** 900 mg po q24h. *National Comprehensive Cancer Network Guidelines on Prevention and Treatment of Cancer-Related Infections, Version 1.2013, Blood 113:5711, 2009, and Biol Blood Marrow Transpl 15:1143, 2009.*
Hepatitis B	SOT	For anti-viral agents with activity against HBV, see *Table 14B, page 178*. For discussion of prevention of HBV re-infection after transplantation and prevention of donor-derived infection see *Am J Transplant 9: S116, 2013*
	HCT	Patients who are anti-HBC positive and anti-HBs positive, but without evidence of active viral replication, can be monitored for ↑LFTs and presence of +HBV-DNA, and given pre-emptive therapy at that time. Alternatively, prophylactic anti-viral therapy can be given, commencing before transplant. (See *guidelines for other specific situations: Biol Blood Marrow Transpl 15:1143, 2009.)* These guidelines recommend Lamivudine 100 mg po q24h as an anti-viral.
Herpes simplex	SOT	**Acyclovir** 400 mg po bid, starting early post-transplant *(Clin Microbiol Rev 10:86, 1997)*
	HCT	**Acyclovir** 250 mg per meter-squared iv q12h **or Acyclovir** 400 mg to 800 mg po bid, from conditioning to engraftment or resolution or mucositis. For those requiring prolonged suppression of HSV, the higher dose (Acyclovir 800 mg po bid) is recommended to minimize the risk of emerging resistance.

* See page 2 for abbreviations

TABLE 15E (2)

OPPORTUNISTIC INFECTION	TYPE OF TRANSPLANT	PROPHYLACTIC REGIMENS
Aspergillus spp.	SOT	Lung and heart/lung transplant: Inhaled **Amphotericin B** and/or a mold active oral azole are commonly used, but optimal regimen not defined. Aerosolized **Amphotericin B** 6 mg q8h (or 25 mg/day) OR aerosolized **LAB** 25 mg/day OR **Voriconazole** 200 mg po bid OR **Itraconazole** 200 mg po bid. 59% centers employ universal prophylaxis for 6 months in lung transplant recipients with 97% targeting Aspergillus. Most use Voriconazole alone or in combination with inhaled Amphotericin B *(Am J Transplant 11:361, 2011)*. Consider restarting prophylaxis during periods of intensified immune suppression. Liver transplant: Consider only in high-risk, re-transplant and/or those requiring renal-replacement therapy. Recommendations on aspergillus prophylaxis in SOT can be found at *(Am J Transplant 13;228, 2013)*
	HCT/Heme malignancy	Indications for prophylaxis against aspergillus include AML and MDS with neutropenia and HCT with GVHD. Posaconazole 200 mg po tid approved this indication *(NEJM 356:335, 2007 and NEJM 356:348,2007)* Posaconazole ER tablets, also approved for prophylaxis (300 mg po BID x 1 day, then 300 daily). Retrospective analysis suggests that Voriconazole would have efficacy in steroid-treated patients with GVHD *(Bone Marrow Transpl 45:662, 2010)*, but is not approved for this indication. Amphotericin B and echinocandins are alternatives as well.
Candida spp.	SOT	Consider in select, high risk patients (liver, small bowel, pancreas): Consider in select, high-risk patients (re-transplants, dialysis). **Fluconazole** 400 mg daily for 4 weeks post-transplant. *(Amer J Transpl 13:200, 2013)*
	HCT	**Fluconazole** 400 mg po or iv once daily from day 0 to engraftment or when ANC consistently >1000, or **Posaconazole** solution 200 mg po tid or Posa ER tablets (300 mg po BID x 1 day, then 300 daily). Approved for high-risk patients (e.g., with GVHD or prolonged neutropenia), or Micafungin 50 mg iv once daily.
Coccidioides immitis	Any	**Fluconazole** 200-400 mg po q24h *(Transpl Inf Dis 5:3, 2003; Am J Transpl 6:340. 2006)*. See COID *21:45, 2008* for approach at one center in endemic area; e.g., for positive serology without evidence of active infection, Fluconazole 400 mg q24h for first year post-transplant, then 200 mg q24h thereafter.
Pneumocystis jiroveci	SOT	**TMP-SMX:** 1 single-strength tab po q24h or 1 double-strength tab po once daily for 3 to 7 days per week. Duration: kidney: 6 mos to 1 year *(Amer J Transpl 9 (Suppl 3): S59, 2009)*; heart, lung, liver: ≥ 1 year to life-long *(Amer J Transpl 4 (Suppl 10): 135, 2004)*.
	HCT	**TMP-SMX:** 1 single-strength tab po q24h or 1 double-strength tab po once daily or once a day for 3 days per week, from engraftment to ≥ 6 mos post transplant.
Toxoplasma gondii	SOT	**TMP-SMX** (1 SS tab po q24h or 1 DS tab po once daily) x 3-7 days/wk for 6 mos post-transplant. *(See Clin Micro Infect 14:1089, 2008)*.
	HCT	**TMP-SMX:** 1 single-strength tab po q24h or 1 double-strength tab po once daily or once a day for 3 days per week, from engraftment to ≥ 6 mos post transplant for seropositive allogeneic transplant recipients.
Trypanosoma cruzi	Heart	May be transmitted from organs or transfusions *(CID 48:1534, 2009)*. Inspect peripheral blood of suspected cases for parasites *(MMWR 55:798, 2006)*. Risk of reactivation during immunosuppression is variable *(JAMA 298:2171, 2007; JAMA 299:1134, 2008; J Cardiac Fail 15:249, 2009)*. If known Chagas disease in donor or recipient, contact CDC for treatment options *(phone 770-488-7775 or in emergency 770-488-7100). Am J Transplant 11:672, 2011*

* See page 2 for abbreviations

TABLE 16 – PEDIATRIC DOSING (AGE > 28 DAYS)

Editorial Note
There are limited data on when to switch adolescents to adult dosing. In general, pediatric weight based dosing is appropriate through mid puberty (Tanner 3) if no maximum dose is specified. Some change to adult dosing at 40 kg. If in doubt, when treating serious infections in peri-pubertal adolescents with drugs that have large margins of safety (e.g. Beta lactams and carbapenems) it may be safer to err on the side of higher doses.

DRUG	DOSE (AGE >28 DAYS) (Daily maximum dose shown, when applicable)
ANTIBACTERIALS	
Aminoglycosides	
Amikacin	15-20 mg/kg/day (once daily); 15-22.5 mg/kg/day (divided q8h)
Gentamicin	5-7 mg/kg/day once daily 2.5 mg/kg q8h
Tobramycin	5-7 mg/kg/day once daily 2.5 mg/kg q8h. Max per day: 8 gm
Beta-Lactams	
Carbapenems	
Ertapenem	30 mg/kg/day (divided q12h). Max per day: 1 gm
Imipenem	60-100 mg/kg/day (divided q6-8h). Max per day: 2-4 gm
Meropenem	60 mg/kg/day (divided q8h); Meningitis: 120 mg/kg/day (divided q8h). Max per day: 2-4 gm
Cephalosporins (po)	
Cefaclor	20-40 mg/kg/day (divided q8-12h). Max per day: 1 gm
Cefadroxil	30 mg/kg/day (divided q12h). Max per day: 2 gm
Cefdinir	14 mg/kg/day (divided q12-24h)
Cefixime	8 mg/kg/day (divided q12-24h)
Cefpodoxime	10 mg/kg/day (divided q12h). Max per day: 400 mg
Cefprozil	15-30 mg/kg/day (divided q12h) -- use 30 for AOM
Ceftibuten	9 mg/kg/day (divided q12-24h). Max per day: 1 gm
Cefuroxime axet	20-30 mg/kg/day (divided q12h) -- use 30 for AOM. Max per day: 1 gm
Cephalexin	25-100 mg/kg/day (divided q6h). Max per day: 4 gm
Loracarbef	15-30 mg/kg/day (divided q12h). Max per day: 800 mg
Cephalosporins (IV)	
Cefazolin	50-150 mg/kg/day (divided q6-8h). Max per day: 6 gm
Cefepime (non-Pseudomonal)	100 mg/kg/day (divided q8h)
Cefepime (Pseudomonal)	150 mg/kg/day (divided q8h)
Cefotaxime	150-200 mg/kg/day (divided q6-8h); Meningitis: 300 mg/kg/day (divided q6h)
Cefotetan	60-100 mg/kg/day (divided q12h). Max per day: 6 gm
Cefoxitin	80-160 mg/kg/day (divided q6-8h)
Ceftazidime	150-200 mg/kg/day (divided q8h); CF: 300 mg/kg/day (divided q8h). Max per day: 6 gm
Ceftizoxime	150-200 mg/kg/day (divided q6-8h)
Ceftriaxone	50-100 mg/kg q24h; Meningitis: 50 mg/kg q12h
Cefuroxime	150 mg/kg/day (divided q8h); Meningitis: 80 mg/kg q8h
Penicillins	
Amoxicillin	25-50 mg/kg/day (divided q8h)
Amoxicillin (AOM, pneumonia)	80-100 mg/kg/day (divided q8-12h; q12h for AOM)
Amoxicillin-clavulanate 7:1 formulation	45 mg/kg/day (divided q12h)
Amoxicillin-clavulanate 14:1 (AOM)	90 mg/kg/day (divided q12h) for wt <40 kg
Ampicillin (IV)	200 mg/kg/day (divided q6h); Meningitis: 300-400 mg/kg/day (divided q6h)
Ampicillin-sulbactam	100-300 mg/kg/day (divided q6h)
Cloxacillin (PO)	If <20 kg: 25-50 mg/kg/day (divided q6h); Otherwise dose as adult
Dicloxacillin (mild - moderate)	12.5-25 mg/kg/day (divided q6h)
Dicloxacillin (osteo articular infection)	100 mg/kg/day (divided q 6h)
Flucloxacillin	Age 2-10: 50% of adult dose; Age<2: 25% of adult dose
Nafcillin	150-200 mg/kg/day (divided q6h)
Oxacillin	150-200 mg/kg/day (divided q6h)
Penicillin G	150,000-300,000 units/kg/day (divided q4-6h). Max per day: 12-20 million units
Penicillin VK	25-75 mg/kg/day (divided q6-8h)
Piperacillin-tazobactam	300 mg/kg/day (divided q6h)
Temocillin	25 mg/kg q12h
Fluoroquinolones * Approved only for CF, anthrax, and complicated UTI	
Ciprofloxacin (PO)	20-40 mg/kg/day (divided q12h) *. Max per day: 1.5 gm
Ciprofloxacin (IV)	20-30 mg/kg/day (divided q12h) *. Max per day: 1.2 gm
Levofloxacin (IV/PO)	16-20 mg/kg/day (divided q12h) *. Max per day: 750 mg

TABLE 16 (2)

DRUG	DOSE (AGE >28 DAYS) (Daily maximum dose shown, when applicable)
Lincosamides	
Clindamycin (PO)	30-40 mg/kg/day (divided q6-8h)
Clindamycin (IV)	20-40 mg/kg/day (divided q6-8h)
Lincomycin	10-20 mg/kg/day (divided q8-12h)
Lipopeptides	
Daptomycin	6-10 mg/kg/day (once daily)
Macrolides	
Azithromycin (po)	5-12 mg/kg/day (once daily)
Azithromycin (IV)	10 mg/kg/day (once daily)
Clarithromycin	15 mg/kg/day (divided q12h). Max per day: 1 gm
Erythromycin (po, IV)	40-50 mg/kg/day (divided q6h)
Monobactams	
Aztreonam	90-120 mg/kg/day (divided q8h). Max per day: 8 gm
Tetracyclines	
Doxycycline (po/IV, age >8 yrs)	2-4 mg/kg/day (divided q12h). Max per day: 200 mg
Fosfomycin (PO)	2 gm once
Fusidic acid (PO)	Age 1-5: 250 mg q8h Age 6-12: 250-500 mg q8h
Minocycline (PO, age >8)	4 mg/kg/day (divided q12h)
Tetracycline	Age >8: 25-50 mg/kg/day (divided q6h). Max per day: 2 gm
Other	
Chloramphenicol (IV)	50-100 mg/kg/day (divided q6h). Max per day: 2-4 gm
Colistin	2.5-5 mg/kg/day (divided q6-12h) CF: 3-8 mg/kg/day (divided q8h)
Linezolid (up to age 12 yrs)	30 mg/kg/day IV/po (divided q8h)
Methenamine hippurate (age 6-12)	500-1000 mg q12h
Methenamine mandelate	Age >2 to 6: 50-75 mg/kg/day (divided q6-8h) Age 6-12: 500 mg q6h
Metronidazole (PO)	30-40 mg/kg/day (divided q6h)
Metronidazole (IV)	22.5-40 mg/kg/day (divided q6h)
Nitrofurantoin (PO Cystitis)	5-7 mg/kg/day (divided q 6h)
Nitrofurantoin (PO UTI prophylaxis)	1-2 mg/kg/day (once daily)
Polymyxin B (age 2 and older)	2.5 mg/kg (load), then 1.5 mg/kg q12h
Rifampin (meningococcal prophylaxis)	10 mg/kg q12h x2 days
Tinidazole (age >3 for Giardia, amebiasis)	50 mg/kg q24h x1-5 days. Max per day: 2 gm
Sulfadiazine	120-150 mg/kg/day (divided q4-6h). Max per day: 6 gm
TMP-SMX (UTI and other)	8-12 mg TMP/kg/day (divided q12h
TMP-SMX (PCP)	15-20 mg TMP/kg/day (divided q12h
Trimethoprim	4 mg/kg/day (divided q12h)
Vancomycin (IV)	40-60 mg/kg/day (divided q6-8h)*
Vancomycin (PO for C. difficile)	40 mg/kg/day (divided q6h)
ANTIMYCOBACTERIALS	
Capreomycin	15-30 mg/kg/day (divided q12-24h). Max per day: 1 gm
Cycloserine	10-15 mg/kg/day (divided q12h). Max per day: 1 gm
Ethambutol	15-25 mg/kg/day (once daily). Max per day: 2.5 gm
Ethionamide	15-20 mg/kg/day (divided q12h). Max per day: 1 gm
Isoniazid (daily dosing)	10-15 mg/kg/day (once daily). Max per day: 300 mg
Isoniazid (2 x/week)	20-30 mg/kg twice weekly. Max per day: 900 mg
Kanamycin	15 -30 mg/kg/day (divided q12-24h). Max per day: 1 gm
Para-aminosalicylic acid	200-300 mg/kg/day (divided q6-12h)
Pyrazinamide (daily)	15-30 mg/kg/day (once daily). Max per day: 2 gm
Pyrazinamide (2 x/week)	50 mg/kg/day (2 days/week). Max per day: 2 gm
Rifabutin (MAC prophylaxis)	5 mg/kg/day (once daily). Max per day: 300 mg
Rifabutin (active TB)	10-20 mg/kg/day (once daily). Max per day: 300 mg
Rifampin	10-20 mg/kg/day (divided q12-24h). Max per day: 600 mg
Streptomycin (age 2 and older)	20-40 mg/kg/day (once daily). Max per day: 1 gm
ANTIFUNGALS	
Amphotericin B deoxycholate	0.5-1 mg/kg/day (once daily)
Amphotericin B lipid complex	5 mg/kg/day (once daily)
Anidulafungin	1.5-3 mg/kg loading dose then .75-1.5 mg/kg/day (once daily)
Caspofungin	70 mg/m2 loading dose then 50 mg/m2 (once daily)

TABLE 16 (3)

DRUG	DOSE (AGE >28 DAYS) (Daily maximum dose shown, when applicable)
ANTIFUNGALS *(continued)*	
Fluconazole	6 mg/kg/day for oral/esophageal Candida; 12 mg/kg/day for invasive disease
Isavuconazole	Not known; adult dose 372 mg q8h x 3 doses loading dose then 744 mg/day (divided q12h)
Itraconazole	5-10 mg/kg/day (divided q12h)
Ketoconazole	3.3-6.6 mg/kg/day (once daily)
Micafungin	Age >4 mon: 2 mg/kg q24h (max 100 mg) for candidiasis; for EC use 3 mg/kg q24h if <30 kg, 2.5 mg/kg q24h (max 150 mg) if ≥30 kg
Posaconazole	Not known; adult dose 300 mg bid loading dose then 300 mg/day (extended release)
Terbinafine	< 20 kg 67.5 mg/day; 20-40 kg 125 mg/day; >40 kg 250 mg/day (adult dose)
Voriconazole	12-20 mg/kg/day (divided q12h) *
ANTIVIRALS	
Acyclovir (IV) neonatal herpes simplex	60 mg/kg/day (divided q8h)
Acyclovir (IV) HSV encephalitis >3 months	30-45 mg/kg/day (divided q8h)
Acyclovir (IV) varicella immunocompromised	<1 year 30 mg/kg/day (divided q8h); > 1 year 30 mg/kg/day or 1500 mg/M2/day (divided q8h)
Acyclovir (IV) HSV immunocompromised	30 mg/kg/day (divided q8h)
Cidofovir	Induction 5 mg/kg once weekly; suppressive therapy 3 mg/kg once weekly (all with hydration and probenecid)
Foscarnet	120-180 mg/kg/day (divided q8-12h)
Ganciclovir	Symptomatic congenital CMV 12 mg/kg/day (divided q12h) CMV treatment or first 2 weeks after SOT 10 mg/kg/day (divided q12h) suppressive therapy or prophylaxis 5 mg/kg/day (divided q24h)
Oseltamivir <1 year old	6 mg/kg/day (divided q12h)
Oseltamivir ≥ 1 year old	<15 kg 30 mg bid; >15 to 23 kg 45 mg bid; >23 - 40 kg 60 mg bid; > 40 kg 75 mg bid (adult dose)
Peramivir	Not studied
Valacyclovir (Varicella or Herpes Zoster)	20 mg/kg/day (divided q8h). Max per day: 3 gm
Valganciclovir	Symptomatic congenital CMV 32 mg/kg/day (divided q12h); Prevention of CMV after SOT: 7 mg x BSA x CrCl (once daily; use Schwartz formula for CrCl)
Zanamivir (age >7 years)	10 mg (two 5-mg inhalations) twice daily

TABLE 17A – DOSAGE OF ANTIMICROBIAL DRUGS IN ADULT PATIENTS WITH RENAL IMPAIRMENT

- For listing of drugs with NO need for adjustment for renal failure, see *Table 17B.*
- Adjustments for renal failure are based on an estimate of creatinine clearance (CrCl) which reflects the glomerular filtration rate.
- **Different methods for calculating estimated CrCl are suggested for non-obese and obese patients.**
  - Calculations for ideal body weight (IBW) in kg:
    - *Men:* 50 kg plus 2.3 kg/inch over 60 inches height.
    - *Women:* 45 kg plus 2.3 kg/inch over 60 inches height.
  - Obese is defined as 20% over ideal body weight or body mass index (BMI) >30

- Calculations of estimated CrCl *(References, see (NEJM 354:2473, 2006 (non-obese), AJM 84:1053, 1988 (obese))*
  - **Non-obese patient**—
    - Calculate ideal body weight (IBW) in kg (as above)
    - Use the following formula to determine estimated CrCl

$$\frac{\text{(140 minus age)(IBW in kg)}}{\text{72 x serum creatinine}} = \text{CrCl in mL/min for men. Multiply answer by 0.85 for women (estimated)}$$

  - **Obese patient**—
    - Weight ≥20% over IBW or BMI >30
    - Use the following formulas to determine estimated CrCl

$$\frac{\text{(137 minus age) x [(0.285 x wt in kg) + (12.1 x ht in meters}^2\text{)]}}{\text{51 x serum creatinine}} = \text{CrCl (obese male)}$$

$$\frac{\text{(146 minus age) x [(0.287 x wt in kg) + (9.74 x ht in meters}^2\text{)]}}{\text{60 x serum creatinine}} = \text{CrCl (obese female)}$$

- If estimated CrCl ≥90 mL/min, see *Tables 10A and 10D for dosing.*
- What weight should be used to calculate dosage on a mg/kg basis?
  - If less than 20% over IBW, use the patient's actual weight for all drugs.
  - **For obese patients** (≥20% over IBW or BMI 30)
    - **Aminoglycosides:** (IBW plus 0.4(actual weight minus IBW) adjusted weight.
    - **Vancomycin:** actual body weight whether non-obese or obese.
    - **All other drugs:** insufficient data *(Pharmacotherapy 27:1081, 2007).*

- For slow or sustained extended daily dialysis **(SLEDD)** over 6-12 hours, adjust does as for CRRT. For details, see *CID 49:433, 2009; CCM 39:560, 2011.*
- General reference: Drug Prescribing in Renal Failure, 5th ed., Aronoff, et al. (eds) *(Amer College Physicians, 2007 and drug package inserts).*

TABLE 17A (2)

ANTIMICROBIAL	Half-life, hrs (renal function normal)	Half-life, hrs (ESRD)	Dose (renal function normal)	CrCl >50-90	CrCl 10-50	CrCl <10	Hemodialysis	CAPD	CRRT
ANTIBACTERIAL ANTIBIOTICS									
AMINOGLYCOSIDES , MDD									
Amikacin[1,2]	2-3	30-70	7.5 mg/kg IM/IV q12h (once-daily dosing below)	7.5 mg/kg q12h	7.5 mg/kg q24h	7.5 mg/kg q48h	7.5 mg/kg q48h (+ extra 3.25 mg/kg AD)	15-20 mg lost per L of dialysate/day	7.5 mg/kg q24h
Gentamicin, Netilmicin NUS, Tobramycin [1,2,3]	2-3	30-70	1.7-2.0 mg/kg IM/IV q8h	1.7-2.0 mg/kg q8h	1.7-2.0 mg/kg q12-24h	1.7-2.0 mg/kg q48h	1.7-2.0 mg/kg q48h (+ extra 0.85-1.0 mg/kg AD)	3-4 mg lost per L of dialysate/day	1.7-2.0 mg/kg q24h
AMINOGLYCOSIDES, ODD *(see Table 10D)*									
			Dose for CrCl >80 (mg/kg q24h)	**CrCl 60-80 (mg/kg q24h)**	**CrCl 40-60 (mg/kg q24h)**	**CrCl 30-40 (mg/kg q24h)**	**CrCl 20-30 (mg/kg q48h)**	**CrCl 10-20 (mg/kg q48h)**	**CrCl 0-10 (mg/kg q72h and AD)**
Gentamicin, Tobramycin	2-3	30-70	5.1	4	3.5	2.5	4	3	2
Amikacin, Kanamycin, Streptomycin	2-3	30-70	15	12	7.5	4	7.5	4	3
Isepamicin[NUS]	2-3	30-70	8	8	8	8 mg/kg q48h	8	8 mg/kg q72h	8 mg/kg q96h
Netilmicin[NUS]	2-3	30-70	6.5	5	4	2	3	2.5	2
BETA-LACTAMS									
Carbapenems									
Doripenem	1	18	500 mg IV q8h	500 mg q8h	CrCl 30-50: 250 mg q8h; CrCl 10-30: 250 mg q12h	No data	No data	No data	500 mg q8h *(JAC 69:2508, 2014)*
Ertapenem	4	>4	1 gm IV q24h	1 gm q24h	CrCl <30: 0.5 gm q24h	0.5 gm q24h	0.5 gm q24h (+ 150 mg AD if given within 6 hr prior to HD)	0.5 gm q24h	0.5-1 gm q24h
Imipenem	1	4	500 mg IV q6h	250-500 mg q6-8h	250 mg q8-12h	125-250 mg q12h	125-250 q12h (give one of the dialysis day doses AD)	125-250 mg q12h	0.5-1 gm q12h *(AAC 49:2421, 2005)*
Meropenem	1	10	1 gm IV q8h	1 gm q8h	CrCl 25-50: 1 gm q12h; CrCl 10-25: 0.5 gm q12h	0.5 gm q24h	0.5 gm q24h (give dialysis day dose AD)	0.5 gm q24h	1 gm q12h

TABLE 17A (3)

ANTIMICROBIAL	Half-life, hrs (renal function normal)	Half-life, hrs (ESRD)	Dose (renal function normal)	CrCl >50-90	CrCl 10-50	CrCl <10	Hemodialysis	CAPD	CRRT
Cephalosporins, IV, 1st gen									
Cefazolin	1.9	40-70	1-2 gm IV q8h	1-2 gm q8h	1-2 g q12h	1-2 gm q24-48h	1-2 gm q24-48h (+ extra 0.5-1 gm AD)	0.5 gm IV q12h	1-2 gm q12h
Cephalosporins, IV, 2nd gen									
Cefotetan	4	13-25	1-2 gm IV q12h	1-2 gm q12h	1-2 gm q24h	1-2 gm q48h	1-2 gm q24h (+ extra 1 gm AD)	1 gm q24h	750 mg q12h
Cefoxitin [4]	0.8	13-23	2 gm IV q8h	2 gm q8h	2 gm q8-12h	2 gm q24-48h	2 gm q24-48h (+ extra 1 gm AD)	1 gm q24h	2 gm q8-12h
Cefuroxime	1.5	17	0.75-1.5 gm IV q8h	0.75-1.5 gm q8h	0.75-1.5 gm q8-12h	0.75-1.5 gm q24h	0.75-1.5 gm q24h (give dialysis day dose AD)	0.75-1.5 gm q24h	0.75-1.5 gm q8-12h
Cephalosporins, IV, 3rd gen, non-antipseudomonal									
Cefotaxime [5]	1.5	15-35	2 gm IV q8h	2 gm q8-12h	2 gm q12-24h	2 gm q24h	2 gm q24h (+ extra 1 gm AD)	0.5-1 gm q24h	2 gm q12-24h
Ceftizoxime	1.7	15-35	2 gm IV q8h	2 gm q8-12h	2 gm q12-24h	2 gm q24h	2 gm q24h (+ extra 1 gm AD)	0.5-1 gm q24h	2 gm q12-24h
Ceftriaxone [5]	8	Unchanged	1-2 gm IV q12-24h	1-2 gm q12-24h	1-2 gm q12-24h	1-2 gm q12-24h	1-2 gm q12-24h	1-2 gm q12-24h	1-2 gm q12-24h
Cephalosporins, IV, antipseudomonal									
Cefepime	2	18	2 gm IV q8h	>60: 2 gm q8-12h	30-60: 2 gm q12h; 11-29: 2 gm q24h	1 gm q24h	1 gm q24h (+ extra 1 gm AD)	1-2 gm q48h	2 gm q12-24h
Ceftazidime	1.9	13-25	2 gm IV q8h	2 gm q8-12h	2 gm q12-24h	2 gm q24-48h	2 gm q24-48h (+ extra 1 gm AD)	No data	1-2 gm q12-24h (depends on flow rate)
Ceftazidime/ avibactam	ceftaz 2.8, avi 2.7	ceftaz 13-25	2.5 gm IV q8h	2.5 gm q8h	30-50: 1.25 gm q8h; 10-30: 0.94 gm q12h	0.94 gm q48h	0.94 gm q48h (give dialysis day dose AD)	No data	No data
Ceftolozane/ tazobactam	ceftolozane 3.1	ceftolozane 40	1.5 gm IV q8h	1.5 gm q8h	30-50: 750 mg q8h 15-30: 375 mg q8h	<15: see HD	750 mg x1, then 150 mg q8h (give dialysis day doses AD)	No data	No data
Cephalosporins, IV, anti-MRSA									
Ceftaroline	2.7	No data	600 mg (over 1 hr) IV q12h	600 mg q12h	30-50: 400 mg q12h; 15-30: 300 mg q12h	<15: 200 mg q12h	200 mg q12h	No data	No data
Ceftobiprole[NUS]	2.9-3.3	21	500 mg IV q8-12h	500 mg q8-12h	30-50: 500 mg q12h over 2 hr; 10-30: 250 mg q12h over 2 hr	No data	No data	No data	No data

TABLE 17A (4)

ANTIMICROBIAL	Half-life, hrs (renal function normal)	Half-life, hrs (ESRD)	Dose (renal function normal)	CrCl >50-90	CrCl 10-50	CrCl <10	Hemodialysis	CAPD	CRRT
Cephalosporins, oral, 1st gen									
Cefadroxil	1.5	20	1 gm po q12h	1 gm q12h	1 gm, then 500 mg q12-24h	1 gm, then 500 mg q36h	1 gm, then 1 gm AD	500 mg q24h	No data
Cephalexin	1	20	500 mg po q6h	500 mg q12h	500 mg q12h	250 mg q12h	250 mg q12h (give one of the dialysis day doses AD)	500 mg q12h	No data
Cephalosporins, oral, 2nd gen									
Cefaclor	0.8	3	500 mg po q8h	500 mg q8h	500 mg q8h	500 mg q12h	500 mg q12h (give one of the dialysis day doses AD)	500 mg q12h	No data
Cefprozil	1.5	5-6	500 mg po q12h	500 mg q12h	500 mg q24h	250 mg q12h	250 mg q12h (give one of the dialysis day doses AD)	250 mg q24h	No data
Cefuroxime axetil	1.5	17	500 mg po q8h	500 mg q8h	500 mg q12h	500 mg q24h	500 mg q24h (give extra 250 mg AD)	500 mg q24h	No data
Cephalosporins, oral, 3rd gen									
Cefdinir	1.7	16	300 mg po q12h	300 mg q12h	300 mg q12h	300 mg q24h	300 mg q24h (dose AD on dialysis days)	300 mg q24h	No data
Cefditoren pivoxil	1.6	5	400 mg po q12h	400 mg q12h	200 mg q12h	200 mg 24h	200 mg q24h (dose AD on dialysis days)	200 mg q24h	No data
Cefixime	3	12	400 mg po q24h	400 mg q24h	300 mg q24h	200 mg q24h	200 mg q24h (dose AD on dialysis days)	200 mg q24h	No data
Cefpodoxime proxetil	2.3	10	200 mg po q12h	200 mg q12h	200 mg q12h	200 mg q24h	200 mg q24h (dose AD on dialysis days)	200 mg q24h	No data
Ceftibuten	2.5	13	400 mg po q24h	400 mg q24h	200 mg q24h	100 mg q24h	100 mg q24h (dose AD on dialysis days)	100 mg po q24h	No data
Monobactams									
Aztreonam	2	6-8	2 gm IV q8h	2 gm q8h	1-1.5 gm q8h	500 mg q8h	500 mg q8h (give additional 250 mg AD)	500 mg q8h	1-1.5 gm q8h
Penicillins (natural)									
Penicillin G	0.5	6-20	0.5-4 million U IV q4h	0.5-4 million U q4h	0.5-4 million U q8h	0.5-4 million U q12h	0.5-4 million U q12h (give one of the dialysis day doses AD)	0.5-4 million U q12h	1-4 million U q6-8h
Penicillin V	0.5	4.1	250-500 mg po q6-8h	250-500 mg q6-8h	250-500 mg q6-8h	250-500 mg q6-8h	250-500 mg q6-8h (give one or more doses AD)	250-500 mg q6-8h	No data

TABLE 17A (5)

ANTIMICROBIAL	Half-life, hrs (renal function normal)	Half-life, hrs (ESRD)	Dose (renal function normal)	CrCl >50-90	CrCl 10-50	CrCl <10	Hemodialysis	CAPD	CRRT
Penicillins (amino)									
Amoxicillin	1.2	5-20	250-500 mg po q8h	250-500 mg q8h	250-500 mg q8-12h	250-500 mg q24h	250-500 mg q24h (give dialysis day dose AD)	250 mg q12h	250-500 mg q8-12h
Amoxicillin ER	1.2-1.5	?	775 mg po q24h	775 mg q24h	30: No data, avoid usage	No data, avoid usage	No data	No data	No data
Amoxicillin/ Clavulanate [6]	amox 1.4, clav 1	amox 5-20, clav 4	500/125 mg po q8h	500/125 mg q8h	250-500 mg (amox component) q12h	250-500 mg (amox) q24h	250-500 mg (amox) q24h (give an extra dose AD on dialysis days)	No data	No data
Ampicillin	1.2	7-20	1-2 gm IV q4-6h	1-2 gm q4-6h	30-50: 1-2 gm q6-8h; 10-30: 1-2 gm q8-12h	1-2 gm q12h	1-2 gm q12h (give one of the dialysis day doses AD)	500 mg - 1 gm q12h	1-2 gm q8-12h
Ampicillin/Sulbactam	amp 1.4, sulb 1.7	amp 7-20, sulb 10	3 gm IV q6h	3 gm q6h	3 gm q8-12h	3 gm q24h	3 gm q24h (give AD on dialysis day)	3 gm q24h	3 gm q12h
Penicillins (penicillinase-resistant)									
Dicloxacillin	0.7	No change	125-500 mg po q6h	125-500 mg q6h	125-500 mg q6h	125-500 mg q6h			
Temocillin	4	No data	1-2 gm IV q12h	1-2 gm q12h	1-2 gm q24h	1 gm q48h	1 gm q48h (give AD on dialysis days)	1 gm q48h	No data
Penicillins (antipseudomonal)									
Piperacillin/ Tazobactam (non-Pseudomonas dose)	pip 1, Tazo 1	pip 3-5, Tazo 2.8	3.375 gm IV q6h (over 30 min)	>40: 3.375 gm q6h	20-40: 2.25 gm q6h; <20: 2.25 gm q8h	2.25 gm q8h	2.25 gm q12h (+ extra 0.75 gm AD)	2.25 gm q12h	2.25 gm q6h
Piperacillin/ Tazobactam (Pseudomonas dose)	pip 1, Tazo 1	pip 3-5, Tazo 2.8	4.5 gm IV q6h (over 30 min)	>40: 4.5 gm q6h	20-40: 3.375 gm q6h; <20: 2.25 gm q6h	2.25 gm q6h	2.25 gm q8h (+ extra 0.75 gm AD)	2.25 gm q8h	3.375 gm q6h
FLUOROQUINOLONES									
Ciprofloxacin po (not XR)	4	6-9	500-750 mg po q12h	500-750 mg q12h	250-500 mg q12h	500 mg q24h	500 mg q24h (dose AD on dialysis days)	500 mg q24h	250-500 mg q12h
Ciprofloxacin XR po	5-7	6-9	500-1000 mg po q24h	500-1000 mg q24h	30-50: 500-1000 mg q24h; 10-30: 500 mg q24h	500 mg q24h	500 mg q24h (dose AD on dialysis days)	500 mg q24h	No data

TABLE 17A (6)

ANTIMICROBIAL	Half-life, hrs (renal function normal)	Half-life, hrs (ESRD)	Dose (renal function normal)	CrCl >50-90	CrCl 10-50	CrCl <10	Hemodialysis	CAPD	CRRT
FLUOROQUINOLONES *(continued)*									
Ciprofloxacin IV	4	6-9	400 mg IV q12h	400 mg q12h	400 mg q24h	400 mg q24h	400 mg q24h (dose AD on dialysis days)	400 mg q24h	200-400 mg q12h
Gatifloxacin[NUS]	7-8	11-40	400 mg po/IV q24h	400 mg q24h	400 mg, then 200 mg q24h	400 mg, then 200 mg q24h	200 mg q24h (give dialysis day dose AD)	200 mg q24h	400 mg, then 200 mg q24h
Gemifloxacin	7	>7	320 mg po q24h	320 mg q24h	160 mg q24h	160 mg q24h	160 mg q24h (give dialysis day dose AD)	160 mg q24h	No data
Levofloxacin	7	76	750 mg po/IV q24h	750 mg q24h	20-49: 750 mg q48h	<20: 750 mg x1, then 500 mg q48h	750 mg x1, then 500 mg q48h	750 mg x1, then 500 mg q48h	750 mg x1, then 500 mg q48h
Norfloxacin	3-4	8	400 mg po q12h	400 mg q12h	30-49: 400 mg q12h; 10-30: 400 mg q24h	400 mg q24h	400 mg q24h	400 mg q24h	Not applicable
Ofloxacin	7	28-37	200-400 mg po q12h	200-400 mg q12h	200-400 mg q24h	200 mg q24h	200 mg q24h (give dialysis day dose AD)	200 mg q24h	200-400 mg q24h
Prulifloxacin[NUS]	10.6-12.1	No data	600 mg po q24h	No data	No data	No data	No data	No data	No data
GLYCOPEPTIDES, LIPOGLYCOPEPTIDES, LIPOPEPTIDES									
Dalbavancin	147-258 (terminal)	No data	1 gm IV x1, then 500 mg IV in 7 days	1 gm x1, then 500 mg in 7 days	30-49: 1 gm x1, then 500 mg in 7 days; <30, non-regular HD: 750 mg x1, then 375 mg in 7 days		Regularly scheduled HD: 1 gm x1, then 500 mg in 7 days	No data	No data
Daptomycin	8-9	30	4-6 mg/kg IV q24h	4-6 mg/kg q24h	30-49: 4-6 mg/kg q24h; <30: 6 mg/kg q48h		6 mg/kg q48h (during or after q48h dialysis); if next planned dialysis is 72 hrs away, give 9 mg/kg *(AAC 57:864, 2013; JAC 69:200, 2014)*	6 mg/kg q48h	6 mg/kg q48h
Oritavancin	245 (terminal)	No data	1200 mg IV x1	1200 mg x1	<30: No data	No data	Not removed by hemodialysis	No data	No data
Teicoplanin[NUS]	70-100	up to 230	6 mg/kg IV q24h	6 mg/kg q24h	6 mg/kg q48h	6 mg/kg q72h	6 mg/kg q72h (give AD on dialysis day)	6 mg/kg q72h	6 mg/kg q48h
Telavancin	8.1	17.9	10 mg/kg IV q24h	10 mg/kg q24h	30-50: 7.5mg/kg q24h; 10-30: 10 mg/kg q48h	10 mg/kg q48h	No data	No data	No data

TABLE 17A (7)

ANTIMICROBIAL	Half-life, hrs (renal function normal)	Half-life, hrs (ESRD)	Dose (renal function normal)	CrCl >50-90	CrCl 10-50	CrCl <10	Hemodialysis	CAPD	CRRT
GLYCOPEPTIDES, LIPOGLYCOPEPTIDES, LIPOPEPTIDES *(continued)*									
Vancomycin [7]	4-6	200-250	15-30 mg/kg IV q12h	15-30 mg/kg q12h	15 mg/kg q24-96h	7.5 mg/kg q2-3 days	For trough conc of 15-20, give 15 mg/kg if next dialysis in 1 day; give 25 mg/kg if next dialysis in 2 days; give 35 mg/kg if next dialysis in 3 days *(CID 53:124, 2011)*	7.5 mg/kg q2-3 days	CAVH/CVVH: 500 mg q24-48h
MACROLIDES, AZALIDES, LINCOSAMIDES, KETOLIDES									
Azithromycin	68	Unchanged	250-500 mg IV/po q24h	250-500 mg q24h	250-500 mg q24h	250-500 mg q24h	250-500 mg q24h	250-500 mg q24h	250-500 mg q24h
Clarithromycin (not ER)	5-7	22	500 mg po q12h	500 mg q12h	500 mg q12-24h	500 mg q24h	500 mg q24h (dose AD on dialysis days)	500 mg q24h	500 mg q12-24h
Telithromycin [5]	10	15	800 mg po q24h	800 mg q24h	30-50: 800 mg 10-30: 600 mg q24h	600 mg q24h	600 mg q24h (give AD on dialysis days)	No data	No data
MISCELLANEOUS ANTIBACTERIALS									
Chloramphenicol [5]	4.1	Unchanged	50-100 mg/kg/day po/IV (divided q6h)	50-100 mg/kg/day (divided q6h)	50-100 mg/kg/day (divided q6h)	50-100 mg/kg/day (divided q6h)	50-100 mg/kg/day (divided q6h)	50-100 mg/kg/day (divided q6h)	50-100 mg/kg/day (divided q6h)
Fosfomycin po	5.7	50	3 gm po x1		Do not use (low urine concentrations)				
Fusidic acid [NUS, 5]	8.9-11	8.9-11	250-750 mg po q8-12h	250-750 mg q8-12h	250-750 mg q8-12h	250-750 mg q8-12h	250-750 mg q8-12h	250-750 mg q8-12h	250-750 mg q8-12h
Metronidazole [5]	6-14	7-21	7.5 mg/kg IV/po q6h	7.5 mg/kg q6h	7.5 mg/kg q6h	7.5 mg/kg q12h	7.5 mg/kg q12h (give one of the dialysis day doses AD)	7.5 mg/kg q12h	7.5 mg/kg q6h
Nitrofurantoin	1	-	100 mg po q12h (Macrobid)	100 mg q12h (Macrobid)	Avoid use	Avoid use	Avoid use	Avoid use	Avoid use
Tinidazole [5]	13	No data	2 gm po q24h x 1-5 days	2 gm q24h x1-5 days	2 gm q24h x1-5 days	2 gm q24h x1-5 days	2 gm q24h x1-5 days (+ extra 1 gm AD)	No data	No data
Trimethoprim	8-15	20-49	100-200 mg po q12h	100-200 mg q12h	>30: 100-200 mg q12h; 10-30: 100-200 mg q18h	100-200 mg q24h	100-200 mg q24h (give dialysis day dose AD)	100-200 mg q24h	100-200 mg q18h

TABLE 17A (8)

ANTIMICROBIAL	Half-life, hrs (renal function normal)	Half-life, hrs (ESRD)	Dose (renal function normal)	CrCl >50-90	CrCl 10-50	CrCl <10	Hemodialysis	CAPD	CRRT
MISCELLANEOUS ANTIBACTERIALS *(continued)*									
TMP/SMX (treatment)	TMP 8-15, SMX 10	TMP 20-49, SMX 20-50	5-20 mg/kg/day po/IV (div q6-12h) base on TMP	5-20 mg/kg/day (divided q6-12h)	30-50: 5-20 mg/kg/day (div q6-12h); 10-29: 5-10 mg/kg/day (div q12h)	Not recommended (but if used: 5-10 mg/kg q24h)	Not recommended (but if used: 5-10 mg/kg q24h, give dialysis day dose AD)	Not recommended (but if used: 5-10 mg/kg q24h)	5 mg/kg q8h
TMP/SMX (prophylaxis)	as above	as above	1 DS tab po q24h or 3x/week	1 DS tab q24h or 3x/week	1 DS tab q24h or 3x/week	1 DS tab q24h or 3x/week			
OXAZOLIDINONES									
Linezolid	5	6-8	600 mg po/IV q12h	600 mg q12h	600 mg q12h	600 mg q12h	600 mg q12h (give one of the dialysis day doses AD)	600 mg q12h	600 mg q12h
Tedizolid	12	Unchanged	200 mg po/IV q24h	200 mg q24h	200 mg q24h	200 mg q24h	200 mg q24h	200 mg q24h	200 mg q24h
POLYMYXINS									
Colistin (polymyxin E) Based on 105 patients *(AAC 55:3284, 2011)*. All doses refer to colistin base in mg	6.3-12	≥48	Load: (2.5) x (2) x (pt wt in kg) Use lower of ideal or actual wt Start maintenance 12 hrs later (see formula) Max daily dose: 340 mg	Daily maintenance dose = 2.5 x [(1.5 x CrCln) + 30] Divide and give q8-12h, max 475 mg daily. CrCln = CrCl x (pt BSA in m^2 divided by 1.73)			75 mg (divided q12h) (non-dialysis days); 112.5 mg (divided q12h) (dialysis days)	160 mg q24h	For Css of 2.5 µg/ml, total daily dose is 80 mg (divided q12h). This dose is necessarily high due to drug removal by the dialysis membrane. See *AAC 55:3284, 2011*
TETRACYCLINES, GLYCYLCYCLINES									
Tetracycline	6-12	57-108	250-500 mg po q6h	250-500 mg q8-12h	250-500 mg q12-24h	250-500 mg q24h	250-500 mg q24h	250-500 mg q24h	250-500 mg q12-24h
ANTIMETABOLITES									
Flucytosine [8]	3-5	75-200	25 mg/kg po q6h	25 mg/kg q6h	25 mg/kg q12h	25 mg/kg q24h	25 mg/kg q24h (give dialysis day dose AD)	0.5-1 gm q24h	25 mg/kg q12h

TABLE 17A (9)

ANTIMICROBIAL	Half-life, hrs (renal function normal)	Half-life, hrs (ESRD)	Dose (renal function normal)	CrCl >50-90	CrCl 10-50	CrCl <10	Hemodialysis	CAPD	CRRT
ALLYLAMINES, AZOLES									
Fluconazole	20-50[7]	100	100-400 mg po/IV q24h	100-400 mg q24h	50-200 mg q24h	50-200 mg q24h	100-400 mg q24h (give dialysis day dose AD)	50-200 mg q24h	200-400 mg q24h
Itraconazole (IV) [5]	35-40	Unchanged	200 mg IV q12h	200 mg q12h	Do not use IV itraconazole if CrCl<30 due to accumulation of cyclodextrin vehicle				
Itraconazole (oral solution) [5]	35-40	Unchanged	100-200 mg po q12h	100-200 mg q12h	100-200 mg q12h	50-100 mg q12h	100 mg q12-24h	100 mg q12-24h	100-200 mg q12h
Terbinafine	36	No data	250 mg po q24h	250 mg q24h	Avoid use	Avoid use	Avoid use	Avoid use	Avoid use
Voriconazole (IV) [5]	dose-dependent	dose-dependent	6 mg/kg IV q12h x2 doses, then 4 mg/kg IV q12h	6 mg/kg q12h x2 doses, then 4 mg/kg q12h	If CrCl< 50, IV vehicle (cyclodextrin) accumulates. Use oral or discontinue.		Avoid use	Avoid use	Avoid use
ANTIMYCOBACTERIALS									
First line, tuberculosis									
Ethambutol [9]	4	7-15	15-25 mg/kg po q24h	15-25 mg/kg q24h	CrCl 30-50: 15-25 mg/kg q24-36h; CrCl 10-30: 15-25 mg/kg q36-48h	15 mg/kg q48h	15 mg/kg q48h (administer AD on dialysis days)	15 mg/kg q48h	15-25 mg/kg q24h
Isoniazid (INH) [5]	0.7-4	8-17	5 mg/kg po q24h	5 mg/kg q24h	5 mg/kg q24h	5 mg/kg q24h	5 mg/kg q24h (administer AD on dialysis days)	5 mg/kg q24h	5 mg/kg q24h
Pyrazinamide	10-16	26	25 mg/kg (max 2.5 gm) po q24h	25 mg/kg q24h	CrCl 21-50: 25 mg/kg q24h; CrCl 10-20: 25 mg/kg q48h	25 mg/kg q48h	25 mg/kg q48h (administer AD on dialysis days)	25 mg/kg q24h	25 mg/kg q24h
Rifabutin [5]	32-67	Unchanged	300 mg po q24h	300 mg q24h	300 mg q24h	300 mg q24h	300 mg q24h	300 mg q24h	300 mg q24h
Rifampin [5]	1.5-5	up to 11	600 mg po q24h	600 mg q24h	300-600 mg q24h	300-600 mg q24h	300-600 mg q24h	300-600 mg q24h	300-600 mg q24h
Rifapentine	13.2-14.1	Unchanged	600 mg po 1-2x/wk	600 mg 1-2x/wk	600 mg 1-2x/wk	600 mg 1-2x/wk	600 mg 1-2x/wk	600 mg 1-2x/wk	600 mg 1-2x/wk
Streptomycin [1,2]	2-3	30-70	15 mg/kg (max 1 gm) IM q24h	15 mg/kg q24h	15 mg/kg q24-72h	15 mg/kg q72-96h	15 mg/kg q72-96h (+ extra 7.5 mg/kg AD)	20-40 mg lost per L of dialysate/day	15 mg/kg q24-72h

TABLE 17A (10)

ANTIMICROBIAL	Half-life, hrs (renal function normal)	Half-life, hrs (ESRD)	Dose (renal function normal)	CrCl >50-90	CrCl 10-50	CrCl <10	Hemodialysis	CAPD	CRRT
ANTIMYCOBACTERIALS *(continued)*									
Second line, tuberculosis									
Bedaquiline	24-30 (terminal 4-5 mo)	No data	400 mg po q24h x2 wk, then 200 mg po 3x/wk x22 wk	400 mg q24h x2 wk, then 200 mg 3x/wk x22 wk	400 mg q24h x2 wk, then 200 mg 3x/wk x22 wk	Use with caution	Use with caution	Use with caution	Use with caution
Capreomycin	2-5	No data	15 mg/kg IM/IV q24h	15 mg/kg q24h	15 mg/kg q24h	15 mg/kg 3x/wk	15 mg/kg 3x/wk (give AD on dialysis days)	No data	No data
Cycloserine [10]	10	No data	250-500 mg po q12h	250-500 mg q12h	250-500 mg q12h-24h (dosing interval poorly defined)	500 mg q48h (or 3x/wk)	500 mg 3x/wk (give AD on dialysis days)	No data	No data
Ethionamide	2	9	500 mg po q12h	500 mg q12h	500 mg q12h	250 mg q12h	250 mg q12h	250 mg q12h	500 mg q12h
Kanamycin [1,2]	2-3	30-70	7.5 mg/kg IM/IV q12h	7.5 mg/kg q12h	7.5 mg/kg q24h	7.5 mg/kg q48h	7.5 mg/kg q48h (+ extra 3.25 mg/kg AD)	15-20 mg lost per L of dialysate/day	7.5 mg/kg q24h
Para-aminosalicylic acid (PAS)	0.75-1.0	23	4 gm po q12h	4 gm q12h	2-3 gm q12h	2 gm q12h	2 gm q12h (dose AD on dialysis days)	No data	No data
ANTIPARASITICS: ANTIMALARIALS									
Artemether/ lumefantrine (20 mg/120 mg)	art, DHA 1.6-2.2, lum 101-119	No data	4 tabs x1, 4 tabs in 8 hr, then 4 tabs q12h x2 days	4 tabs x1, 4 tabs in 8 hr, then 4 tabs q12h x2 days	4 tabs x1, 4 tabs in 8 hr, then 4 tabs q12h x2 days	4 tabs x1, 4 tabs in 8 hr, then 4 tabs q12h x2 days	No data	No data	No data
Atovaquone	67	No data	750 mg po q12h	750 mg q12h	CrCl 30-50: 750 mg q12h; CrCl 10-30: use with caution	Use with caution	No data	No data	No data
Atovaquone/ Proguanil (250 mg/100 mg)	atov 67, pro 12-21	No data	4 tabs po q24h x3 days	4 tabs q24h x3 days	CrCl <30: use with caution	Use with caution	No data	No data	No data
Chloroquine phosphate	45-55 days (terminal)	No data	2.5 gm po over 3 days	2.5 gm over 3 days	2.5 gm over 3 days	2.5 gm over 3 days (consider reducing dose 50%)	2.5 gm over 3 days (consider reducing dose 50%)	No data	No data

TABLE 17A (11)

ANTIMICROBIAL	Half-life, hrs (renal function normal)	Half-life, hrs (ESRD)	Dose (renal function normal)	CrCl >50-90	CrCl 10-50	CrCl <10	Hemodialysis	CAPD	CRRT
ANTIPARASITICS, ANTIMALARIALS *(continued)*									
Mefloquine	13-24 days	No data	750 mg po, then 500 mg po in 6-8 hrs	750 mg, then 500 mg in 6-8 hrs	750 mg, then 500 mg in 6-8 hrs	750 mg, then 500 mg in 6-8 hrs	No data	No data	No data
Quinine	9.7-12.5	up to 16	648 mg po q8h	648 mg q8h	648 mg q8-12h	648 mg q24h	648 mg q24h (give dialysis day dose AD)	648 mg q24h	648 mg q8-12h
OTHER									
Albendazole	8-12	No data	400 mg po q12-24h	400 mg q12-24h	400 mg q12-24h	400 mg q12-24h	No data	No data	No data
Dapsone	10-50	No data	100 mg po q24h	No data	No data	No data	No data	No data	No data
Ivermectin	20	No data	200 µg/kg/day po x1-2 days	200 µg/kg/day x1-2 days	200 µg/kg/day x1-2 days	200 µg/kg/day x1-2 days	No data	No data	No data
Miltefosine	7-31 days	No data	50 mg po q8h	No data	No data	No data	No data	No data	No data
Nitazoxanide	tizoxanide 1.3-1.8	No data	500 mg po q12h	No data	No data	No data	No data	No data	No data
Pentamidine	3-12	73-118	4 mg/kg IM/IV q24h	4 mg/kg q24h	4 mg/kg q24h	4 mg/kg q24-36h	4 mg/kg q48h (give dialysis day dose AD)	4 mg/kg q24-36h	4 mg/kg q24h
ANTIVIRALS **HEPATITIS B**									
Adefovir	7.5	15	10 mg po q24h	10 mg q24h	10 mg q48-72h	10 mg q72h	10 mg weekly (dose AD on dialysis days)	No data	No data
Entecavir	128-149	?	0.5 mg po q24h	0.5 mg q24h	0.15-0.25 mg q24h	0.05 mg q24h	0.05 mg q24h (dose AD on dialysis days)	0.05 mg q24h	No data
Telbivudine	40-49	No data	600 mg po q24h	600 mg q24h	30-49: 600 mg q48h; 10-30: 600 mg q72h	600 mg q96h	600 mg q96h (dose AD on dialysis days)	No data	No data
HEPATITIS C (SINGLE AGENTS)									
Daclatasvir	12-15	No data	60 mg po q24h	60 mg q24h	60 mg q24h	60 mg q24h	No data	No data	No data
Ribavirin	44	No data	Depends on indication	No dosage adjustment	Use with caution	Use with caution	No data	No data	No data
Simeprevir	41	Unchanged	150 mg po q24h	150 mg q24h	Use with caution (no data for use in patients with CrCl<30)		No data	No data	No data
Sofosbuvir	sofosbuvir 0.5-0.75	Unchanged	400 mg po q24h	400 mg q24h	Use with caution (no data for use in patients with CrCl<30)		No data	No data	No data

TABLE 17A (12)

ANTIMICROBIAL	Half-life, hrs (renal function normal)	Half-life, hrs (ESRD)	Dose (renal function normal)	CrCl >50-90	CrCl 10-50	CrCl <10	Hemodialysis	CAPD	CRRT
HEPATITIS C (FIXED-DOSE COMBINATIONS)									
Harvoni (Ledipasvir, Sofosbuvir)	ledipasvir 47	No data	1 tab po q24h	1 tab q24h	Use with caution (no data for use in patients with CrCl<30)		No data	No data	No data
Technivie (Ombitasvir, Paritaprevir, RTV)	ombit 28-34, parita 5.8	No data	2 tabs po q24h	2 tabs q24h	2 tabs q24h	2 tabs q24h	No data	No data	No data
Viekira Pak (Dasabuvir, Ombitasvir, Paritaprevir, RTV)	dasabuvir 5-8	No data	2 Ombit/Parita/RTV tabs q24h, Dasa 250 mg q12h	2 Ombit/Parita/RTV tabs q24h, Dasa 250 mg q12h	2 Ombit/Parita/RTV tabs q24h, Dasa 250 mg q12h	2 Ombit/Parita/RTV tabs q24h, Dasa 250 mg q12h	No data	No data	No data
HERPESVIRUS									
Acyclovir (IV) [11]	2.5-3.5	20	5-12.5 mg/kg IV q8h	5-12.5 mg/kg q8h	5-12.5 mg/kg q12-24h	2.5-6.25 mg/kg q24h	2.5-6.25 mg/kg q24h (dose AD on dialysis days)	2.5-6.25 mg/kg q24h	5-10 mg/kg q24h
Cidofovir (induction)	2.6	No data	5 mg/kg IV q-week x2 weeks	CrCl>55: 5 mg/kg q-week x2 weeks	Contraindicated in patients with CrCl of 55 ml/min or less		Contraindicated	Contraindicated	Contraindicated
Cidofovir (maintenance)	2.6	No data	5 mg/kg IV every 2 weeks	CrCl>55: 5 mg/kg every 2 weeks	Contraindicated in patients with CrCl of 55 ml/min or less		Contraindicated	Contraindicated	Contraindicated
Famciclovir	penciclovir 2-3	10-22	500 mg po q8h (VZV)	500 mg q8h	500 mg q12-24h	250 mg q24h	250 mg q24h (dose AD on dialysis days)	No data	No data
Ganciclovir (IV induction)	3.5	30	5 mg/kg IV q12h	CrCl 70-90, 5 mg/kg q12h; CrCl 50-69, 2.5 mg/kg q12h	CrCl 25-49, 2.5 mg/kg q24h; CrCl 10-24, 1.25 mg/kg q24h	1.25 mg/kg 3x/week	1.25 mg/kg 3x/week (dose AD on dialysis days)	1.25 mg/kg 3x/week	CVVHF: 2.5 mg/kg q24h *(AAC 58:94, 2014)*
Ganciclovir (IV maintenance)	3.5	30	5 mg/kg IV q24h	2.5-5 mg/kg q24h	0.625-1.25 mg/kg q24h	0.625 mg/kg 3x/week	0.625 mg/kg 3x/week (dose AD on dialysis days)	0.625 mg/kg 3x/week	No data
Ganciclovir (oral)	3.5	30	1 gm po q8h	0.5-1 gm q8h	0.5-1 gm q24h	0.5 gm 3x/week	0.5 gm 3x/week (dose AD on dialysis days)	No data	No data
Valacyclovir	3	14	1 gm po q8h (VZV)	1 gm q8h	1 gm q12-24h	0.5 gm q24h	0.5 gm q24h (dose AD on dialysis days)	0.5 gm q24h	1 gm q12-24h
Valganciclovir	ganciclovir 4	ganciclovir 67	900 mg po q12h	900 mg q12h	450 mg q24-48h	Do not use	See prescribing information	No data	No data

TABLE 17A (13)

ANTIMICROBIAL	Half-life, hrs (renal function normal)	Half-life, hrs (ESRD)	Dose (renal function normal)	CrCl >50-90	CrCl 10-50	CrCl <10	Hemodialysis	CAPD	CRRT
HERPESVIRUS *(continued)*									
			CrCl above 1.4 ml/min/kg (foscarnet only)	**CrCl >1 to 1.4 mL/min/kg (foscarnet only)**	**CrCl >0.8 to 1.0 mL/min/kg (foscarnet only)**	**CrCl >0.6 to 0.8 mL/min/kg (foscarnet only)**	**CrCl >0.5 to 0.6 mL/min/kg (foscarnet only)**	**CrCl 0.4 to 0.5 mL/min/kg (foscarnet only)**	**CrCl <0.4 mL/min/kg (foscarnet only)**
Foscarnet (induction) special dosing scale	3 (terminal 18-88)	Very long	60 mg/kg IV q8h	45 mg/kg q8h	50 mg/kg q12h	40 mg/kg q12h	60 mg/kg q24h	50 mg/kg q24h	Not recommended
Foscarnet (maintenance) special dosing scale	3 (terminal 18-88)	Very long	90-120 mg/kg IV q24h	70-90 mg/kg q24h	50-65 mg/kg q24h	80-105 mg/kg q48h	60-80 mg/kg q48h	50-65 mg/kg q48h	Not recommended
INFLUENZA									
Amantadine	14.8	500	100 mg po q12h	100 mg q12h	100 mg q24-48h	100 mg weekly	100 mg weekly (give AD on dialysis days)	100 mg weekly	100 mg q24-48h
Oseltamivir [12]	carboxylate 6-10	carboxylate >20	75 mg po q12h	CrCl >60: 75 mg q12h	CrCl 31-60: 30 mg q12h; CrCl 10-30: 30 mg q24h	No recommendation unless HD	30 mg after each dialysis, no drug on non-HD days *(see comments)*	30 mg after a dialysis exchange	No data
Peramivir	20	No data	600 mg IV q24h	600 mg q24h	CrCl 31-49: 200 mg q24h; CrCl 10-30: 100 mg q24h	100 mg x1, then 15 mg q24h	100 mg x1, then 100 mg 2 hrs AD on dialysis days only	No data	No data
Rimantadine [5]	24-36	prolonged	100 mg po q12h	100 mg q12h	100 mg q12-24h	100 mg q24h	No data	No data	Use with caution
ANTIRETROVIRALS (NRTIs)									
Abacavir (ABC) [5]	1.5	No data	600 mg po q24h	600 mg q24h	600 mg q24h	600 mg q24h	No data	No data	No data
Didanosine enteric coated (ddI)	1.6	4.5	400 mg EC po q24h	400 mg EC q24h	125-200 mg EC q24h	Do not use	No data	No data	No data
Emtricitabine capsules (FTC)	10	>10	200 mg po q24h	200 mg q24h	CrCl 30-49: 200 mg q48h; CrCl 15-29: 200 mg q72h	CrCl <15: 200 mg q96h	200 mg q96h	No data	No data
Emtricitabine oral solution (FTC)	10	>10	240 mg po q24h	240 mg q24h	CrCl 30-49: 120 mg q24h; CrCl 15-29: 80 mg q24h	CrCl <15: 60 mg q24h	60 mg q24h	No data	No data
Lamivudine (3TC)	5-7	15-35	300 mg po q24h (HIV dose)	300 mg q24h (HIV)	50-150 mg q24h (HIV)	25-50 mg q24h (HIV)	25-50 mg q24h (dose AD on dialysis days) (HIV)	25-50 mg po q24h (HIV)	100 mg first day, then 50 mg q24h (HIV)

TABLE 17A (14)

ANTIMICROBIAL	Half-life, hrs (renal function normal)	Half-life, hrs (ESRD)	Dose (renal function normal)	CrCl >50-90	CrCl 10-50	CrCl <10	Hemodialysis	CAPD	CRRT
ANTIRETROVIRALS (NRTIs) *(continued)*									
Stavudine (d4T)	1.2-1.6	5.5-8	30-40 mg po q12h	30-40 mg q12h	15-20 mg q12h	≥60 kg: 20 mg q24h; <60 kg, 15 mg q24h	≥60 kg: 20 mg q24h; <60 kg, 15 mg q24h (dose AD on dialysis days)	No data	30-40 mg q12h
Tenofovir (TDF)	17	Prolonged	300 mg po q24h	300 mg q24h	CrCl 30-49: 300 mg q48h; CrCl 10-29: 300 mg q72-96h	No data	300 mg after every 3rd dialysis, or q7 days if no dialysis	No data	No data
Zidovudine (ZDV)	0.5-3	1.3-3	300 mg po q12h	300 mg q12h	300 mg q12h	100 mg q8h	100 mg q8h (dose AD on dialysis days)	No data	300 mg q12h
FUSION/ENTRY INHIBITORS									
Enfuvirtide (ENF, T20) [5]	3.8	Unchanged	90 mg sc q12h	90 mg q12h	Not studied in patients with CrCl<35; DO NOT USE		Avoid use	Avoid use	Avoid use
Maraviroc (MVC)	14-18	No data	300 mg po q12h	300 mg q12h	No data	No data	No data	No data	No data
FIXED-DOSE COMBINATIONS									
Atripla (EFV/FTC/TDF)	See components	See components	1 tab po q24h	1 tab q24h	Do not use	Do not use	Do not use	Do not use	Do not use
Combivir (3TC/ZDV)	See components	See components	1 tab po q12h	1 tab q12h	Do not use	Do not use	Do not use	Do not use	Do not use
Complera, Eviplera (RPV/FTC/TDF)	See components	See components	1 tab po q24h	1 tab q24h	Do not use	Do not use	Do not use	Do not use	Do not use
Dutrebis (3TC/RAL)	See components	See components	1 tab po q12h	1 tab q12h	Do not use	Do not use	Do not use	Do not use	Do not use
Epzicom, Kivexa (ABC/3TC)	See components	See components	1 tab po q24h	1 tab q24h	Do not use	Do not use	Do not use	Do not use	Do not use
Evotaz (ATV/cobi) [13]	See components	See components	1 tab po q24h	1 tab q24h	1 tab q24h	1 tab q24h	Do not use	No data	No data
Genvoya (EVG/FTC/TAF/cobi)	See components	See components	1 tab po q24h	1 tab po q24h	CrCl 30-49: 1 tab po q24h; do not use if CrCl <30	Do not use	Do not use	Do not use	Do not use
Prezcobix (DRV/cobi) [13]	See components	See components	1 tab po q24h	1 tab q24h	1 tab q24h	1 tab q24h	1 tab q24h	1 tab q24h	1 tab q24h

TABLE 17A (15)

ANTIMICROBIAL	Half-life, hrs (renal function normal)	Half-life, hrs (ESRD)	Dose (renal function normal)	CrCl >50-90	CrCl 10-50	CrCl <10	Hemodialysis	CAPD	CRRT
FIXED-DOSE COMBINATIONS *(continued)*									
Stribild (EVG/FTC/TDF/cobi)	See components	See components	1 tab po q24h	Do not use if CrCl <70	Do not use	Do not use	Do not use	Do not use	Do not use
Triumeq (DTG/ABC/3TC)	See components	See components	1 tab po q24h	1 tab q24h	Do not use	Do not use	Do not use	Do not use	Do not use
Trizivir (ABC/3TC/ZDV)	See components	See components	1 tab po q12h	1 tab q12h	Do not use	Do not use	Do not use	Do not use	Do not use
Truvada (FTC/TDF)	See components	See components	1 tab po q24h	1 tab q24h	CrCl 30-49: 1 tab q48h; do not use if CrCl <30	Do not use	Do not use	Do not use	Do not use

[1] High flux HD membranes lead to unpredictable drug Cl; measure post-dialysis drug levels.
[2] Check levels with CAPD, PK highly variable. Usual method w/CAPD: 2L dialysis fluid replaced qid (Example amikacin: give 8L x 20 mg lost/L = 160 mg amikacin IV supplement daily).
[3] Gentamicin SLEDD dose: 6 mg/kg IV q48h beginning 30 min before start of SLEDD *(AAC 54:3635, 2010)*
[4] May falsely increase Scr by interference with assay.
[5] Dosage adjustment may be required in hepatic disease.
[6] Clav cleared by liver; thus, as dose of combination is decreased, a clav deficiency may occur (JAMA 285:386, 2001). If CrCl≤30, do not use 875/125 or 1000/62.5.
[7] New hemodialysis membranes increase vancomycin clearance; check levels.
[8] Goal peak serum concentration: 25-100 µg/ml.
[9] Monitor serum concentrations if possible in dialysis patients.
[10] Goal peak serum concentration: 20-35 µg/ml.
[11] Rapid infusion can increase SCr.
[12] Dosing for age >1 yr (dose after each hemodialysis): ≤15 kg, 7.5 mg; 16-23 kg, 10 mg; 24-40 kg, 15 mg; >40 kg, 30 mg *(CID 50:127, 2010)*.
[13] Do not use with tenofovir if CrCl <70.

TABLE 17B – NO DOSAGE ADJUSTMENT WITH RENAL INSUFFICIENCY BY CATEGORY

Antibacterials		Antifungals	Anti-TBc	Antivirals	
Azithromycin	Minocycline	Anidulafungin	Bedaquiline	Abacavir	
Ceftriaxone	Moxifloxacin	Caspofungin	Ethionamide	Atazanavir	Nelfinavir
Chloramphenicol	Nafcillin	Itraconazole oral solution	Isoniazid	Darunavir	Nevirapine
Ciprofloxacin XL	Oritavancin	Ketoconazole	Rifampin	Delavirdine	Raltegravir
Clindamycin	Polymyxin B	Micafungin	Rifabutin	Efavirenz	Ribavirin
Doxycycline	Pyrimethamine	Posaconazole, **po only**	Rifapentine	Enfuvirtide[1]	Saquinavir
Linezolid[3]	Rifaximin	Voriconazole, **po only**		Fosamprenavir	Simeprevir[2]
	Tedizolid			Indinavir	Sofosbuvir[2]
	Tigecycline			Lopinavir	Tipranavir

[1] Enfuvirtide: Not studied in patients with CrCl <35 mL/min. DO NOT USE
[2] No data for CrCl <30 mL/min
[3] Increased risk of bone marrow toxicity

TABLE 17C – ANTIMICROBIAL DOSING IN OBESITY

The number of obese patients is increasing. Intuitively, the standard doses of some drugs may not achieve effective serum concentrations. Pertinent data on anti-infective dosing in the obese patient is gradually emerging. Though some of the data needs further validation, the following table reflects what is currently known. **Obesity is defined as ≥ 20% over Ideal Body Weight (Ideal BW) or Body Mass Index (BMI) > 30. Dose =** suggested body weight (BW) for dose calculation in obese patient; or specific dose if applicable. In general, the absence of a drug in the table indicates a lack of pertinent information in the published literature.

Drug	Dose	Comments
Acyclovir	Use **Ideal BW** Example: for HSV encephalitis, give 10 mg/kg of Ideal BW q8h	Unpublished data from 7 obese volunteers *(Davis, et al., ICAAC abstract, 1991).*
Aminoglycosides	Use **Adjusted BW** Example: Critically ill patient. Gentamicin or Tobramycin (not Amikacin) 7 mg/kg of Adjusted BW IV q24h (See Comment)	Adjusted BW = Ideal BW + 0.4(Actual BW – Ideal BW). Ref: *Pharmacother 27:1081, 2007.* Follow levels so as to lower dose once hemodynamics stabilize.
Cefazolin (surgical prophylaxis)	No dose adjustment needed: 2 gm x 1 dose (repeat q 3 hours?)	Conflicting data; unclear whether dose should be repeated, or if an even higher dose is required. Patients with BMI 40-80 studied. Refs: *Surg 136:738, 2004; Eur J Clin Pharmacol 67:985, 2011; Surg Infect 13:33, 2012.*
Cefepime	Modest dose increase: 2 gm IV q8h instead of the usual q12h	Data from 10 patients (mean BMI 48) undergoing bariatric surgery; regimen yields free T > MIC of 60% for MIC of 8 µg/mL. Ref: *Obes Surg 22:465, 2012.*
Daptomycin	Use **Actual BW** Example: 4-12 mg/kg of Actual BW IV q24h	Data from a single-dose PK study in 7 obese volunteers. Ref: *Antimicrob Ag Chemother 51:2741, 2007.*
Flucytosine	Use **Ideal BW** Example: Crypto meningitis, give 25 mg/kg of Ideal BW po q6h	Date from one obese patient with cryptococcal disease. Ref: *Pharmacother 15:251, 1995.*
Levofloxacin	**No dose adjustment** required Example: 750 mg po/IV q24h	Data from 13 obese patients; variability in study findings renders conclusion uncertain. Refs: *AAC 55:3240, 2011; JAC 66:1653, 2011.* A recent PK study (requiring clinical validation) in patients with BMI of 40 or more suggests that higher doses may be necessary to achieve adequate drug exposure *(Clin Pharmacokin 53:753, 2014).*
Linezolid	**No dose adjustment required** Example: 600 mg po/IV q12h	Data from 20 obese volunteers up to 150 kg body weight suggest standard doses provide AUC values similar to nonobese subjects. In a recent case report, standard dosing in a 265 kg male with MRSA pneumonia seemed to have reduced clinical effectiveness. Refs: *Antimicrob Ag Chemother 57:1144, 2013; Ann Pharmacother 47: e25, 2013.*
Meropenem	**No dose adjustment required.** Example: 1 gm IV q8h.	PK data in ten hospitalized (non-ICU) patients similar to non-obese patients *(Ann Pharmacother 48:178, 2014).*

[1] Ref. for NRTIs and NNRTIs: *Kidney International 60:821, 2001*

TABLE 17C (2)

Drug	Dose	Comments
Moxifloxacin	**No dose adjustment** required Example: 400 mg po/IV q24h	Data from 12 obese patients undergoing gastric bypass. Ref: *J Antimicrob Chemother 66:2330, 2011.*
Oseltamivir	**No dose adjustment** required Example: 75 mg po q12h	Data from 10 obese volunteers, unclear if applicable to patients >250 kg (OK to give 150 mg po q12h). Ref: *J Antimicrob Chemother 66:2083, 2011.*
Piperacillin-tazobactam	6.75 gm IV over 4 hours and dosed every 8 hours. No data for pt with impaired renal function	Data need confirmation. Based on 14 obese patients with actual BW >130 kg and BMI >40 kg/m^2. Ref: *Int J Antimicrob Ag 41:52, 2013.* High dose to optimize dose for pathogens with MIC ≤16 mcg/mL. May enhance bleeding propensity in uremic patients.
Telavancin	If weight is 30% or more over ideal BW, dose using adjusted BW as for aminoglycosides.	The correct dosing weight to use for Telavancin is unclear. Actual BW may overdose and increase nephrotoxicity, ideal BW may underdose *(JAC 67:723, 2012; JAC 67:1300, 2012).* Problematic because serum levels are not routinely available.
Vancomycin	Use **Actual BW** Example: in critically ill patient give 25-30 mg/kg of Actual BW IV load, then 15-20 mg/kg of Actual BW IV q8h-12h (infuse over 1.5-2 hr). No single dose over 2 gm. Check trough levels.	Data from 24 obese patients; Vancomycin half-life appears to decrease with little change in Vd. Ref: *Eur J Clin Pharmacol 54:621, 1998.*
Voriconazole po	**No dose adjustment** required Example: 400 mg po q12h x2 doses then 200 mg po q12h. Check trough concentrations (underdosing common with Voriconazole).	Data from a 2-way crossover study of oral voriconazole in 8 volunteers suggest no adjustment required, but data from one patient suggest use of adjusted BW. Recommended IV voriconazole dose based on actual BW (no supporting data). Refs: *Antimicrob Ag Chemother 55:2601, 2011; Clin Infect Dis 53:745, 2011.*

TABLE 18 – ANTIMICROBIALS AND HEPATIC DISEASE: DOSAGE ADJUSTMENT*

The following alphabetical list indicates antibacterials excreted/metabolized by the liver **wherein a dosage adjustment may be indicated** in the presence of hepatic disease. Space precludes details; consult the PDR or package inserts for details. List is **not** all-inclusive:

Antibacterials		Antifungals	Antivirals[§]	
Ceftriaxone	Nafcillin	Caspofungin	Abacavir	Indinavir
Chloramphenicol	Rifabutin	Itraconazole	Atazanavir	Lopinavir/ritonavir
Clindamycin	Rifampin	Voriconazole	Darunavir	Nelfinavir
Fusidic acid	Synercid**		Delavirdine	Nevirapine
Isoniazid	Telithromycin++		Efavirenz	Rimantadine
Metronidazole	Tigecycline		Enfuvirtide	Ritonavir
	Tinidazole		Fosamprenavir	Stavudine

§ Ref. on antiretrovirals: *CID 40:174, 2005* ** Quinupristin/dalfopristin ++ Telithromycin reduce dose in renal & hepatic failure

TABLE 19 – TREATMENT OF CAPD PERITONITIS IN ADULTS*

(Periton Dial Intl 30:393, 2010)[1]

EMPIRIC Intraperitoneal Therapy: Culture Results Pending *(For MRSA see footnote*[2]*)*

Drug		Residual Urine Output	
		<100 mL per day	**>100 mL per day**
(Cefazolin or Vanco) +	Can mix in same bag	1 gm per bag, q24h	20 mg per kg BW per bag, q24h
Ceftazidime		3 gm LD, then 1-2 gm IP q24h *(AAC 58:19, 2014)*	20 mg per kg BW per bag, q24h

Drug	Intermittent Dosing (once per day)		Continuous Dosing (per liter exchange)	
	Anuric	**Non-Anuric**	**Anuric**	**Non-Anuric**
Amphotericin B	NA	NA	MD 1.5 mg	NA
Ampicillin	250–500 mg po bid	ND	No LD, MD 125 mg	ND
Amp-sulbactam	2 gm q12h	ND	LD 1 gm, MD 100 mg	LD 1 gm, MD ↑ 25%
Cefazolin	15 mg per kg	20 mg per kg	LD 500 mg, MD 125 mg	LD 500 mg, ↑ MD 25%
Cefepime	1 gm in one exchange/day	1.25 gm	LD 500 mg, MD 125 mg	LD 500 mg, ↑ MD 25%
Ceftazidime	1000–2000 mg	ND	LD 500 mg, MD 125 mg	LD 500 mg; ↑ MD 25%
Ciprofloxacin	500 mg po bid	ND	LD 50 mg, MD 25 mg	ND
Daptomycin			LD 100 mg, MD 20 mg	LD 500 mg, ↑ MD 25%
Fluconazole	200 mg q24h	ND	200 mg q24h	ND
Gentamicin	0.6 mg per kg	↑ dose 25%	Not recommended	Not recommended
Imipenem	1 gm in one exchange q12h		LD 250 mg, MD 50 mg	LD 250 mg, ↑ MD 25%
Itraconazole	100 mg q12h	100 mg q12h	100 mg q12h	100 mg q12h
Metronidazole	250 mg po bid	ND	250 mg po bid	ND
TMP-SMX	160/800 mg po bid	ND	LD 320/1600 mg po, MD 80/400 mg po q24h	ND
Vancomycin	15–30 mg per kg q3–7 days	↑ dose 25%	LD 1 gm; MD 25 mg	LD 1 gm, ↑ MD 25%

CAPD = continuous ambulatory peritoneal dialysis

Indications for catheter removal: 1) Relapse with same organism within 1 mo; 2) Failure to respond clinically within 5 days; 3) Exit site and tunnel infection; 4) Fungal peritonitis; 5) Fecal flora peritonitis (suggests bowel perforation).

[1] **All doses IP unless indicated otherwise.**
LD = loading dose, **MD** = maintenance dose, **ND** = no data; **NA** = not applicable—dose as normal renal function.
Anuric = <100 mL per day, **non-anuric** = >100 mL per day

[2] **Does not provide treatment for MRSA.** If gram-pos cocci on gram stain, include vanco.

TABLE 20A – ANTI-TETANUS PROPHYLAXIS, WOUND CLASSIFICATION, IMMUNIZATION

WOUND CLASSIFICATION		
Clinical Features	**Tetanus Prone**	**Non-Tetanus Prone**
Age of wound	> 6 hours	≤ 6 hours
Configuration	Stellate, avulsion	Linear
Depth	> 1 cm	≤ 1 cm
Mechanism of injury	Missile, crush, burn, frostbite	Sharp surface (glass, knife)
Devitalized tissue	Present	Absent
Contaminants (dirt, saliva, etc.)	Present	Absent

IMMUNIZATION SCHEDULE				
History of Tetanus Immunization	**Dirty, Tetanus-Prone Wound**		**Clean, non-Tetanus-Prone Wound**	
	Td[1,2]	Tetanus Immune Globulin	Td[1,2]	Tetanus Immune Globulin
Unknown or < 3 doses[3]	Yes	Yes	Yes	No
3 or more doses	No[4]	No	No[5]	No

Ref: *MMWR 60:13, 2011; MMWR 61:468, 2012; MMWR 62:131, 2013 (pregnancy)*

[1] Td = Tetanus & diphtheria toxoids, adsorbed (adult). For adult who has not received Tdap previously, substitute one dose of Tdap for Td when immunization is indicated *(MMWR 61::468, 2012)*.
[2] For children < 7 years, use DTaP unless contraindicated; for persons > 7 years, Td is preferred to tetanus toxoid alone, but single dose of Tdap can be used if required for catch-up series.
[3] Individuals who have not completed vaccine series should do so.
[4] Yes, if >5 years since last booster.
[5] Yes, if >10 years since last booster.

TABLE 20B – RABIES POSTEXPOSURE PROPHYLAXIS

All wounds should be cleaned immediately & thoroughly with soap & water.
This has been shown to protect 90% of experimental animals![1]

Animal Type	Evaluation & Disposition of Animal	Recommendations for Prophylaxis
Dogs, cats, ferrets	Healthy & available for 10-day observation	Don't start unless animal develops sx, then immediately begin HRIG + vaccine
	Rabid or suspected rabid	Immediate HRIG + vaccine
	Unknown (escaped)	Consult public health officials
Skunks, raccoons, bats,* foxes, coyotes, most carnivores	Regard as rabid	Immediate vaccination
Livestock, horses, rodents, rabbits; includes hares, squirrels, hamsters, guinea pigs gerbils, chipmunks, rats, mice, woodchucks	Consider case-by-case	Consult public health officials. Bites of squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, other small rodents, rabbits, and hares **almost never** require rabies post-exposure prophylaxis.

* Most recent cases of human rabies in U.S. due to contact (not bites) with silver-haired bats or rarely big brown bats but risk of acquiring rabies from non-contact bat exposure is exceedingly low *(CID 48:1493, 2009)*. For more detail, see *CID 30:4, 2000; JAVMA 219:1687, 2001; CID 37:96, 2003 (travel medicine advisory); Ln 363:959, 2004; EID 11:1921, 2005; MMWR 55 (RR-5), 2006.*

Postexposure Rabies Immunization Schedule

IF NOT PREVIOUSLY VACCINATED

Treatment	Regimen[2]
Local wound cleaning	**All postexposure treatment should begin with immediate, thorough cleaning of all wounds with soap & water.**
Human rabies immune globulin - HRIG	20 units per kg body weight given once on day *0*. If anatomically feasible, the full dose should be infiltrated around the wound(s), the rest should be administered IM in the gluteal area. If the calculated dose of HRIG is insufficient to inject all the wounds, it should be diluted with normal saline to allow infiltration around additional wound areas. HRIG should **not** be administered in the **same syringe**, **or** into the **same anatomical site** as vaccine, or more than 7 days after the initiation of vaccine. Because HRIG may partially suppress active production of antibody, no more than the recommended dose should be given.[3]
Vaccine	Human diploid cell vaccine (HDCV), rabies vaccine adsorbed (RVA), or purified chick embryo cell vaccine (PCECV) 1 mL **IM (deltoid area[4])**, one each days *0*, 3, 7, 14[5].

IF PREVIOUSLY VACCINATED[6]

Treatment	Regimen[2]
Local wound cleaning	All postexposure treatment should begin with immediate, thorough cleaning of all wounds with soap **&** water.
HRIG	HRIG should **not** be administered
Vaccine	HDCV or PCEC, 1 mL **IM (deltoid area[4])**, one each on days *0* & *3*

CORRECT VACCINE ADMINISTRATION SITES

Age Group	Administration Site
Children & adults	**DELTOID[4]** only (**NEVER** in gluteus)
Infants & young children	Outer aspect of thigh (anterolateral thigh) may be used (**NEVER** in gluteus)

[1] From *MMWR 48:RR-1, 1999; CID 30:4, 2000;* B. T. Matyas, Mass. Dept. of Public Health. *MMWR 57:1, 2008*

[2] These regimens are applicable for all age groups, including children.

[3] In most reported post-exposure treatment failures, only identified deficiency was failure to infiltrate wound(s) with HRIG *(CID 22:228, 1996)*. However, several failures reported from SE Asia in patients in whom WHO protocol followed *(CID 28:143, 1999)*.

[4] The **deltoid** area is the **only** acceptable site of vaccination for adults & older children. For infants & young children, outer aspect of the thigh (anterolateral thigh) may be used. Vaccine should **NEVER** be administered in gluteal area.

[5] Note that this is a change from previous recommendation of 5 doses (days *0*, *3*, 7, 14 & 28) based on new data & recommendations from ACIP. Note that the number of doses for persons with altered immunocompetence remains unchanged (5 doses on days 0, 3, 7, 14 & 28) and recommendations for pre-exposure prophylaxis remain 3 doses administered on days 0, 7 and 21 or 28 *(MMWR 59 (RR-2), 2010)*.

[6] Any person with a history of pre-exposure vaccination with HDCV, RVA, PCECV; prior post-exposure prophylaxis with HDCV, PCEC or rabies vaccine adsorbed (RVA); or previous vaccination with any other type of rabies vaccine & a documented history of antibody response to the prior vaccination.

TABLE 21 SELECTED DIRECTORY OF RESOURCES

ORGANIZATION	PHONE/FAX	WEBSITE(S)
ANTIPARASITIC DRUGS & PARASITOLOGY INFORMATION		
CDC Drug Line	Weekdays: 404-639-3670 Evenings, weekends, holidays: 404-639-2888	http://www.cdc.gov/ncidod/srp/drugs/drug-service.html
DPDx: Lab ID of parasites		www.dpd.cdc.gov/dpdx/default.htm
Malaria	daytime: 770-488-7788 other: 770-488-7100 US toll free: 855-856-4713	www.cdc.gov/malaria
Expert Compound. Pharm.	800-247-9767/Fax: 818-787-7256	www.expertpharmacy.org
World Health Organization (WHO)		www.who.int
Parasites & Health		www.dpd.cdc.gov/dpdx/HTML/Para_Health.htm
BIOTERRORISM		
Centers for Disease Control & Prevention	770-488-7100	www.bt.cdc.gov
Infectious Diseases Society of America	703-299-0200	www.idsociety.org
Johns Hopkins Center Civilian Biodefense		www.jhsph.edu
Center for Biosecurity of the Univ. of Pittsburgh Med. Center		www.upmc-biosecurity.org
US Army Medical Research Institute of Inf. Dis.		www.usamriid.army.mil
HEPATITIS B		
Hepatitis B Foundation		www.hepb.org, www.natap.org
HEPATITIS C		
CDC		www.cdc.gov/ncidod/diseases/hepatitis/C
Individual		http://hepatitis-central.com
		www.natap.org
HCV Guidelines		www.hcvguidelines.org
HIV		
General		
HIV InSite		http://hivinsite.ucsf.edu
		www.natap.org
Drug Interactions		
Liverpool HIV Pharm. Group		www.hiv-druginteractions.org
Other		http://AIDS.medscape.com
Prophylaxis/Treatment of Opportunistic Infections; HIV Treatment		www.aidsinfo.nih.gov
IMMUNIZATIONS		
CDC, Natl. Immunization Program	404-639-8200	www.cdc.gov/vaccines
FDA, Vaccine Adverse Events	800-822-7967	www.fda.gov/cber/vaers/vaers.htm
National Network Immunization Info.	877-341-6644	www.immunizationinfo.org
Influenza vaccine, CDC	404-639-8200	www.cdc.gov/vaccines
Institute for Vaccine Safety		www.vaccinesafety.edu
OCCUPATIONAL EXPOSURE, BLOOD-BORNE PATHOGENS (HIV, HEPATITIS B & C)		
Clinicians Consultation Center	888-448-4911	www.ucsf.edu/hivcntr
PEPline (exposed clinicians)		
WARMline (clinicians of HIV pts)		
Perinatal HIV Hotline	888-448-8765	www.ucsf.edu/hivcntr
Q-T_c INTERVAL PROLONGATION BY DRUGS		www.qtdrugs.org; www.crediblemeds.org
TRAVELERS' INFO: Immunizations, Malaria Prophylaxis, More		
Amer. Soc. Trop. Med. & Hyg.		www.astmh.org
CDC, general	877-394-8747	http://www.cdc.gov/travel/default.asp
CDC, Malaria:		www.cdc.gov/malaria
Prophylaxis		http://www.cdc.gov/travel/default.asp
MD Travel Health		www.mdtravelhealth.com
Pan American Health Organization		www.paho.org
World Health Organization (WHO)		www.who.int/home-page

TABLE 22A – ANTI-INFECTIVE DRUG-DRUG INTERACTIONS

Importance: ± = theory/anecdotal; + = of probable importance; ++ = of definite importance
To check for interactions between more than 2 drugs, *see: http://www.drugs.com/drug_interactions.html; http://www.healthline.com/druginteractions; www.medscape.com*

ANTI-INFECTIVE AGENT (A)	OTHER DRUG (B)	EFFECT	IMPORT
Abacavir	Methadone	↓ levels of B	++
Amantadine (Symmetrel)	Alcohol	↑ CNS effects	+
	Anticholinergic and anti-Parkinson agents (ex. Artane, scopolamine)	↑ effect of B: dry mouth, ataxia, blurred vision, slurred speech, toxic psychosis	+
	Trimethoprim	↑ levels of A & B	+
	Digoxin	↑ levels of B	±
Aminoglycosides—parenteral (amikacin, gentamicin, kanamycin, netilmicin, sisomicin, streptomycin, tobramycin)	Amphotericin B	↑ nephrotoxicity	++
	Cis platinum (Platinol)	↑ nephro & ototoxicity	+
	Cyclosporine	↑ nephrotoxicity	+
	Neuromuscular blocking agents	↑ apnea or respiratory paralysis	+
	Loop diuretics (e.g., furosemide)	↑ ototoxicity	++
	NSAIDs	↑ nephrotoxicity	+
	Non-depolarizing muscle relaxants	↑ apnea	+
	Radiographic contrast	↑ nephrotoxicity	+
	Vancomycin	↑ nephrotoxicity	+
Aminoglycosides—oral (kanamycin, neomycin)	**Warfarin**	↑ prothrombin time	+
Amphotericin B and ampho B lipid formulations	Antineoplastic drugs	↑ nephrotoxicity risk	+
	Digitalis	↑ toxicity of B if K^+ ↓	+
	Nephrotoxic drugs: aminoglycosides, cidofovir, cyclosporine, foscarnet, pentamidine	↑ nephrotoxicity of A	++
Ampicillin, amoxicillin	Allopurinol	↑ frequency of rash	++
Artemether-lumefantrine	CYP3A4 inhibitors: amiodarone, atazanavir, fluconazole, ritonavir, voriconazole	↑ levels of A; ↑ QTc interval	++
	CYP2D6 substrates: flecainide, imipramine, amitriptyline	↑ levels of B; ↑ QTc interval	++
Atazanavir	*See protease inhibitors and Table 22B*		
Atovaquone	Rifampin (perhaps rifabutin)	↓ serum levels of A; ↑ levels of B	+
	Metoclopramide	↓ levels of A	+
	Tetracycline	↓ levels of A	++

Azole Antifungal Agents [**Flu** = fluconazole; **Itr** = itraconazole; **Ket** = ketoconazole; **Posa** = posaconazole **Vor** = voriconazole; **Isa** = isavuconazole + = occurs; **blank space** = either studied & no interaction OR no data found (may be in pharm. co. databases)]

Flu	Itr	Ket	Posa	Vor	Isa			
+	+					Amitriptyline	↑ levels of B	+
					+	Bupropion	↓ levels of B	++
+	+	+		+		Calcium channel blockers	↑ levels of B	++
	+			+		Carbamazepine (vori contraindicated)	↓ levels of A	++
+	+	+	+	+	+	Cyclosporine	↑ levels of B, ↑ risk of nephrotoxicity	+
	+	+				Didanosine	↓ absorption of A	+
					+	Digoxin	↑ levels of B	++
	+	+	+	+		Efavirenz	↓ levels of A, ↑ levels of B	++ **(avoid)**
	+	+	+			H_2 blockers, antacids, sucralfate	↓ absorption of A	+
+	+	+	+	+		Hydantoins (phenytoin, Dilantin)	↑ levels of B, ↓ levels of A	++
	+	+				Isoniazid	↓ levels of A	+
	–	–	+	+	+	Lovastatin/simvastatin, atorvastatin	Rhabdomyolysis reported; ↑ levels of B	++
				+		Methadone	↑ levels of B	+
					+	Mycophenolate	↑ levels of B	++
+	+	+	+	+		Midazolam/triazolam, po	↑ levels of B	++
+	+			–		Warfarin	↑ effect of B	++
+	+			+		Oral hypoglycemics	↑ levels of B	++
			+	+		Pimozide	↑ levels of B—**avoid**	++
	+	+		+	+	Protease inhibitors, e.g., LPV	↑ levels of B	++
	+	+	+	+		Proton pump inhibitors	↓ levels of A, ↑ levels of B	++
+	+	+	+	+	+	Rifampin/rifabutin (vori contraindicated)	↑ levels of B, ↓ serum levels of A	++
	+					Rituximab	Inhibits action of B	++
			+	+	+	Sirolimus (vori and posa contraindicated)	↑ levels of B	++
+		+	+	+	+	Tacrolimus	↑ levels of B with toxicity	++
+		+				Theophyllines	↑ levels of B	+
		+				Trazodone	↑ levels of B	++
+						Zidovudine	↑ levels of B	+

TABLE 22A (2)

ANTI-INFECTIVE AGENT (A)	OTHER DRUG (B)	EFFECT	IMPORT
Bedaquiline	Rifampin	↓ levels of A	++
	Ketoconazole	↑ levels of A	
Caspofungin	Cyclosporine	↑ levels of A	++
	Tacrolimus	↓ levels of B	++
	Carbamazepine, dexamethasone, efavirenz, nevirapine, phenytoin, rifamycin	↓ levels of A; ↑ dose of caspofungin to 70 mg/d	++
Chloramphenicol	Hydantoins	↑ toxicity of B, nystagmus, ataxia	++
	Iron salts, Vitamin B12	↓ response to B	++
	Protease inhibitors—HIV	↑ levels of A & B	++
Clindamycin (Cleocin)	Kaolin	↓ absorption of A	++
	Muscle relaxants, e.g., atracurium, baclofen, diazepam	↑ frequency/duration of respiratory paralysis	++
	St John's wort	↓ levels of A	++
Cobicistat	*See Integrase Strand Transfer Inhibitors*		
Cycloserine	Ethanol	↑ frequency of seizures	+
	INH, ethionamide	↑ frequency of drowsiness/dizziness	+
Dapsone	Atazanavir	↑ levels of A - Avoid	++
	Didanosine	↓ absorption of A	–
	Oral contraceptives	↓ effectiveness of B	+
	Pyrimethamine	↑ in marrow toxicity	–
	Rifampin/Rifabutin	↓ serum levels of A	+
	Trimethoprim	↑ levels of A & B (methemoglobinemia)	–
	Zidovudine	May ↑ marrow toxicity	+
Daptomycin	HMG-CoA inhibitors (statins)	Consider DC statin while on dapto	++
Delavirdine (Rescriptor)	*See Non-nucleoside reverse transcriptase inhibitors (NNRTIs) and Table 22B*		
Didanosine (ddI) (Videx)	Allopurinol	↑ levels of A—**AVOID**	++
	Cisplatin, dapsone, INH, metronidazole, nitrofurantoin, stavudine, vincristine, zalcitabine	↑ risk of peripheral neuropathy	+
	Ethanol, lamivudine, pentamidine	↑ risk of pancreatitis	+
	Fluoroquinolones	↓ absorption 2° to chelation	+
	Drugs that need low pH for absorption: dapsone, indinavir, Itraconazole, ketoconazole, pyrimethamine, rifampin, trimethoprim	↓ absorption	+
	Methadone	↓ levels of A	++
	Ribavirin	↑ levels ddI metabolite—**avoid**	++
	Tenofovir	↑ levels of A **(reduce dose of A)**	++
Dolutegravir	*See Integrase Strand Transfer Inhibitors*		
Doripenem	Probenecid	↑ levels of A	++
	Valproic acid	↓ levels of B	–+
Doxycycline	Aluminum, bismuth, iron, Mg^{++}	↓ absorption of A	+
	Barbiturates, hydantoins	↓ serum t 2 of A	–
	Carbamazepine (Tegretol)	↓ serum t/2 of A	+
	Digoxin	↑ serum levels of B	–
	Warfarin	↑ activity of B	++
Efavirenz (Sustiva)	*See non-nucleoside reverse transcriptase inhibitors (NNRTIs) and Table 22B*		
Elvitegravir	*See Integrase Strand Transfer Inhibitors*		
Ertapenem (Invanz)	Probenecid	↑ levels of A	++
	Valproic acid	↓ levels of B	++
Ethambutol (Myambutol)	Aluminum salts (includes didanosine buffer)	↓ absorption of A & B	+
Etravirine	*See non-nucleoside reverse transcriptase inhibitors (NNRTIs) and Table 22B*		

Fluoroquinolones (**Cipro** = ciprofloxacin; **Gati** = gatifloxacin; **Gemi** = gemifloxacin; **Levo** = levofloxacin; **Moxi** = moxifloxacin; **Oflox** = ofloxacin)

Cipro	Gati	Gemi	Levo	Moxi	Oflox	NOTE: **Blank space** = *either studied and no interaction OR no data found*		
	+		+	+		**Antiarrhythmics (procainamide, amiodarone)**	↑ Q-T interval (torsade)	++
+	+		+	+	+	Insulin, oral hypoglycemics	↑ & ↓ blood sugar	++
+						Caffeine	↑ levels of B	+
+					+	Cimetidine	↑ levels of A	+
+					+	Cyclosporine	↑ levels of B	±
+	+		+	+	+	Didanosine	↓ absorption of A	++
+	+	+	+	+	+	**Cations: Al+++, Ca++, Fe++, Mg++, Zn++ (antacids, vitamins, dairy products), citrate/citric acid**	↓ absorption of A (some variability between drugs)	++
+						Methadone	↑ levels of B	++
+			+		+	**NSAIDs**	↑ risk CNS stimulation/seizures	++
+						Phenytoin	↑ or ↓ levels of B	+

TABLE 22A (3)

ANTI-INFECTIVE AGENT (A)						OTHER DRUG (B)	EFFECT	IMPORT
Fluoroquinolones *(continued)*								
Cipro	Gati	Gemi	Levo	Moxi	Oflox	**NOTE: Blank space** = either studied and no interaction OR no data found		
+	+	+			+	Probenecid	↓ renal clearance of A	+
+						Rasagiline	↑ levels of B	++
				+		Rifampin	↓ levels of A *(CID 45:1001, 2007)*	++
+	+	+	+		+	**Sucralfate**	**↓ absorption of A**	++
+						Theophylline	↑ levels of B	++
+						Thyroid hormone	↓ levels of B	++
+						Tizanidine	↑ levels of B	++
–			+	+	+	Warfarin	↑ prothrombin time	+
Ganciclovir (Cytovene) & **Valganciclovir** (Valcyte)						Imipenem	↑ risk of seizures reported	+
						Probenecid	↑ levels of A	+
						Zidovudine	↓ levels of A, ↑ levels of B	+
Gentamicin						*See Aminoglycosides—parenteral*		
Imipenem & Meropenem						BCG	↓ effectiveness of B–avoid combination	++
						Divalproex	↓ levels of B	++
						Ganciclovir	↑ seizure risk	++
						Probenecid	↑ levels of A	++
						Valproic acid	↓ levels of B	++
Indinavir						*See protease inhibitors and Table 22B*		

Integrase Strand Transfer Inhibitors (INSTI): Dolutegravir (**DTG**), Raltegravir (**RAL**), Elvitegravir (**ELV**)
NOTE: Interactions involving Stribild (elvitegravir + cobicistat + emtricitabine + tenofovir) reflect one or more of its components (the specifics may not be known).

ANTI-INFECTIVE AGENT (A)			OTHER DRUG (B)	EFFECT	IMPORT
DTG	RAL	Stribild (ELV)			
x	x	x	Antacids (polyvalent cations)	↓ levels of A—space dosing	++
		x	Antiarrhythmics: digoxin	↑ levels of B—monitor	+
	x		Atazanavir/RTV	↑ levels of A—monitor	±
		x	Atorvastatin	↑ levels of B—monitor	+
		x	Benzodiazepines	↑ levels of B—monitor	+
		x	Beta-blockers	↑ levels of B—monitor	+
		x	Bosentan	**↑ levels of B—adjust dose or avoid**	++
		x	Buprenorphine	↑ levels of B—monitor	+
		x	Buspirone	↑ levels of B—monitor	+
		x	Calcium channel blockers	↑ levels of B—monitor	+
x			Carbamazepine	**↓ levels of A—avoid**	++
		x		**↓ levels of A, ↑ levels of B—avoid**	++
		x	Clarithromycin	↑ levels of A and B—monitor	+
		x	Clonazepam	↑ levels of B—monitor	+
		x	Colchicine	↑ levels of B—adjust dose	+
		x	Cyclosporine	↑ levels of B—monitor	+
		x	Dexamethasone	**↓ levels of A—avoid**	++
x			Dofetilide	**↑ levels of B—avoid**	++
x			Efavirenz	↓ levels of A—adjust dose	++
	x			↓ levels of A—monitor	+
		x	Ethosuximide	↑ levels of B—monitor	+
x			Etravirine	**↓ levels of A—avoid**	++
	x			↓ levels of A—monitor	+
		x	Fluticasone	**↑ levels of B—avoid**	++
x			Fosamprenavir/RTV	**↓ levels of A—adjust dose or avoid**	++
x		x	Fosphenytoin/phenytoin	**↓ levels of A—avoid**	++
		x	Fluconazole	**↑ levels of A—avoid**	++
		x	Itraconazole	**↑ levels of A and B—adjust dose or avoid**	++
		x	Ketoconazole	**↑ levels of A and B—adjust dose or avoid**	++
x			Metformin	↑ levels of B—monitor	++
x			Nevirapine	**↓ levels of A—avoid**	++
	x		Omeprazole	↑ levels of A—monitor	±
		x	Oral contraceptives	**↑ or ↓ levels of B—avoid**	++
x		x	Oxcarbazepine	**↓ levels of A—avoid**	++

TABLE 22A (4)

Integrase Strand Transfer Inhibitors (INSTI) *(continued)*

ANTI-INFECTIVE AGENT (A)			OTHER DRUG (B)	EFFECT	IMPORT
DTG	RAL	Stribild (ELV)			
x		x	Phenobarbital	↓ **levels of A—avoid**	++
		x	Phenothiazines	↑ levels of B—monitor	+
		x	Phosphodiesterase-5 inhibitors	↑ **levels of B—adjust dose or avoid**	++
x			Primidone	↓ **levels of A—avoid**	++
x	x	x	Rifampin, rifabutin, rifapentine	↓ **levels of A—adjust dose or avoid**	++
		x	Risperidone	↑ levels of B—monitor	+
		x	Salmeterol	↑ **levels of B—avoid**	++
		x	Sirolimus	↑ levels of B—monitor	+
x		x	St. John's wort	↓ **levels of A—avoid**	++
		x	SSRIs	↑ levels of B—monitor	+
x	x	x	Sucralfate	↓ levels of A—space dosing	++
		x	Tacrolimus	↑ levels of B—monitor	++
x			Tipranavir/RTV	↓ **levels of A—adjust dose or avoid**	−−
	x			↓ levels of A—monitor	=
		x	Trazodone	↑ levels of B—monitor	+
		x	Tricyclic antidepressants	↑ levels of B—monitor	−
		x	Voriconazole	↑ **levels of A and B—adjust dose or avoid**	++
		x	Warfarin	↑ or ↓ levels of B—monitor	+
		x	Zolpidem ("Z" drugs)	↑ levels of B—monitor	+
Isoniazid			**Alcohol, rifampin**	**↑ risk of hepatic injury**	**++**
			Aluminum salts	↓ absorption (take fasting)	++
			Carbamazepine, phenytoin	↑ levels of B with nausea, vomiting, nystagmus, ataxia	++
			Itraconazole, ketoconazole	↓ levels of B	+
			Oral hypoglycemics	↓ effects of B	+
Lamivudine			Zalcitabine	**Mutual interference—do not combine**	++
Linezolid (Zyvox)			Adrenergic agents	Risk of hypertension	++
			Aged, fermented, pickled or smoked foods —↑ tyramine	Risk of hypertension	+
			Clarithromycin	↑ levels of A	++
			Meperidine	Risk of serotonin syndrome	++
			Rasagiline (MAO inhibitor)	Risk of serotonin syndrome	−
			Rifampin	↓ levels of A	++
			Serotonergic drugs (SSRIs)	Risk of serotonin syndrome	++
Lopinavir			*See protease inhibitors*		

Macrolides [**Ery** = erythromycin; **Azi** = azithromycin; **Clr** = clarithromycin. + = occurs. **blank space** = either studied and no interaction OR no data]

Ery	Azi	Clr			
	+		Calcium channel blockers	↑ serum levels of B	++
+		+	Carbamazepine	↑ serum levels of B, nystagmus, nausea, vomiting, ataxia	++ **(avoid w/ erythro)**
+		+	Cimetidine, **ritonavir**	↑ levels of B	+
+			Clozapine	↑ serum levels of B, CNS toxicity	+
		+	**Colchicine**	**↑ levels of B (potent, fatal)**	**++(avoid)**
+			Corticosteroids	↑ effects of B	+
+	+	+	Cyclosporine	↑ serum levels of B with toxicity	+
+	+	+	Digoxin, digitoxin	↑ serum levels of B (10% of cases)	+
		+	Efavirenz	↓ levels of A	++
+		+	Ergot alkaloids	↑ levels of B	++
		+	Linezolid	↑ levels of B	++
+		+	Lovastatin/simvastatin	↑ levels of B; rhabdomyolysis	++
+			Midazolam, triazolam	↑ levels of B, ↑ sedative effects	+
+		+	Phenytoin	↑ levels of B	+
+	+	+	Pimozide	**↑ Q-T interval**	++
+		+	Rifampin, rifabutin	↓ levels of A	+
+		+	Tacrolimus	↑ levels of B	++
+		+	Theophylline	↑ serum levels of B with nausea, vomiting, seizures, apnea	++
+		+	Valproic acid	↑ levels of B	+
+		+	Warfarin	May ↑ prothrombin time	+
		+	Zidovudine	↓ levels of B	+

TABLE 22A (5)

ANTI-INFECTIVE AGENT (A)	OTHER DRUG (B)	EFFECT	IMPORT
Maraviroc	Clarithromycin	↑ serum levels of A	++
	Delavirdine	↑ levels of A	++
	Itraconazole/ketoconazole	↑ levels of A	++
	Nefazodone	↑ levels of A	++
	Protease Inhibitors (not tipranavir/ritonavir)	↑ levels of A	++
	Anticonvulsants: carbamazepine, phenobarbital, phenytoin	↓ levels of A	++
	Efavirenz	↓ levels of A	++
	Rifampin	↓ levels of A	++
Mefloquine	ß-adrenergic blockers, calcium channel blockers, quinidine, quinine	↑ arrhythmias	+
	Divalproex, valproic acid	↓ level of B with seizures	++
	Halofantrine	Q-T prolongation	++ **(avoid)**
	Calcineurin inhibitors	Q-T prolongation (avoid)	++
Meropenem	*See Imipenem*		
Methenamine mandelate or hippurate	Acetazolamide, sodium bicarbonate, thiazide diuretics	↓ antibacterial effect 2° to ↑ urine pH	++
Metronidazole /Tinidazole	**Alcohol**	Disulfiram-like reaction	+
	Cyclosporin	↑ levels of B	++
	Disulfiram (Antabuse)	Acute toxic psychosis	+
	Lithium	↑ levels of B	++
	Warfarin	↑ anticoagulant effect	++
	Phenobarbital, hydantoins	↑ levels of B	++
Micafungin	Nifedipine	↑ levels of B	+
	Sirolimus	↑ levels of B	+
Nafcillin	Warfarin	↓ Warfarin effect	++
Nelfinavir	*See protease inhibitors and Table 22B*		
Nevirapine (Viramune)	*See non-nucleoside reverse transcriptase inhibitors (NNRTIs) and Table 22B*		
Nitrofurantoin	Antacids	↓ absorption of A	+

Non-nucleoside reverse transcriptase inhibitors (NNRTIs): For interactions with protease inhibitors, *see Table 22B*.
Del = delavirdine; **Efa** = efavirenz; **Etr** = etravirine; **Nev** = nevirapine

Del	Efa	Etr	Nev	Co-administration contraindicated *(See package insert)*:		IMPORT
+		+		Anticonvulsants: carbamazepine, phenobarbital, phenytoin		++
+		+		Antimycobacterials: rifabutin, rifampin		++
+				Antipsychotics: pimozide		++
+	+	+		Benzodiazepines: alprazolam, midazolam, triazolam		++
+	+			Ergotamine		++
+	+	+		HMG-CoA inhibitors (statins): lovastatin, simvastatin, atorvastatin, pravastatin		++
+		+		St. John's wort		++
				Dose change needed:		
+				Amphetamines	↑ levels of B—**caution**	++
+		+	+	Antiarrhythmics: amiodarone, lidocaine, others	↓ or ↑ levels of B—**caution**	++
+	+	+	+	Anticonvulsants: carbamazepine, phenobarbital, phenytoin	↓ levels of A and/or B	++
+	+	+	+	Antifungals: itraconazole, ketoconazole, voriconazole, posaconazole	Potential ↓ levels of B, ↑ levels of A	++ **(avoid)**
+			+	Antirejection drugs: cyclosporine, rapamycin, sirolimus, tacrolimus	↑ levels of B	++
+			+	Calcium channel blockers	↑ levels of B	++
+		+	+	Clarithromycin	↑ levels of B metabolite, ↑ levels of A	++
+		+	+	Cyclosporine	↑ levels of B	++
+		+		Dexamethasone	↓ levels of A	++
+	+	+	+	Sildenafil, vardenafil, tadalafil	↑ levels of B	++
+			+	Fentanyl, methadone	↑ levels of B	++
+				Gastric acid suppression: antacids, H-2 blockers, proton pump inhibitors	↓ levels of A	++
	+		+	Mefloquine	↓ levels of B	++
	+	+	+	Methadone, fentanyl	↓ levels of B	++
	+		+	Oral contraceptives	↑ or ↓ levels of B	++
+	+	+	+	Protease inhibitors—*see Table 22B*		
+	+	+	+	**Rifabutin, rifampin**	↑ or ↓ levels of rifabutin; ↓ levels of A—**caution**	++
+	+	+	+	St. John's wort	↓ levels of B	
+		+	+	Warfarin	↑ levels of B	++
Oritavancin				Warfarin	↑ levels of B	++
Pentamidine, IV				Amphotericin B	↑ risk of nephrotoxicity	+
				Pancreatitis-assoc drugs, eg, alcohol, valproic acid	↑ risk of pancreatitis	+
PIP-TZ				Methotrexate	↑ levels of B	++
Polymyxin B				Curare paralytics	Avoid: neuromuscular blockade	++

TABLE 22A (6)

ANTI-INFECTIVE AGENT (A)	OTHER DRUG (B)	EFFECT	IMPORT
Polymyxin E (Colistin)	Curare paralytics	Avoid: neuromuscular blockade	++
	Aminoglycosides, Ampho B, Vanco	↑ nephrotoxicity risk	++
Primaquine	Chloroquine, dapsone, INH, probenecid, quinine, sulfonamides, TMP/SMX, others	**↑ risk of hemolysis in G6PD-deficient patients**	++

Protease Inhibitors—Anti-HIV Drugs. (**Atazan** = atazanavir; **Darun** = darunavir; **Fosampren** = fosamprenavir; **Indin** = *indinavir;* **Lopin** = lopinavir; **Nelfin** = nelfinavir ; **Saquin** = saquinavir; **Tipran** = tipranavir). For interactions with antiretrovirals, see *Table 22B* **Only a partial list—check package insert**

Also see http://aidsinfo.nih.gov
To check for interactions between more than 2 drugs, see:
http://www.drugs.com/drug_interactions.html and http://www.healthline.com/druginteractions

Atazan	Darun	Fosampren	Indin	Lopin	Nelfin	Saquin	Tipran		
								Analgesics:	
							+	1. Alfentanil, fentanyl, hydrocodone, tramadol	↑ levels of B	+
	+			+		+	+	2. Codeine, hydromorphone, morphine, methadone	↓ levels of B *(JAIDS 41:563, 2006)*	+
+	+	+	+	+	+		+	**Anti-arrhythmics: amiodarone, lidocaine, mexiletine, flecainide**	↑ levels of B; **do not co-administer or use caution** *(See package insert.*	++
	+		+	+	+	+		**Anticonvulsants: carbamazepine, clonazepam, phenobarbital**	↓ levels of A, ↑ levels of B	++
+		+	+				+	Antidepressants, all tricyclic	↑ levels of B	++
+	+						+	Antidepressants, all other	↑ levels of B; do not use pimozide	++
	+							Antidepressants: SSRIs	↓ levels of B - avoid	++
							+	Antihistamines	**Do not use**	++
+	+	+	+	+	+		+	**Benzodiazepines, e.g., diazepam, midazolam, triazolam**	**↑ levels of B—do not use**	++
+	+			+				Boceprevir	↓ levels of A & B	++
+	+	+	+	+	+	+	+	Calcium channel blockers (all)	↑ levels of B	++
+	+			+	+	+	+	Clarithro, erythro	↑ levels of B if renal impairment	+
+	+			+	+		+	Contraceptives, oral	↓ levels of A & B	++
	+	+		+		+		Corticosteroids: prednisone, dexamethasone	↓ levels of A, ↑ levels of B	+
+	+	+	+	+	+	+	+	Cyclosporine	↑ levels of B, monitor levels	+
						+		Digoxin	↑ levels of B	++
+	+	+	+	+	+	+	+	Ergot derivatives	**↑ levels of B—do not use**	++
		+	+		+	+		Erythromycin, clarithromycin	↑ levels of A & B	+
			+		+	+		Grapefruit juice (>200 mL/day)	↓ indinavir & ↑ saquinavir levels	++
+	+	+	+	+	+	+		H2 receptor antagonists	↓ levels of A	++
+	+	+	+	+	+	+	+	**HMG-CoA reductase inhibitors (statins): lovastatin, simvastatin**	**↑ levels of B—do not use**	++
+								Irinotecan	**↑ levels of B—do not use**	++
	+	+	+	+	+	+	+	Ketoconazole, itraconazole. ? vori.	↑ levels of A, ↑ levels of B	–
	+	+	+	+	+	+	+	Posaconazole	↑ levels of A, no effect on B	+–
				+			+	Metronidazole	Poss. disulfiram reaction, a concl	–
				+				Phenytoin *(JAIDS 36:1034, 2004)*	↑ levels of A & B	++
+	+	+	+	+	+	+	+	**Pimozide**	**↑ levels of B—do not use**	++
+	+		+	+	+	+		Proton pump inhibitors	↓ levels of A	++
+	+	+	+	+	+	+	+	Rifampin, rifabutin	↓ levels of A, ↑ levels of B **(avoid)**	++
+	+	+	+	+	+	+	+	Sildenafil (Viagra), tadalafil, vardenafil	Varies, some ↑ & some ↓ levels of B	++
+	+	+	+	+	+	+	+	**St. John's wort**	**↓ levels of A—do not use**	++
+	+	+	+	+	+	+	+	**Sirolimus, tracrolimus**	**↑ levels of B**	++
+								Tenofovir	↓ levels of A—add ritonavir	++
	+		+	+				Theophylline	↓ levels of B	+
+		+		+			+	Warfarin	↑ levels of B	+
Pyrazinamide								INH, rifampin	May ↑ risk of hepatotoxicity	±
Pyrimethamine								Lorazepam	↑ risk of hepatotoxicity	+
								Sulfonamides, TMP/SMX	↑ risk of marrow suppression	+
								Zidovudine	↑ risk of marrow suppression	+
Quinine								Digoxin	↑ digoxin levels; ↑ toxicity	++
								Mefloquine	↑ arrhythmias	+
								Warfarin	↑ prothrombin time	++
Quinupristin- dalfopristin (Synercid)								Anti-HIV drugs: NNRTIs & PIs	↑ levels of B	++
								Antineoplastic: vincristine, docetaxel, paclitaxel	↑ levels of B	++
								Calcium channel blockers	↑ levels of B	++
								Carbamazepine	↑ levels of B	++
								Cyclosporine, tacrolimus	↑ levels of B	++

TABLE 22A (7)

ANTI-INFECTIVE AGENT (A)	OTHER DRUG (B)	EFFECT	IMPORT
Quinupristin-dalfopristin (Synercid) *(continued)*	Lidocaine	↑ levels of B	++
	Methylprednisolone	↑ levels of B	++
	Midazolam, diazepam	↑ levels of B	++
	Statins	↑ levels of B	++
Raltegravir	*See Integrase Strand Transfer Inhibitors*		
Ribavirin	Didanosine	↑ levels of B → toxicity—**avoid**	++
	Stavudine	↓ levels of B	++
	Zidovudine	↓ levels of B	++
Rifamycins (rifampin, rifabutin) Ref.: *ArIM 162:985, 2002* **The following is a partial list of drugs with rifampin-induced ↑ metabolism and hence lower than anticipated serum levels: ACE inhibitors, dapsone, diazepam, digoxin, diltiazem, doxycycline, fluconazole, fluvastatin, haloperidol, moxifloxacin, nifedipine, progestins, triazolam, tricyclics, voriconazole, zidovudine** *(Clin Pharmacokinetic 42:819, 2003).*	Al OH, ketoconazole, PZA	↓ levels of A	+
	Atovaquone	↑ levels of A, ↓ levels of B	+
	Beta adrenergic blockers (metoprolol, propranolol)	↓ effect of B	+
	Caspofungin	↓ levels of B—increase dose	++
	Clarithromycin	↑ levels of A, ↓ levels of B	++
	Corticosteroids	↑ replacement requirement of B	++
	Cyclosporine	↓ effect of B	++
	Delavirdine	**↑ levels of A, ↓ levels of B—avoid**	++
	Digoxin	↓ levels of B	++
	Disopyramide	↓ levels of B	++
	Fluconazole	↑ levels of A	+
	Amprenavir, indinavir, nelfinavir, ritonavir	↑ levels of A (↓ dose of A), ↓ levels of B	++
	INH	Converts INH to toxic hydrazine	++
	Itraconazole, ketoconazole	↓ levels of B, ↑ levels of A	++
	Linezolid	↓ levels of B	++
	Methadone	↓ serum levels (withdrawal)	+
	Nevirapine	**↓ levels of B—avoid**	++
	Warfarin	Suboptimal anticoagulation	++
	Oral contraceptives	↓ effectiveness; spotting, pregnancy	+
	Phenytoin	↓ levels of B	+
	Protease inhibitors	**↓ levels of A, ↑ levels of B—CAUTION**	++
	Quinidine	↓ effect of B	+
	Raltegravir	↓ levels of B	++
	Sulfonylureas	↓ hypoglycemic effect	+
	Tacrolimus	**↓ levels of B**	++
	Theophylline	↑ levels of B	+
	TMP/SMX	↓ levels of A	+
	Tocainide	↓ effect of B	+
Rimantadine	*See Amantadine*		
Ritonavir	*See protease inhibitors and Table 22B*		
Saquinavir	*See protease inhibitors and Table 22B*		
Stavudine	Ribavirin	↓ levels of A—**AVOID**	++
	Zidovudine	Mutual interference—do not combine	++
Strand Transfer Integrase Inhibitors (INSTI)	*See Integrase Strand Transfer Inhibitors*		
Sulfonamides	Beta blockers	↑ levels of B	++
	Cyclosporine	↓ cyclosporine levels	+
	Methotrexate	↑ antifolate activity	+
	Warfarin	↑ prothrombin time; bleeding	+
	Phenobarbital, rifampin	↓ levels of A	+
	Phenytoin	↑ levels of B; nystagmus, ataxia	+
	Sulfonylureas	↑ hypoglycemic effect	+
Telithromycin (Ketek)	Carbamazine	↓ levels of A	++
	Digoxin	↑ levels of B—do digoxin levels	++
	Ergot alkaloids	**↑ levels of B—avoid**	++
	Itraconazole; ketoconazole	↑ levels of A; no dose change	+
	Metoprolol	↑ levels of B	++
	Midazolam	↑ levels of B	++
	Warfarin	↑ prothrombin time	+
	Phenobarbital, phenytoin	↓ levels of A	++
	Pimozide	**↑ levels of B; QT prolongation—AVOID**	++
	Rifampin	**↓ levels of A—avoid**	++
	Simvastatin & other "statins"	↑ levels of B (↑ risk of myopathy)	++
	Sotalol	↓ levels of B	++
	Theophylline	↑ levels of B	++

TABLE 22A (8)

ANTI-INFECTIVE AGENT (A)	OTHER DRUG (B)	EFFECT	IMPORT
Tenofovir	Atazanavir	↓ levels of B—add ritonavir	++
	Didanosine (ddI)	↑ **levels of B (reduce dose)**	++
Terbinafine	Cimetidine	↑ levels of A	+
	Phenobarbital, rifampin	↓ levels of A	+
Tetracyclines	*See Doxycycline, plus:*		
	Atovaquone	↓ levels of B	+
	Digoxin	↑ toxicity of B (may persist several months—up to 10% pts)	++
	Methoxyflurane	↑ toxicity; polyuria, renal failure	+
	Sucralfate	↓ absorption of A (separate by ≥2 hrs)	+
Thiabendazole	Theophyllines	↑ serum theophylline, nausea	+
Tigecycline	Oral contraceptives	↓ levels of B	++
Tinidazole (Tindamax)	*See Metronidazole—similar entity, expect similar interactions*		
Tobramycin	*See Aminoglycosides*		
Trimethoprim	Amantadine, dapsone, digoxin, methotrexate, procainamide, zidovudine	↑ serum levels of B	++
	Potassium-sparing diuretics	↑ serum K^+	++
	Repaglinide	↑ levels of B (hypoglycemia)	−−
	Thiazide diuretics	↓ serum Na^+	±
Trimethoprim-Sulfamethoxazole	Ace inhibitors	↑ serum K+	−−
	Amantadine	↑ levels of B (toxicity)	++
	Azathioprine	Reports of leukopenia	−
	Cyclosporine	↓ levels of B, ↑ serum creatinine	+
	Loperamide	↑ levels of B	+
	Methotrexate	Enhanced marrow suppression	++
	Oral contraceptives, pimozide, and 6-mercaptopurine	↓ effect of B	+
	Phenytoin	↑ levels of B	+
	Rifampin	↑ levels of B	+
	Spironolactone, sulfonylureas	↑ levels K+	++
	Warfarin	↑ activity of B	+
Valganciclovir (Valcyte)	*See Ganciclovir*		
Vancomycin	Aminoglycosides	↑ frequency of nephrotoxicity	++
Zalcitabine (ddC) (HIVID)	Valproic acid, pentamidine (IV), alcohol, lamivudine	↑ pancreatitis risk	+
	Cisplatin, INH, metronidazole, vincristine, nitrofurantoin, d4T, dapsone	↑ risk of peripheral neuropathy	+
Zidovudine (ZDV) (Retrovir)	Atovaquone, fluconazole, methadone	↑ levels of A	+
	Clarithromycin	↓ levels of A	±
	Indomethacin	↑ levels of ZDV toxic metabolite	+
	Nelfinavir	↓ levels of A	++
	Probenecid, TMP/SMX	↑ levels of A	+
	Rifampin/rifabutin	↓ levels of A	++
	Stavudine	**Interference—DO NOT COMBINE!**	++
	Valproic Acid	↑ levels of A	++

TABLE 22B – DRUG-DRUG INTERACTIONS BETWEEN NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIS) AND PROTEASE INHIBITORS
(Adapted from Guidelines for the Use of Antiretroviral Agents in HIV Infected Adults & Adolescents; see *www.aidsinfo.nih.gov*)

NAME (Abbreviation, Trade Name)	Atazanavir (ATV, Reyataz)	DARUNAVIR (DRV, Prezista)	Fosamprenavir (FOS-APV, Lexiva)	Indinavir (IDV, Crixivan)	Lopinavir/Ritonavir (LP/R, Kaletra)	Nelfinavir (NFV, Viracept)	Saquinavir (SQV, Invirase)	Tipranavir (TPV)
Delavirdine (DLV, Rescriptor)	No data	No data	**Co-administration not recommended**	IDV levels ↑ 40%. Dose: IDV 600 mg q8h, DLV standard	Expect LP levels to ↑. No dose data	NFV levels ↑ 2X; DLV levels ↓ 50%. Dose: No data	SOV levels ↑ 5X. Dose: SQV 800 mg q8h, DLV standard	No data
Efavirenz (EFZ, Sustiva)	ATV AUC ↓ 74%. Dose: EFZ standard; ATA/RTV 300/100 mg q24h with food	Standard doses of both drugs	FOS-APV levels ↓. Dose: EFZ standard; FOS-APV 1400 mg + RTV 300 mg q24h or 700 mg FOS-APV + 100 mg RTV q12h	Levels: IDV ↓ 31%. Dose: IDV 1000 mg q8h, EFZ standard	Level of LP ↓ 40%. Dose: LP/R 533/133 mg q12h, EFZ standard	Standard doses	Level: SOV ↓ 62%. Dose: SQV 400 mg + RTV 400 mg q12h	No dose change necessary
Etravirine (ETR, Intelence)	↑ ATV & ↑ ETR levels.	Standard doses of both drugs	↑ levels of FOS-APV.	↓ level of IDV.	↑ levels of ETR, ↓ **levels of LP/R.**	↑ levels of NFV.	↓ ETR levels 33%; SOV/R no change. Standard dose of both drugs.	↓ levels of ETR, ↑ levels of TPV & RTV. **Avoid combination.**
Nevirapine (NVP, Viramune)	Avoid combination. ATZ increases NVP concentrations > 25%; NVP decreases ATZ AUC by 42%	Standard doses of both drugs	Use with caution. NVP AUC increased 14% (700/100 Fos/rit; NVP AUC inc 29% (Fos 1400 mg bid).	IDV levels ↓ 28%. Dose: IDV 1000 mg q8h or combine with RTV; NVP standard	LP levels ↓ 53%. Dose: LP/R 533/133 mg q12h; NVP standard	Standard doses	Dose: SQV + RTV 400/400 mg, both q12h	**Standard doses**

TABLE 23 – LIST OF GENERIC AND COMMON TRADE NAMES

GENERIC NAME: TRADE NAMES	GENERIC NAME: TRADE NAMES	GENERIC NAME: TRADE NAMES
Abacavir: Ziagen	Elvitegravir: Vitekta	Paritaprevir, ritonavir, ombitasvir: Technivie
Abacavir + Lamivudine: Epzicom	Elvitegravir + Cobicistat + Emtricitabine + Tenofovir: Stribild	Paritaprevir, ritonavir, ombitasvir, dasabuvir: Viekira Pak
Abacavir + Lamivudine + Dolutegravir: Triumeq	Emtricitabine: Emtriva	Paromomycin: Humatin
Abacavir + Lamivudine + Zidovudine: Trizivir	Emtricitabine + tenofovir: Truvada	Pentamidine: NebuPent, Pentam 300
Acyclovir: Zovirax	Emtricitabine + tenofovir + rilpivirine: Complera	Peramivir: Rapivab
Adefovir: Hepsera	Enfuvirtide (T-20): Fuzeon	Piperacillin/tazobactam: Zosyn, Tazocin
Albendazole: Albenza	Entecavir: Baraclude	Piperazine: Antepar
Amantadine: Symmetrel	Ertapenem: Invanz	Podophyllotoxin: Condylox
Amikacin: Amikin	Etravirine: Intelence	Polymyxin B: Poly-Rx
Amoxicillin: Amoxil, Polymox	Erythromycin(s): Ilotycin	Posaconazole: Noxafil
Amoxicillin extended release: Moxatag	*Ethyl succinate:* Pediamycin	Praziquantel: Biltricide
Amox./clav.: Augmentin, Augmentin ES-600; Augmentin XR	*Glucoheptonate:* Erythrocin	Primaquine: Primachine
Amphotericin B: Fungizone	*Estolate:* Ilosone	Proguanil: Paludrine
Ampho B-liposomal: AmBisome	Erythro/sulfisoxazole: Pediazole	Pyrantel pamoate: Antiminth
Ampho B-lipid complex: Abelcet	Ethambutol: Myambutol	Pyrimethamine: Daraprim
Ampicillin: Omnipen, Polycillin	Ethionamide: Trecator	Pyrimethamine/sulfadoxine: Fansidar
Ampicillin/sulbactam: Unasyn	Famciclovir: Famvir	Quinupristin/dalfopristin: Synercid
Artemether-Lumefantrine: Coartem	Fidaxomicin: Dificid	Raltegravir: Isentress
Atazanavir: Reyataz	Fluconazole: Diflucan	Retapamulin: Altabax
Atovaquone: Mepron	Flucytosine: Ancobon	Ribavirin: Virazole, Rebetr
Atovaquone + proguanil: Malarone	Fosamprenavir: Lexiva	Rifabutin: Mycobutin
Azithromycin: Zithromax	Foscarnet: Foscavir	Rifampin: Rifadin, Rimactane
Azithromycin ER: Zmax	Fosfomycin: Monurol	Rifapentine: Priftin
Aztreonam: Azactam, Cayston	Fusidic acid: Taksta	Rifaximin: Xifaxan
Bedaquiline: Sirturo	Ganciclovir: Cytovene	Rilpivirine: Edurant
Boceprevir: Victrelis	Gatifloxacin: Tequin	Rimantadine: Flumadine
Caspofungin: Cancidas	Gemifloxacin: Factive	Ritonavir: Norvir
Cefaclor: Ceclor, Ceclor CD	Gentamicin: Garamycin	Saquinavir: Invirase
Cefadroxil: Duricef	Griseofulvin: Fulvicin	Spectinomycin: Trobicin
Cefazolin: Ancef, Kefzol	Halofantrine: Halfan	Stavudine: Zerit
Cefdinir: Omnicef	Idoxuridine: Dendrid, Stoxil	Stibogluconate: Pentostam
Cefditoren pivoxil: Spectracef	INH + RIF: Rifamate	Silver sulfadiazine: Silvadene
Cefepime: Maxipime	INH + RIF + PZA: Rifater	Simeprevir: Olysio
Cefixime[NUS]: Suprax	Interferon alfa: Intron A	Sofosbuvir: Sovaldi
Cefoperazone-sulbactam: Sulperazon[NUS]	Interferon, pegylated: PEG-Intron, Pegasys	Sulfamethoxazole: Gantanol
Cefotaxime: Claforan	Interferon + ribavirin: Rebetron	Sulfasalazine: Azulfidine
Cefotetan: Cefotan	Imipenem + cilastatin: Primaxin, Tienam	Sulfisoxazole: Gantrisin
Cefoxitin: Mefoxin	Imiquimod: Aldara	Tedizolid: Sivextro
Cefpodoxime proxetil: Vantin	Indinavir: Crixivan	Telaprevir: Incivek
Cefprozil: Cefzil	Isavuconazole: Cresemba	Telavancin: Vibativ
Ceftaroline: Teflaro	Itraconazole: Sporanox	Telbivudine: Tyzeka
Ceftazidime: Fortaz, Tazicef, Tazidime	Iodoquinol: Yodoxin	Telithromycin: Ketek
Ceftazidime-avibactam: Avycaz	Ivermectin: Stromectol, Sklice	Temocillin: Negaban, Temocen
Ceftibuten: Cedax	Ketoconazole: Nizoral	Tenofovir: Viread
Ceftizoxime: Cefizox	Lamivudine: Epivir, Epivir-HBV	Terbinafine: Lamisil
Ceftobiprole: Zeftera	Lamivudine + abacavir: Epzicom	Thalidomide: Thalomid, Thiabendazole: Mintezol
Ceftolozane-tazobactam: Zerbaxa	Levofloxacin: Levaquin	Tigecycline: Tygacil
Ceftriaxone: Rocephin	Linezolid: Zyvox	Tinidazole: Tindamax
Cefuroxime: Zinacef, Ceftin	Lomefloxacin: Maxaquin	Tipranavir: Aptivus
Cephalexin: Keflex	Lopinavir/ritonavir: Kaletra	Tobramycin: Nebcin
Cephradine: Anspor, Velosef	Loracarbef: Lorabid	Tretinoin: Retin A
Chloroquine: Aralen	Mafenide: Sulfamylon	Trifluridine: Viroptic
Cidofovir: Vistide	Maraviroc: Selzentry	Trimethoprim: Primsol
Ciprofloxacin: Cipro, Cipro XR	Mebendazole: Vermox	Trimethoprim/sulfamethoxazole: Bactrim, Septra
Clarithromycin: Biaxin, Biaxin XL	Mefloquine: Lariam	Valacyclovir: Valtrex
Clindamycin: Cleocin	Meropenem: Merrem	Valganciclovir: Valcyte
Clofazimine: Lamprene	Mesalamine: Asacol, Pentasa	Vancomycin: Vancocin
Clotrimazole: Lotrimin, Mycelex	Methenamine: Hiprex, Mandelamine	Voriconazole: Vfend
Cloxacillin: Tegopen	Metronidazole: Flagyl	Zalcitabine: HIVID
Colistimethate: Coly-Mycin M	Micafungin: Mycamine	Zanamivir: Relenza
Cycloserine: Seromycin	Minocycline: Minocin	Zidovudine (ZDV): Retrovir
Daclatasvir: Daklinza	Moxifloxacin: Avelox	Zidovudine + 3TC: Combivir
Daptomycin: Cubicin	Mupirocin: Bactroban	Zidovudine + 3TC + abacavir: Trizivir
Dalbavancin: Dalvance	Nafcillin: Unipen	Abelcet: Ampho B-lipid complex
Darunavir: Prezista	Nelfinavir: Viracept	Albenza: Albendazole
Delavirdine: Rescriptor	Nevirapine: Viramune	Aldara: Imiquimod
Dicloxacillin: Dynapen	Nitazoxanide: Alinia	Alinia: Nitazoxanide
Didanosine: Videx	Nitrofurantoin: Macrobid, Macrodantin	Altabax: Retapamulin
Diethylcarbamazine: Hetrazan	Nystatin: Mycostatin	AmBisome: Ampho B-liposomal
Diloxanide furoate: Furamide	Ofloxacin: Floxin	Amikin: Amikacin
Dolutegravir: Tivicay	Olysio: Simeprevir	Amoxil: Amoxicillin
Doripenem: Doribax	Oritavancin: Orbactiv	Ancef: Cefazolin
Doxycycline: Vibramycin	Oseltamivir: Tamiflu	Ancobon: Flucytosine
Efavirenz: Sustiva	Oxacillin: Prostaphlin	Anspor: Cephradine
Efavirenz/Emtricitabine/Tenofovir: Atripla	Palivizumab: Synagis	

TABLE 23 (2)
LIST OF COMMON TRADE AND GENERIC NAMES

TRADE NAME: GENERIC NAME	TRADE NAME: GENERIC NAME	TRADE NAME: GENERIC NAME
Antepar: Piperazine	Isentress: Raltegravir	Stromectol: Ivermectin
Antiminth: Pyrantel pamoate	Kantrex: Kanamycin	Sulfamylon: Mafenide
Aptivus: Tipranavir	Kaletra: Lopinavir/ritonavir	Sulperazon[NUS]: Cefoperazone-sulbactam
Aralen: Chloroquine	Keflex: Cephalexin	Suprax: Cefixime[NUS]
Asacol: Mesalamine	Ketek: Telithromycin	Sustiva: Efavirenz
Atripla: Efavirenz/emtricitabine/tenofovir	Lamisil: Terbinafine	Symmetrel: Amantadine
Augmentin, Augmentin ES-600	Lamprene: Clofazimine	Synagis: Palivizumab
Augmentin XR: Amox./clav.	Lariam: Mefloquine	Synercid: Quinupristin/dalfopristin
Avelox: Moxifloxacin	Levaquin: Levofloxacin	Taksta: Fusidic acid
Avycaz: Ceftazidime-avibactam	Lexiva: Fosamprenavir	Tamiflu: Oseltamivir
Azactam: Aztreonam	Lorabid: Loracarbef	Tazicef: Ceftazidime
Azulfidine: Sulfasalazine	Macrodantin, Macrobid: Nitrofurantoin	Technivie: Paritaprevir, ritonavir, ombitasvir
Bactroban: Mupirocin	Malarone: Atovaquone + proguanil	Teflaro: Ceftaroline
Bactrim: Trimethoprim/ sulfamethoxazole	Mandelamine: Methenamine mandel	Tegopen: Cloxacillin
Baraclude: Entecavir	Maxaquin: Lomefloxacin	Tequin: Gatifloxacin
Biaxin, Biaxin XL: Clarithromycin	Maxipime: Cefepime	Thalomid: Thalidomide
Biltricide: Praziquantel	Mefoxin: Cefoxitin	Tienam: Imipenem
Cancidas: Caspofungin	Mepron: Atovaquone	Tinactin: Tolnaftate
Cayston: Aztreonam (inhaled)	Merrem: Meropenem	Tindamax: Tinidazole
Ceclor, Ceclor CD: Cefaclor	Minocin: Minocycline	Tivicay: Dolutegravir
Cedax: Ceftibuten	Mintezol: Thiabendazole	Trecator SC: Ethionamide
Ceftzox: Ceftizoxime	Monocid: Cefonicid	Triumeq: Abacavir + Lamivudine + Dolutegravir
Cefotan: Cefotetan	Monurol: Fosfomycin	Trizivir: Abacavir + ZDV + 3TC
Ceftin: Cefuroxime axetil	Moxatag: Amoxicillin extended release:	Trobicin: Spectinomycin
Cefzil: Cefprozil	Myambutol: Ethambutol	Truvada: Emtricitabine + tenofovir
Cipro, Cipro XR: Ciprofloxacin & extended release	Mycamine: Micafungin	Tygacil: Tigecycline
Claforan: Cefotaxime	Mycobutin: Rifabutin	Tyzeka: Telbivudine
Coartem: Artemether-Lumefantrine	Mycostatin: Nystatin	Unasyn: Ampicillin/sulbactam
Coly-Mycin M: Colistimethate	Nafcil: Nafcillin	Unipen: Nafcillin
Combivir: ZDV + 3TC	Nebcin: Tobramycin	Valcyte: Valganciclovir
Complera: Emtricitabine + tenofovir – rilpivirine	NebuPent: Pentamidine	Valtrex: Valacyclovir
Cresemba: Isavuconazole	Nizoral: Ketoconazole	Vancocin: Vancomycin
Crixivan: Indinavir	Norvir: Ritonavir	Vantin: Cefpodoxime proxetil
Cubicin: Daptomycin	Noxafil: Posaconazole	Velosef: Cephradine
Cytovene: Ganciclovir	Olysio: Simeprevir	Vermox: Mebendazole
Daklinza: Daclatasvir	Omnicef: Cefdinir	Vfend: Voriconazole
Dalvance: Dalbavancin	Omnipen: Ampicillin	Vibativ: Telavancin
Daraprim: Pyrimethamine	Orbactiv: Oritavancin	Vibramycin: Doxycycline
Dificid: Fidaxomicin	Pediamycin: Erythro. ethyl succinate	Victrelis: Boceprevir
Diflucan: Fluconazole	Pediazole: Erythro. ethyl succinate + sulfisoxazole	Videx: Didanosine
Doribax: Doripenem	Pegasys, PEG-Intron: Interferon, pegylated	Viekira Pak: Paritaprevir, ritonavir, ombitasvir, dasabuvir
Duricef: Cefadroxil	Pentam 300: Pentamidine	Viracept: Nelfinavir
Dynapen: Dicloxacillin	Pentasa: Mesalamine	Viramune: Nevirapine
Edurant: Rilpivirine	Polycillin: Ampicillin	Virazole: Ribavirin
Emtriva: Emtricitabine	Polymox: Amoxicillin	Viread: Tenofovir
Epivir, Epivir-HBV: Lamivudine	Poly-Rx: Polymyxin B	Vistide: Cidofovir
Epzicom: Lamivudine + abacavir	Prezista: Darunavir	Vitekta: Elvitegravir
Factive: Gemifloxacin	Priftin: Rifapentine	Xifaxan: Rifaximin
Famvir: Famciclovir	Primaxin: Imipenem + cilastatin	Yodoxin: Iodoquinol
Fansidar: Pyrimethamine + sulfadoxine	Primsol: Trimethoprim	Zerit: Stavudine
Flagyl: Metronidazole	Prostaphlin: Oxacillin	Zeftera: Ceftobiprole
Floxin: Ofloxacin	Rapivab: Peramivir	Zerbaxa: Ceftolozane-tazobactam
Flumadine: Rimantadine	Rebetol: Ribavirin	Ziagen: Abacavir
Foscavir: Foscarnet	Rebetron: Interferon + ribavirin	Zinacef: Cefuroxime
Fortaz: Ceftazidime	Relenza: Zanamivir	Zithromax: Azithromycin
Fulvicin: Griseofulvin	Rescriptor: Delavirdine	Zmax: Azithromycin ER
Fungizone: Amphotericin B	Retin A: Tretinoin Retrovir: Zidovudine (ZDV)	Zovirax: Acyclovir
Furadantin: Nitrofurantoin	Reyataz: Atazanavir	Zosyn: Piperacillin/tazobactam
Fuzeon: Enfuvirtide (T-20)	Rifadin: Rifampin	Zyvox: Linezolid
Gantanol: Sulfamethoxazole	Rifamate: INH + RIF	
Gantrisin: Sulfisoxazole	Rifater: INH + RIF + PZA	
Garamycin: Gentamicin	Rimactane: Rifampin	
Halfan: Halofantrine	Rocephin: Ceftriaxone	
Hepsera: Adefovir	Selzentry: Maraviroc	
Herplex: Idoxuridine	Septra: Trimethoprim/sulfa	
Hiprex: Methenamine hippurate	Seromycin: Cycloserine	
HIVID: Zalcitabine	Silvadene: Silver sulfadiazine	
Humatin: Paromomycin	Sirturo: Bedaquiline	
Ilosone: Erythromycin estolate	Sivextro: Tedizolid	
Ilotycin: Erythromycin	Sklice: Ivermectin lotion	
Incivek: Telaprevir	Solvadi: Sofosbuvir	
Intelence: Etravirine	Spectracef: Cefditoren pivoxil	
Intron A: Interferon alfa	Sporanox: Itraconazole	
Invanz: Ertapenem	Stoxil: Idoxuridine	
Invirase: Saquinavir	Stribild: Elvitegravir + Cobicistat + Emtricitabine + Tenofovir	

PAGES (page numbers bold if major focus)

A

Abacavir 97, 183, **192**, 229, 230, 235, 244, 245
Abortion, prophylaxis/septic **25**, **202**
Acanthamoeba **14**, 152
Acinetobacter 22, 40, 47, 50, **69**, 81, 103
Acne rosacea and vulgaris **51**, 162, 177
Actinomycosis 40, 45, 69
Acute complicated urinary tract infection **35**
Acyclovir 96, **169**, 170, 171, 172, **177**, 178, 209, 229, 244, 245
Adefovir 95, **178**, 196, 244, 245
Adenovirus 13, 36, 38, 42, 166
Adverse reactions
- Antibacterials **115**
- **Antifungals** **134**
- **Antimycobacterials** **148**
- **Antiparasitic drugs** **162**, **165**
- **Antiviral drugs** **177**

Aeromonas hydrophila 18, 55, 69
Aggregatibacter aphrophilus 70
AIDS 6, **10**, 15, **20**, 21, 24, 27, 36, **44**, 45, 51, 57, 72, **127**, 128, 132, 136, 141, 144, 145, 148, 151, 152, 156, 161, 168, 170, 172, 177, 207, 234
Albendazole 95, 152, 157, 158, 159, 160, **162** **164**, 244
Allergic bronchopulmonary aspergillosis 121
Alligator bite **52**
Amantadine **180**, 235, 241, 242, 244, 245
Amebiasis 18, 20, 36, **151**
Amebic meningoencephalitis **152**
Amikacin 88, 94, 115, **118** 120, 145, 146, 149, 215, 235, 244
Aminoglycosides, single daily dose 118
Amnionitis, septic abortion **25**
Amoxicillin 89, 102, 115, 202, 235, 244, 245
Amoxicillin extended release 89, 102, 244, 245
Amoxicillin-clavulanate 89, 90, 102, 115, 121, 202
Amphotericin B 93, 152
Amphotericin B, ampho B 118, 121, 122, 127, 128, 131, **134**, 135, 210, 231, 235, 239, 244, 245
- lipid ampho B preps 121, 127, 131 **134** 235

Amphotericin B-lipid complex 93
Ampicillin 8, 28, 29, 90, **102** **103** 115, 231, 235, 244, 245
Ampicillin-sulbactam 90, **103**, 115, 201, 202, 203, 231
Anaerobic lung infection 43
Anaplasma (Ehrlichia) 58, 70
Ancylostoma caninum 158
Anemia 192
Angiostrongylus cantonensis (Angiostrongyliasis) 10, 158, 165
Anidulafungin 93, 135, 229
Anisakiasis **157**
Antacids 237
Anthrax **40**, **51**, 53, 56, 69
Antibacterials, Prolonged/Continuous Dosing 119
Antifungals **121**
Antimicrobial dosing in obesity **229**
Antimony compounds **162**
Antiretroviral Drugs & Therapy/Antiviral Drugs **166**
Aphthous stomatitis **45**, 149
Appendicitis 20, **47**
Arcanobacterium haemolyticum 69
Artemether 162
Artemether-Lumefantrine 94, 100, 154, 155, **156**, 162, 235, 244, 245
Artesunate 162
Artesunate (AS) 94
Arthritis, septic 18, 23, **31**, **32**, 33, 62, 72, 107, 163, 171
- reactive (Reiter's) 27, **31**

Ascariasis **157**
Aspergilloma 121
Aspergillosis 14, 15, 30, 50, 64, 66, **121**, **122**, 135, 136, 210
Asplenia 52, 64, 152
Atabrine **162**
Atazanavir 97, 101, 181, 185, 187, 194, 208, 229, 230, 235, 236, 237, 240, 242, 243, 244, 245
Athlete's foot (Tinea pedis) **129**
Atovaquone 95
Atovaquone, atovaquone + proguanil 132, 152, 153, 155, 156, **162**, 235, 241, 242, 244, 245
Atripla 181, 184
Avibactam 88
Avycaz 245
Azithromycin 10, 72, 91, 99, 108, 116, 144, 145, 152, 229, 238, 244, 245
Azithromycin ER 91
Azole antifungals 112, **121**
AZT (zidovudine) 177, 208, 235, 236, 237, 239, 240, 241, 242, 244, 245
Aztreonam 89, **104**, 105, 115, 120, 202, 244, 245

B

Babesia, babesiosis **57**, 58, **152**
Bacillary angiomatosis 51, **57**
Bacillus anthracis (anthrax) 40, 51, 53, 56, 69
Bacillus cereus, subtilis **15**, 69
Bacitracin 114
Bacterial endocarditis 21, 28, 29, 30, 31, 56, 72, 107, 204
Bacterial peritonitis 17, 22, 26, 36, 46, **47**, 55, 56, 63, 134, 201, 203
Bacterial vaginosis **26**, 70
Bacteriuria, asymptomatic **35**, 72, 199
Bacteroides species 6, 17, **22**, 25, 26, 36, 43, 47, 52, 55, 56, 69
Balanitis **26**, 31
Balantidiasis **151**
Bartonella henselae, quintana 30, 36, 44, 45, 51, **57**, 69
Bartonellosis 158
BCG 137, **144**
Bedaquiline 94, 100, 140 **149** 229, 236, 244
Bell's palsy **169**
Benzamide 89
Benzathine penicillin, Bicillin 62, 102
Benznidazole 95, 157, **163**
Biliary sepsis **17**, 22, 63
Biloma, post-transplant 36
Biological weapons 234
Bites 27 **52** **53** 55, 171, 175, 233
Bithionol 117
Blastocystis hominis **151**
Blastomyces dermatitidis 122
Blastomycosis 56 **122** 131
Blepharitis **12**
Boceprevir 244, 245
Boils (furunculosis) **53**, **54**, 82
Bordetella pertussis (whooping cough) **37** 69
Borrelia burgdorferi, B. garinii, B. afzelii 32, **58**, 69
Bosentan 237
Botulism (food-borne, infant, wound) **65**
Brain abscess **6**, **7**, 156
Breast infection (mastitis, abscess) 6
Bronchitis, bronchiolitis 36, 37, 38, 108, 174
Bronchopneumonia **38**

Bold numbers indicate major considerations.
Antibiotic selection often depends on modifying circumstances and alternative agents.

PAGES (page numbers bold if major focus)

Brucellosis 32, **61**, 69, 72
Bubonic plague **45**
Buccal cellulitis 45
Bunyaviridae 166
Burkholderia (Pseudomonas) cepacia **43**, 69
Burkholderia pseudomallei (melioidosis) **41**, 56, **69**
Burns **53**, 65, 66, 232
  non-infected 53
  sepsis 53
Bursitis, septic **33**
Buruli Ulcer 146

C

Calymmatobacterium granulomatis **24**
Campylobacter jejuni, fetus 17, 18, 20, 31, 69
Canaliculitis 15
Candida albicans, glabrata, krusei, lusitaniae 21, 26, 134, 136
Candida Stomatitis, Thrush **45**
Candidemia, candidiasis 14, 15, 17, 21, 26, 27, 30, 36, 46, 54, 56, 63, 64, 66, **122**, 134, 135, 136, 210
Candidiasis
  Bloodstream - Neutropenic patient **123**
  Bloodstream - Non-neutropenic patient **122**
  Candida esophagitis **124**
  CNS Infection **125**
  Cutaneous **125**
  Cystitis **126**
  Endocarditis **123**
  Endophthalmitis **125**
  Myocarditis **123**
  Neonatal candidiasis **126**
  Oropharyngeal candidiasis **124**
  Osteomyelitis **123**
  Pericarditis **124**
  Peritonitis **126**
  Pyelonephritis **126**
  Septic arthritis **123**
  Vulvovaginitis **125**
Canimorsus 52
CAPD peritonitis 47, 231
Capillariasis 157
Capnocytophaga ochracea, canimorsus **52**, 64, 69
Capreomycin 94, 139, **149**
Carbapenems 81, 103, 115
Caspofungin 93, 121, **134**, 229, 230, 236, 244, 245
Cat bite **52**
Catfish sting 52
Cat-scratch disease 36, 44, 45, 51, 52, 57
Cayetanensis **151**
CDC Drug Service 151
Cefaclor, Cefaclor–ER 89, **106**, 116, 244, 245
Cefadroxil 89, **106**, 116, 244, 245
Cefazolin 88, **104**, 116, 201, 202, 203, 229, 231, 244
Cefdinir 89, 106, 116, 244, 245
Cefditoren pivoxil 89, **106**, 116, 244, 245
Cefepime 81, 88, 105, 116, **119**, 229, 231, 244, 245
Cefixime 89, 106, 116
Cefoperazone-sulbactam 104
Cefotaxime 88, **104**, 105, 116, 117, 244, 245
Cefotetan 88, **104**, 116, 201, 202, 244, 245
Cefoxitin 88, **104**, 105, 116, 145, 201, 202, 244, 245
Cefpirome **105**
Cefpodoxime 89
Cefpodoxime proxetil **106**, 116, 244, 245
Cefprozil 89, **106**, 116, 244, 245
Ceftaroline 81, 88, 107, **116**, 244
Ceftaroline fosamil 105
Ceftazidime 88, 104, 105, 116, 117, 119, 120, 231, 244, 245
Ceftazidime-avibactam **104**, **105**, 116, 244

PAGES (page numbers bold if major focus)

Ceftibuten 89, **106**, 116, 244, 245
Ceftizoxime 88, **104**, 116, 244, 245
Ceftobiprole 16, 88, 105, 116, 244, 245
Ceftolozane 88
Ceftolozane-tazobactam 105, 116, 244, 245
Ceftriaxone 10, 72, 81, 88, **104**, 116, 201, 202, 229, 230, 244, 245
  desensitization 83
Cefuroxime 88, 89, **104**, 106, 116, 201, 202, 244, 245
Cefuroxime axetil **106**, 116, 245
Cellulitis (erysipelas) 16, 45, 52, 54, 65, 72
Cephalexin 89, **106**, 116, 244, 245
Cephalosporins 105
Cephalosporins, overall/generations 104, 106
Cephradine 244, 245
Certolizumab 33
Cervicitis **23**, **25**, 72
Cestodes (tapeworms) **160**, **161**, 164
Chagas disease 157
Chancroid **22**, 44, 70
Chickenpox 13, 15, 65, 171
Chlamydia trachomatis 12, **13**, 23, 24, 25, 27, 31, 38, 69
Chlamydophila pneumoniae (Chlamydia) 36, 37, 69
Chloramphenicol 72, 91, 99, **108**, 116, 229, 230, 236
Chloroquine 100, 153, 154, 155, **163**, 164, 240, 244, 245
Chloroquine phosphate 95
Cholangitis **17**, 36, 201
Cholecystitis 17, 201
Cholera 17, **19**, 71
Chorioretinitis **125**
Chromoblastomycosis **126**, 136
Cidofovir 96, 100, 166, 174, 175, **177**, 235, 244, 245
Ciprofloxacin 62, 72, 90, 99, **110**, 116, 139, 140, 145, 146, **149**, 151, 152, 201, 202, 203, 229, 231, 236, 244, 245
Citrobacter 69
Clarithromycin 91, 99, **108**, 116, 144, 145, 146, 150, 238, 239, 240, 241, 242, 244, 245
Clindamycin 91, 99, **108**, 116, 132, 152, 154, 155, 156, 202, 203, 229, 230, 236, 244
Clofazimine 131, 146, 147, **149**, 244, 245
Clonorchis sinensis **159**
Clostridial myonecrosis **45**, 55, 72
Clostridium difficile colitis 17, **18**, 69, 104, 106, 108
Clostridium perfringens 25, 45, 55, 69
Clotrimazole 244
Cloxacillin 90, 102, 244, 245
Cobicistat 97, 101, 190, 236, 244, 245
Coccidioides immitis 127, 210
Coccidioidomycosis 10, 43, 54, 127, 136
Colchicine 237
Colistin 63, 81, 116, 120
Colistin, Polymyxin E 92
Colitis, antibiotic-associated *See C. difficile colitis*
Combivir 182, 184
Complera/Eviplera 181, 184, 187
Conjunctivitis (all types) 7, **12**, **13**, 23, 31, 62, 170
Contaminated traumatic wound **45**
Continuous Dosing, Antibacterials 119
Coronavirus 42, **166**
Corticosteroids and meningitis **8**, **10**
Corynebacterium diphtheriae 69
Corynebacterium jeikeium 66, 69
Corynebacterium minutissimum 69
Coxiella burnetii 30, 31, **69**
"Crabs" (Phthirus pubis) 24, 161
Creeping eruption 158
Cryptococcosis **10**, 27, **127**, **128**, 131, 136
Cryptococcus neoformans **10**, 27
Cryptosporidium 17, 18, 20, 118, **151**

PAGES (page numbers bold if major focus)

C-Section 25
CSF 7, 8, 9, 10, 58, 102, 130, 135, 141, 149, 156, 166, 167, 169, **170**, 177, 202
Cycloserine 94, 139, 145, 146, **149**, 236, 244, 245
Cyclospora **17**, **18**, 20, **151**
Cyclosporiasis **151**
Cyclosporine 109, 118, 134, 235, 236, 237, 238, 239, 240, 241, 242
Cystic fibrosis **43**, 118
Cysticercosis **164**
Cystitis **34**, **35**, 72, 102, 166
Cystoisospora belli **152**
Cystoscopy 203
Cystoscopy with manipulation 203
Cytochrome P450 Interactions 99
Cytomegalovirus
Colitis, Esophagitis, Gastritis **168**
Neurologic disease, Encephalitis **168**
Cytomegalovirus (CMV) 15, 21, 38, 168, 177, 209
Congenital/Neonatal **168**
retinitis 15, 168

D

d4T (stavudine) 208, 236, 241, 242, 244, 245
Daclatasvir 96, 100, 179, 197, 244
Dacryocystitis 15
Daklinza 245
Dalbavancin 91, 106, 116
Dandruff (seborrheic dermatitis) **54**, 206
Dapsone 95, 100, 117, 132, 147, **149**, 156, **163**, 236, 240, 242
Daptomycin 81, 82, 91, 99, 106, **107**, 116, **229**, 231, 236, 244, 245
Darunavir 97, 101, 181, 187, 194, 229, 230, 240, 243, 244, 245
Dasabuvir 96, 100, 197
ddC (zalcitabine) 236, 238, 242, 244, 245
ddI (didanosine) 192, 235, 236, 241, 242, 244, 245
Delavirdine 97, 101, 185, 193, 229, 230, 236, 239, 241, 243, 244, 245
Dengue 62, **167**
Dental (Tooth) abscess 45
Dermatophytosis **129**
Desensitization
Ceftaroline **84**
Ceftriaxone 83
Penicillin 83
TMP-SMX 83
Valganciclovir **84**
Dexamethasone 9, 237
Diabetic foot 5, **16**, 54
Dialysis: Hemo- and peritoneal 47, 203
Diarrhea **17**, **20**, 72, 102, 104, 106, 108, 112, 113, 115, 116, 134, 135, 136, **150**, 151, 152, 162, 163, 164, 166, 174, 176, 177, 178, 180, 188, 192, 193, 194, 195, 206
Dicloxacillin 90, **102**, 115, 244, 245
Didanosine 97
Didanosine (ddI) 192, 235, 236, 241, 242, 244, 245
Didanosine (ddI) 183
Dientamoeba fragilis 151
Diethylcarbamazine 95, 158, **164**, 244
Digoxin 237, 240
Diloxanide **151**, **162**, 244
Diphtheria; C. diphtheriae 49, 72
Dipylidium caninum 160
Dirofilariasis (heartworms) 159
Disulfiram reactions 108, 135, 148, 162, 239, 240
Diverticulitis 17, 22, 47
Dog bite (also see Rabies) **52**
Dolutegravir 98, 101, 181, 191, 195, 236, 237, 238, 244
Donovanosis **24**

PAGES (page numbers bold if major focus)

Doripenem 16, 25, 81, 88, 103, 115, **119**, 236, 244, 245
Doxycycline 72, 82, **92**, **109**, 116, 117, 145, 146, 153, **154**, 155, 202, 229, 236, 242, 244, 245
Dracunculus (guinea worm) **158**
Drug-drug interactions 108, 109, 134, 135, 136, **144**, 148, 162, 178, **191**, 234, 235, 236, 237, 238, 239, 240, 242, 243
Duodenal ulcer (Helicobacter pylori) 21, 70, 72
Dysentery, bacillary 72, 151

E

Ear Infections **10**, 11, 72
Ebola virus 167
Ebola/Marburg virus 167
EBV (Epstein-Barr virus) **44**, **169**
Echinococcosis 160
Efavirenz 97, 101, 117, 181, 186, 187, 193, 237, 243, 244, 245
Efavirenz (Sustiva) 208, 229, 230, 235, 236, 238, 239, 244, 245
Efinaconazole 129
Eflornithine **157**, **163**
Ehrlichiosis, monocytic & granulocytic 57, 58, 60, 70
Eikenella 30, 49, 52, **70**
Elephantiasis (tilariasis) 158
Elizabethkingae 70
Elvitegravir 98, 101, 190, **191**, 195, 236, 244, 245
Empyema, lung 43
Empyema, subdural 7
Emtricitabine 97, 184, 192, 196, 244, 245
Emtricitabine/tenofovir 193
Emtricitabine/tenofovir/efavirenz 184
Emtricitabine/tenofovir/rilpivirine 184
Encephalitis **7**, 57, 58, 157, **169**, 171
Encephalitozoon 152
Endocarditis
Native valve 28, 29, 30, 72
Prosthetic valve 30
Endomyometritis 22, **25**
Endophthalmitis **15**
Endotoxin shock (septic shock) **64**
Enfuvirtide 189, 195
Enfuvirtide (T20, fusion inhibitor) 98, 229, 230, 244, 245
Entamoeba histolytica 17, 18, 20, 36, **151**
Enterobacter 95, 178, 196, 244, 245
Enteric fever (typhoid fever) 62
Enterobacter 11, 53, 62, 70, 105
Enterobius vermicularis **157**
Enterococci 8, 15, 17, 22, **27**, **28**, **29**, 30, 36, 46, 47, 56, 63, 70, 72, 104
Drug-resistant **29**, 73, 104
Vancomycin-resistant **29**, 36
Enterococcus faecalis **29**, 53, 70, 81
Enterococcus faecium 29, 70, 81, 104
Enterocolitis, pseudomembranous or neutropenic 17, **20**, 72, 106
Enterocytozoon bieneusi 20, 152
Enterohemorrhagic Escherichia coli (EHEC) 18
Enterovirus 7, 46, **166**
Eosinophilic meningitis 159
Epididymitis **27**
Epiglottitis 49, 70
Epstein-Barr virus (infectious mono) **44**, **169**
Epzicom 181, 184
Ertapenem 88, **103**, **115**, 236, 244, 245
Erysipelas 16, 54, 65
Erysipelothrix **70**
Erythema multiforme **54**, 106
Erythema nodosum **54**, 147, 149, 150
Erythrasma **54**, 69, 129

PAGES (page numbers bold if major focus)

Erythromycin 91, 99, **108**, 116, 118, 146, 201, 238, 240, 244, 245
Erythrovirus B19 175
Escherichia coli 6, 8, 9, 17, **20**, 46, 50, 53, 62, 70, 81, 151
  0157 H7 17
  enterotoxigenic (traveler's diarrhea) 17
Etanercept 33
Ethambutol 94, 139, 140, 141, 143, 144, 145, 146, **148**, 236, 244, 245
Ethionamide 94, 139, 147, **149**, 229, 236, 244, 245
Etravirine 97, 101, 186, 193, 236, 239, 243, 244, 245
Eviplera (Complera) 184, 187
Extended-spectrum β-lactamases (ESBL) 41, 46

F

F. moniliforme 129
F. oxysporum 129
F. verticillioides 129
Famciclovir 96, 169, 170, 171, 172, **178**, 244, 245
Fansidar (pyrimethamine sulfadoxine) 163, 164, 244, 245
Fasciola buski, gigantica 159
Fasciola buski, hepatica 159
Fever blisters (cold sores) **170**
Fever in Returning Travelers 62
Fidaxomicin 108, 244, 245
Filariasis **158**, **159**, 164
Fitzhugh-Curtis syndrome 25
Flucloxacillin **102**
Fluconazole 93, 99, 117, 121, 122, 127, 128, 129, 134, 135, 152, 210, 231, 235, 237, 241, 242, 244, 245
Flucytosine 93, 127, 127, **128**, **135**, 229, 244
Fluke infestation (Trematodes) 159, 160
Fluoroquinolones 20, 62, 72, 108, **110**, **111**, 116, 117, 140, 145, 236
Folliculitis; hot tub folliculitis 54, 56
Foot, diabetic 5, 16, 54
Fosamprenavir 97, 101, 188, 194, 208, 229, 230, 240, 243, **244**, 245
Foscarnet 96, **177**, 235, 244, 245
Foscavir 244, 245
Fosfomycin 91, **112**, 120, 244, 245
Fournier's gangrene **56**
Francisella tularensis 40, **42**, 44, 56, **60**, 70, 72
Fumagillin 152, 163
Furunculosis **53**, **54**
Fusariosis 129, 136
Fusarium solani 129
Fusarium sp. 136
Fusidic acid 82, 91, 114, 230, 244, 245
Fusobacterium necrophorum 15, 36, 49, **52**

G

G6PD deficiency 53, 113, 149, 150, 153, 155, 162, 163, 240
Ganciclovir 96, 169, 171, **177**, **178**, 209, 237, 242, 244, 245
Gardnerella vaginalis **26**, 70
Gas gangrene **45**, 55, 56, 64, 72
Gastric ulcer, gastritis (H. pylori) **21**, 70, 72
Gastroenteritis 17, 18, 19, 20, 174
Gatifloxacin **110**, 116, 144, 236, 237, 244, 245
Gemifloxacin 90, 110, 116, 236, 237, 244, 245
Genital herpes 7, 27, 169, **170**
Gentamicin 28, 29, 72, 88, 115, **118**, 202, 229, 231, 235, 237, 244, 245
Genvoya 181, **227**
Giardiasis 18, 20
Gnathostoma 10, 159
Golimumab 33
Gongylonemiasis 157
Gonococcal arthritis, disseminated GC **32**, 72

PAGES (page numbers bold if major focus)

Gonococcal ophthalmia **12**
Gonorrhea 12, 13, **23**, 25, 26, 27, 32, 70
Granuloma inguinale **24**
Griseofulvin 117, 129, **135**, 244, 245
Group B strep, including neonatal 4, 8, 25, 27, 32, 38, **62**, **199**
Guillain-Barré syndrome 192

H

HACEK acronym; infective endocarditis **30**
Haemophilus aphrophilus, H. ducreyi 22, **30**, 70
Haemophilus influenzae 8, **9**, **10**, **11**, 12, 13, 15, 16, 32, 36, 37, 38, 41, 43, 44, 45, 49, 50, 62, 63, 64, 67, 70, 72
Halofantrine 100
Hantavirus pulmonary syndrome **42**, 159, 167
Headache 185, 187, 192
Heartworms (dirofilariasis) 159
Helicobacter pylori 21, 70, 72
Hemodialysis (drug dosages) 66
Hemolytic uremic syndrome **17**, 178
Hemolytic Uremic Syndrome (HUS) 18
Hemorrhagic bullae (Vibrio skin infection) 54
Hemorrhagic fevers 166, 167
Hepatic abscess **36**, **151**
Hepatic disease/drug dosage adjustment 230
Hepatitis 194
Hepatitis A 196
Hepatitis A, B & C 32, 36, 57, 148, 178, 179, 205, 206, 208, 209, 234, 244, 245
Hepatitis B 184, 185, 192, 193, 196
Hepatitis B occupational exposure 205
Hepatitis B prophylaxis **205**, 234
Hepatitis C
  Response to Therapy 197
  Treatment Regimens 197
Herpes infections 7, 13, 15, 20, 23, 24, 27, 45, 54, 63, 169, 170, 171, 172, 178, 209
  mucocutaneous **170**
Herpes simiae 52, **171**
Herpes simplex 7, 13, 15, 21, 24, 27, 44, 45, **169**, **170**, **171**, 209
Herpes zoster 54, 172
Heterophyes (intestinal fluke) 159
HHV-6, HHV-7, HHV-8 infections **169**
Hidradenitis suppurativa 53
Histoplasma capsulatum 130
Histoplasmosis 10, 43, 44, **130**, 136
HIV **6**, **7**, 10, 15, 20, 21, 22, 43, 44, 51, 57, 127, 128, 131, 135, 137, 138, 141, 143, 144, 146, 148, 151, 152, 168, 170, 171, 172, 177, 178, 205, 206, 207, 208, 234, 236, 240, 243
  Prophylaxis: needlestick & sexual **206**, **207**, **208**
Hookworm 157, 158
Hordeolum (stye) 12
Hot tub folliculitis **56**
Human T-cell Leukotrophic Virus-1 (HTLV-1) **172**
Hymenolepis diminuta **160**
Hyperalimentation, sepsis **66**

I

Imidazoles, topical **135**
Imipenem 81, 88, 103, 115, 145, 231, 237, 244, 245
Imiquimod 180, 244
Immune globulin, IV (IVIG) 7, 62, 65, 196
Impetigo 55
Inclusion conjunctivitis 13
Indinavir 97, 101, 188, 194, 229, 230, 236, 237, 240, 241, 243, 244, 245
Infectious mononucleosis (see EBV) 169, 206
Inflammatory bowel disease 54, 162
Infliximab 33, 171

PAGES (page numbers bold if major focus)

Influenza A 127, **173**, 180, 234
INH (isoniazid) 137, 138, 139, 140, 141, 143, 144, 145, 146, **148**, 150, 230, 235, 236, 238, 240, 241, 242, 244, 245
Interferon alfa 179
Interferons 127, 144, 166, 175, 180, 244, 245
Iodoquinol 151, **162**, 244, 245
Isavuconazole 93, 99, **135**, 244
Isentress 190, 195
Isepamicin **118**
Isoniazid 94, 100, 117, 229
Isospora belli 20
Itraconazole **93**, 99, 117, 121, 122, 127, 128, 129, 131, 133, **135**, 152, 229, 230, 231, 235, 236, 237, 238, 239, 240, 241, 244, 245
IV line infection & prophylaxis 15, 66, 67
Ivermectin 95, 157, 158, 159, 161, **164**, 244, 245

J

Jock itch (T. cruris) 129

K

Kala-azar 163
Kaletra 182, 188, 194, 243
Kanamycin 88, 94, 115, **118**, 139, 140, 146, 235, 245
Kaposi's sarcoma 44, 169
Katayama fever 160
Kawasaki syndrome **62**
Keratitis 13, 14, 15, 152, 170
Ketoconazole 93, 99, 117, 129, **131**, **135**, 229, 235, 236, 237, 238, 239, 240, 241, 244, 245
Kikuchi-Fujimoto (necrotizing lymphadenitis) **44**
Kivexa 181
Klebsiella species 11, **36**, 41, 43, 46, 62, 70, **81**

L

Lactobacillus sp. 66, **70**
Lamivudine (3TC) 97, 178, 182, 183, 184, 192, 196, 208, 209, 236, 238, 242, 244, 245
Larva migrans **159**
Laryngitis 49
Lassa fever, Ebola **167**
Ledipasvir 96, 100, **179**, 197
Ledipasvir + Sofosbuvir **179**
Legionnaire's disease/Legionella sp. 30, 41, 44, 63, 70, 72
Leishmaniasis 44, 56, **152**
Lemierre's **syndrome** (jugular vein **suppurative** phlebitis) 49
Leprosy **146**, 149, 159
Leptospirosis 7, 36, **61**, 70, 109
Leuconostoc 66, **70**
Leukemia 102
Levofloxacin 90, 99, **111**, 116, 120, 138, 139, 140, 229, 236, 237, 244, 245
Lexiva 244
Lice
  body, head, pubic, & scabies 24, 30, 57, **161**, 164
Lincomycin **108**
Lindane 161
Line sepsis 15, **66**, **67**
Linezolid 81, 82, 92, 99, 107, **109**, 115, 140, 145, 146, 150, 229, 238, 244, 245
Liposomal Amikacin 120
Listeria monocytogenes 7, 8, 9, 10, 14, 19, 38, 62, 70, 72
Liver abscess 36, **151**
Liver disease/drug dosage adjustment **230**
Loa loa **158**
Lobomycosis 131
Loiasis **158**
Lomefloxacin 237, 244, 245
Lopinavir 101, 188, 194, 243
Lopinavir/ritonavir 97

PAGES (page numbers bold if major focus)

Lopinavir/ritonavir & lopinavir 208, 229, 230, 238, 240, 244, 245
Loracarbef 244, 245
Ludwig's angina 45, **49**
Lumefantrine 162
Lumpy jaw 45
Lung abscess 43
  putrid 72
Lyme disease 10, **31**, **32**, 44, 57, **58**, 72
Lymphadenitis 44, 51, 57
Lymphangitis, nodular **44**
Lymphatic filariasis 158
Lymphedema (congenital = Milroy's disease) **54**
Lymphogranuloma venereum **24**, 44

M

MAC, MAI (Mycobacterium avium-intracellulare complex) **144**, **146**
Macrolide antibiotics 11, 41, 108, 116, 238
Madura foot **131**
Malaria 62, 109, 151, **153**, **156**, 163, 164, 234
Malarone (atovaquone + proguanil) 153, 155, 156, **162**
Malassezia furfur (Tinea versicolor) 54, 66, **129**
Malathion 161
Mansonella **159**
Maraviroc 98, 101, 190, 195, 239, 244, 245
Mastitis 6
Mastoiditis **12**
Measles, measles vaccine 106, **174**
Mebendazole 157, 159, **164**, 244, 245
Mefloquine 95, 100, 153, 154, 155, **163**, 239, 240, 244, 245
Meibomianitis 12
Melarsoprol 157, **163**
Meleney's gangrene **55**, **56**
Melioidosis (Burkholderia pseudomallei) **41**, 56, **69**
Membranous pharyngitis 49
Meningitis
  Aseptic 7, 10, 113, 166, 167
  Bacterial (acute and chronic) **7**, **8**, **9**, **10**, 58, 70, 104, 141
  eosinophilic 10, **157**, 158
Meningococci 8, 9, 15, 32, 63, 64, 70, 72, 109
Meningococcus, meningitis **8**, 9, 10, 15, 32, 64, 70, 72
  Prophylaxis 10
Meropenem 81, 88, 103, 115, 119, 229, 237, 244, 245
Mesalamine 244, 245
Metagonimus 159
Metapneumovirus 42, 174
Methenamine mandelate & hippurate **112**, 239, 244, 245
Methicillin 29, 30, 71
Methicillin-resistant Staph. aureus (MRSA) 4, 5, 6, 8, 13, 15, 16, 27, 29, 31, 32, 33, 38, 42, 43, 45, 50, 53, 54, 55, 56, 62, 63, 65, 66, 71, 201
Methotrexate 239
Metronidazole 7, 92, 99, **112**, 116, 151, 152, 162, 201, 202, 230, 231, 236, 239, 240, 242, 244, 245
Micafungin 93, 121, 134, 210, 229, 239, 244, 245
Miconazole **136**
Microsporidia 20, 152
Miltefosine 95, 152, 163
Minocycline 67, 81, 82, 92, 109, 145, 146, 147, 229, 244, 245
Mollaret's recurrent meningitis 170
Monkey bite **52**, 166, 171
Monobactams **104**, 115
Moraxella 52
Moraxella catarrhalis 11, 12, 16, 37, 41, 50, 70
Morganella species 70
Moxifloxacin 90, **111**, 116, 138, 140, 144, 145, 146, 147, 150, 229, 230, 236, 237, 244, 245

PAGES (page numbers bold if major focus)

MRSA 4, 5, 6, 8, 13, 15, 16, 27, 29, 31, 32, 33, 38, 42, 43, 45, 47, 50, 53, 54, 55, 56, 62, 63, 65, 66, 71, 104, 107, 201
Mucormycosis 50, **131**
Multidrug-resistant TB **139**, **140**
Mumps 46
Mupirocin 114, 201, 244, 245
Mycobacteria 10, 32, 33, 43, 44, 46, 56, 109, 137, **139**, **140**, **141**, 144, 145, 146
Mycobacterium abscessus, M. bovis, M. celatum, M.chelonae, M. genavense, M. gordonae, M. haemophilum, M. kansasii, M. marinum, M. scrofulaceum, M. simiae, M. ulcerans, M. xenopi, M. leprae **28**, 33, 44, 52, 109, 144, **145**, **146**, **171**
Mycobacterium tuberculosis 10, 33, 43, 44, 54, 137, 139, 140, 141, 144
  Directly observed therapy (DOT) **139**, 141
  Drug-resistant **144**
  Pulmonary 43, 44, **139**, **140**
Mycoplasma pneumoniae 36, 37, 70
Mycotic aneurysm **67**
Myiasis 161
Myositis 45, 65

N

Naegleria fowleri 152
Nafcillin 42, 46, 90, 99, 102, 116, 229, 230, 239, 244, 245
Necrotizing enterocolitis **17**
Necrotizing fasciitis 54, 55, 56, 65
Needlestick, HIV, Hepatitis B & C **205**, 206, **208**
Neisseria
  gonorrhoeae 12, 13, 23, 25, 26, 27, 32, 70
  meningitis 9, 15, 32, 64, **70**, 72
Nelfinavir 98, 101, 188, 194, 229, 230, 239, 240, 241, 242, 243, 244, 245
Nematodes (roundworms) **157**, 164
Neomycin 88, 114, **118**, **162**, 201, 235
Neonatal sepsis 62, 199
Netilmicin 115, 118, 235
Neurocysticercosis 160
Neurosyphilis **24**
Neutropenia 20, 50, 63, 64, 66, 102, 109, **115**, **116**, 121, 134, 152, 163, 177
Nevirapine 97, 101, **182**, 186, 193, 208, 229, 230, 236, 237, 239, 241, 243, 244, 245
Niclosamide 160
Nifurtimox **157**, **163**
Nitazoxanide 95, 113, 151, 162, 244
Nitrofurantoin 112, **113**, 236, 239, 242, 244, 245
Nocardia brasiliensis, asteroides 70, 109
Nocardiosis **6**, **7**, **41**, 44, 70, 109, **131**
Non-gonococcal urethritis
  Mycoplasma genitalium 23
Norfloxacin 90, 99
Norovirus (Norwalk-like virus) 18, 174
NRTIs 183, 184, 185, 186, 187, 192, 193, 194
Nursing (breast milk) & antibiotics 6, 25
Nystatin **136**, 244, 245

O

Ofloxacin 90, **111**, 116, 139, 145, 146, 147, **150**, 236, 237, 244, 245
Olysio 244, 245
Ombitasvir 96, 100, 197
Onchocerca volvulus **158**
Onchocerciasis **158**, 164
Onychomycosis 17, 129, 135, 136
Ophthalmia neonatorum **12**, **13**
Orbital cellulitis **16**
Orchitis **27**
Oritavancin 91, 99, **106**, 116, 229, 239

PAGES (page numbers bold if major focus)

Orthopedic Surgery 202
Oseltamivir 96, **173**, **180**, 230, 244, 245
Osteomyelitis
  Chronic 5, 72
  Contiguous (post-operative, post-nail puncture) **5**
  Foot 16
  Hematogenous 5, 72
  Osteonecrosis of the jaw **5**
  Vertebral **4**, 57
Otitis externa—chronic, malignant, & swimmer's ear **10**
Otitis media 7, **11**, 72, 108
Oxacillin 42, 46, 90, **102**, 115, 244, 245

P

P. knowlesi 154
Palivizumab 175, **180**, 244, 245
Pancreatitis 183, 185, 192, 194
  pancreatic abscess **46**, 62, 104, **110**, 163, 236, 239, 242
Papillomavirus **174**
Papovavirus/Polyoma virus **175**
Para-aminosalicylic acid 94
Paracoccidioidomycosis **131**
Paragonimus 160
Parapharyngeal space infection 49
Parasitic infections 151-62
Paritaprevir 96, 100, 197
Paromomycin 118, 151, 152, 162, 244, 245
Paronychia 27
Parotitis **46**
Parvovirus B19 32, **175**
PAS (para-aminosalicylic acid) **150**
Pasteurella canis 52
Pasteurella multocida 52, 70
Pegylated interferon 166, 179, 197, 244, 245
Pegylated-Interferon-alpha 2a 196, 197
Peliosis hepatis **36**, **57**
Pelvic actinomycosis 25
Pelvic inflammatory disease (PID) **25**, **26**, **72**
Pelvic suppurative phlebitis 25
Penciclovir 169, 170, 178
Penicillin
  desensitization 83
Penicillin allergy 8, 9, 24, 28, 29, 47, 52, 54, 55, 58, 102, 103, 104, 106
Penicillin G 9, 28, 29, 62, 89, **102**, 115
Penicillin V 89, **102**, 200
Penicilliosis **131**
Pentamidine 132, 152, 157, **163**, 235, 236, 239, 242, 244, 245
Peptostreptococcus 6, 71
Peramivir 96, **180**, 244, 245
Pericarditis **31**, 72, 141
Perirectal abscess **22**
Peritoneal dialysis, infection 47, 203, **231**
Peritonitis
  Bacterial/spontaneous **17**, 22, 46
  Spontaneous—prevention 46
Peritonsillar **abscess** 48
Pertussis **37**, 69
Phaeohyphomycosis **131**
Pharmacodynamics 99
Pharmacokinetics, pharmacology **99**
Pharyngitis
  Diffuse erythema 48
  Exudative 48, 49
  Membranous 49
  Vesicular, ulcerative pharyngitis 49
Pharyngitis/tonsillitis 23, 31, 62, 72
Phlebitis, septic 25, **66**
Photosensitivity 51, 110, 113, 117, 135, 148, 163

PAGES (page numbers bold if major focus)

PID **25**, **26**, 72
Pinworms 157, 164
Piperacillin-tazobactam 90, 103, 115, 119, 121, 230, 239, 244, 245
Plague 40, 56, 71
  bacteremic 59
Plesiomonas shigelloides 18, 70
PML (progressive multifocal leukoencephalopathy) **175**
Pneumococci, drug-resistant 11, 42, 44, **71**
Pneumocystis (carinii) jiroveci 44, 72, 113, 210
Pneumocystis jiroveci 132
Pneumonia 42, **168**
  adult 38, 40, 41, 42, 43, 44, 60, 72, 82, 132, 166, 171, 175, 176, 180
  adult, community acquired, outpatient **39**
  adult, healthcare, hospital-acquired, or ventilator-associated **40**
  adult, hospitalized (not ICU) **39**
  adult, hospitalized in ICU **39**
  aspiration 43
  chronic 43
  community-acquired **63**, 176
  community-associated 82
  Infants, Children 38
  neonatal/infants/children **38**
  Q Fever 41
  ventilator-acquired 82
Podofilox 174, **180**
Polymyxin B 92, **111**, 114, 116, 229, 239, 244, 245
Polymyxin E, Colistin 81, 112, 116, 240
Polyoma virus 175
Posaconazole 93, 99, 121, 126, 127, 131, 132, 136, 210, 229, 235, 239, 240, 244, 245
PPD (TST) 137
Praziquantel 95, 100, 159, 160, **164**, 244, 245
Prednisone 159
Pregnancy
  Acute pyelonephritis **34**
  antibiotics in 9, 23, 24, 26, 40, 41, 42, 58, 109, 110, 127, 134, 135, 138, 141, 148, 150, 151, 153, 155, 156, 159, 163, 164, 171, 178, 179, 206, 208, 241
  Asymptomatic bacteriuria & cystitis **34**
Pregnancy Risk and Safety in Lactation **85**
Primaquine 132, 153, 155, **163**, 240, 244
Proctitis 20, 23
Progressive multifocal leukoencephalopathy (PML) **175**
Proguanil 95, 100
  atovaquone-proguanil 153, 155, 156, 162, 244, 245
Prolonged Dosing, Antibacterials 119
Prostatitis, prostatodynia 23, 27, 72
Prosthetic joint infection/prophylaxis 5, 19, 33
Prosthetic valve endocarditis 30, 201
Protease inhibitors (PI) 141, 146, 185, 186, 188, 189, 193, 194, 195, 235, 236, 237, 238, 239, 240, 241
Protein binding (antimicrobials) **88–98**
Providencia species 70
Prulifloxacin 90
Pseudallescheria boydii (Scedosporium sp.) 131, 136
Pseudomembranous enterocolitis 72, 108
Pseudomonas aeruginosa 5, 8, 9, 10, 12, 14, 15, 17, 20, 22, 27, 30, 32, 33, 36, 38, 41, 43, 44, 47, 53, 54, 56, 70, 81, 103, 105, 120
Pseudotumor cerebri 109, 110
Puncture wound 56
Pyelonephritis **34**, **35**, 63, 72, 112
Pyomyositis 45
Pyrantel pamoate 158, 164, 244, 245
Pyrazinamide 94, 117, 138, **139**, **140**, **141**, **143**, 144, 145, 146, **148**, 240, 241, 244, 245
Pyridoxine 141, 148, 149

PAGES (page numbers bold if major focus)

Pyrimethamine 95, 117, 132, 152, 156, **163**, 164, 229, 236, 240, 244, 245

Q

Q fever 31, 69
QTc prolongation **108**, **110**, **111**, 136, 155, 187, 194
Quinacrine HCl 151, 162
Quinidine gluconate 155, 163, 239, 241
Quinine 117, 152, 154, 163, **164**, 239, 240
Quinine sulfate 95, 100, 155
Quinolones 99
Quinupristin-dalfopristin 82, 92, 99, **109**, 116, 230, 240, 241, 244, 245

R

Rabies, rabies vaccine 52, 163, 175, 233
Raltegravir 98, 101, 181, 190, 195, 229, 237, 238, 241, 244, 245
Rape victim 200
Rat bite **52**
Recurrent urinary tract infection **34**
Red neck syndrome & vancomycin **107**
Reiter's syndrome 27, **31**
Relapsing fever 59
  Louse-borne 59
  Tick-borne 59
Renal failure, dosing 229
Resistance
  Acinetobacter 81
  Carbapenemase 81
  Enterococcus sp. 81
  Escherichia coli 81
  Gram Negative Bacilli 81
  Gram Positive Bacteria 81
  Klebsiella species 81
  Staph. aureus 81
  Stenotrophomonas maltophilia 81
  Streptococcus pneumoniae 81
Resistant bacteria 73
Resource directory (phone numbers, websites) 234
Respiratory syncytial virus (RSV) 36, 38, 42, 174, 180
Retapamulin 114, 244
Retinal necrosis, progressive outer 16
Retinitis **15**, 156
Rheumatic fever 31, 32, 48, 62
Rheumatoid arthritis, septic joint **32**, 72
Rhinosinusitis 11, 50
Rhinovirus 38, **176**
Rhodococcus equi 71
Ribavirin 96, 166, 167, 174, 175, 179, 197, 229, 236, 241, 244, 245
Rickettsial diseases **60**, 62, 71
Rifabutin 94, 100, 138, 139, 141, 144, 145, 146, **150**, 229, 230, 235, 236, 238, 239, 240, 241, 242, 244, 245
Rifampin 92, 94, 99, 146, 152, 229, 238
Rifampin, Rifamate, Rifater 67, 82, 113, 116, 136, 138, 139, 140, 141, 143, 144, 145, 146, 147, **148**, 150, 230, 235, 236, 238, 239, 240, 241, 242, 244, 245
Rifamycins 141, 241
Rifapentine 94, 100, 138, 139, 141, 143, **150**, 229, 238, 244, 245
Rifaximin 92, 113, 229, 244, 245
Rilpivirine 97, 101, 182, 187, 194, 244, 245
Rimantadine 96, **180**, 230, 241, 244, 245
Ringworm 129
Ritonavir 96, 98, 101, 187, 189, 194, 195, 197, 208, 230, 238, 240, 241, 242, 243, 244, 245
Rocky Mountain spotted fever 63, 72
Rubella vaccine 32

PAGES (page numbers bold if major focus)

S

Salmonellosis, bacteremia 5, **17**, **19**, **20**, 31, 32, 61, **62**, 71
Salpingitis 26
Saquinavir 98, 101, 117, 189, 195, 229, 240, 241, 243, 244, 245
SARS (Severe Acute Resp. Syndrome) 42, 166
SBE (subacute bacterial endocarditis) 28, 29, 30, 31
SBP (spontaneous bacterial peritonitis) 46
Scabies & Norwegian scabies 24, 161, 164
Scedosporium sp. (Pseudallescheria boydii) 131, 136
Schistosomiasis 160, 165
Scrofula **44**
Seborrheic dermatitis (dandruff) 54, 206
"Sepsis" and "septic shock" 17, 52, 55, 62, 63, **64**, 144, 201
Sepsis, abortion; amnionitis **25**
Sepsis, neonatal **62**
Septata intestinalis 20, 152
Serratia marcescens 71, 105
Severe acute respiratory distress syndrome (SARS) 42, 166
Severe fever with thrombocytopenia syndrome virus (SFTSV) 166, 167
Sexual contacts/assaults 12, 13, **22**, 26, 44, 135, **200**, 206, 208
SFTSV (Severe fever with thrombocytopenia syndrome virus) 166, 167
Shiga Toxin Escherichia coli (STEC) 18
Shigellosis **17**, **19**, **20**, 31, 71
Shingles 54, 172
Sickle cell disease 5, 32, 200
Silver sulfadiazine 114
Simeprevir 96, 100, **179**, 197, 229, 244
Sinecatechins 174, 180
Sinusitis 7, 36, **50**, 72, 108, 121, **131**, 180
  acute 50
Sirturo 245
Skin 184, 193, 194
  Ulcerated 56
Smallpox 176
Snake bite, spider bite 52, 53
Sofosbuvir 96, 100, **179**, **180**, 197, 229, 244
Sofosbuvir + Ledipasvir 197
Solvadi 245
Sparganosis **161**
Spectinomycin 118, 244, 245
Spinal implant infection 5
Spiramycin 164
Spirochetosis 19
Splenectomy 52, 56, 64, 152, **199**
Splenic abscess **56**
Sporotrichosis **44**, 133
Spotted fevers 60, **63**, 72
Staph. aureus 4, 5, 6, 8, 10, 12, 13, 14, 15, 16, 17, 27, 28, 29, 30, 31, 32, 33, 38, 42, 43, 44, 45, 46, 49, 50, 52, 53, 54, 55, 56, 62, 63, 65, 66, 67, 71, 72, **81**, 105, 107, 201
  Community-associated 56, 71
  Endocarditis 29, 72, 107
Staph. epidermidis 5, **8**, 12, 14, 15, 17, 30, 31, 46, 47, 52, 53, 62, 66, 71, 82
Staph. hemolyticus **71**
Staph. lugdunensis 6, **71**
Staph. saprophyticus 71
Staph. scalded skin syndrome **56**
Stavudine (d4T) 97, 185, 192, 208, 236, 241, 242, 244, 245
Stenotrophomonas maltophilia 42, 71, 81
Stevens-Johnson syndrome 188, 193, 194, 195

PAGES (page numbers bold if major focus)

Stibogluconate **162**, 244
Stomatitis **45**, 149, 170
Streptobacillus moniliformis **52**, 71
Streptococcal toxic shock 56, 65
Streptococci 4, 6, 8, 12, 15, 16, 25, 27, 28, 29, 30, 31, 32, 36, 38, 42, 43, 44, 45, 49, 50, 52, 53, 54, 55, 56, 62, 63, 64, 65, 71, 72, 103, 146, 199
Streptococcus
  anginosus group 71
  bovis **28**, 144
  group B, prophylaxis **199**
  milleri complex 43
  pneumoniae 8, 9, 11, 12, 13, 14, 15, 16, 31, 38, 42, 43, 44, 49, 63, 64, 71, 72, **81**, 200
  pyogenes 6, 8, 14, 15, 16, 32, 48, 49, 53, 54, 65, **71**
Streptococcus sp. 54, 56
Streptomycin 29, 72, 94, 118, 139, 140, 146, **148**, 235
Stribild 181, 190, 230
Stribild/Elvitegravir 237, 238
Strongyloidiasis **157**, 164
Subdural empyema **7**
Submandibular space infection, bilateral 45
Sulfadiazine 67, 156, 163, 164, 244, 245
Sulfadoxine + pyrimethamine 163, 164, 244, 245
Sulfasalazine 244, 245
Sulfisoxazole **113**, 244, 245
Sulfonamides 54, 113, 164, 240, 241, 242, 244, 245
Supraglottis 49
Suramin 157, **164**
Surgical procedures, prophylaxis 200, 202, 203
Synercid® (quinupristin-dalfopristin) 82, **109**, 116, 230, 240, 241, 244, 245
Syphilis 10, 20, **23**, **24**, **25**, 38, 44, 200

T

Tacrolimus 238
Tapeworms
  Taenia saginata, T. solium, D. latum, D. caninum 158, **160**
Tazobactam 88
Technivie 245
Tedizolid 92, 115, 229, 245
Teicoplanin 91, **107**
Telaprevir 244, 245
Telavancin 81, 91, **107**, 116, 230, 244, 245
Telbivudine 95, 178, 196, 244, 245
Telithromycin 91, 99, **108**, 230, 241, 244, 245
Temocillin **103**, 119, 244
Tenofovir 97, 183, 184, 185, 187, 193, 196, 236, 240, 242, 244, 245
Tenofovir alafenamide (TAF) 185
Terbinafine 99, 126, 129, 133, **136**, 242, 244, 245
Tetanus prophylaxis 52, 53, **232**
Tetanus, Clostridium tetani 17, 52, 53, 55, 56, 66, 69, **232**
Tetracycline 13, 92, 109, 110, 116, 117, **151**, 154, 155, **164**, 235
Thalidomide 100, 150, 244, 245
Thiabendazole 242, 244, 245
Thrombophlebitis
  Cavernous Sinus 67
  Jugular Vein 68
  Jugular vein suppurative phlebitis (Lemierre's syndrome) **49**
  Lateral Sinus 67
  Lemierre's Syndrome 68
  Pelvic Vein **25**, 68
  Portal Vein 68
  Sagittal Sinus 67
  Suppurative (septic) **66**
  Suppurative (Septic) 67, 68
Thrush 206

PAGES (page numbers bold if major focus)

Tigecycline 92, 110, 116, 145, 229, 230, 242, 244, 245
Tinea capitis, corporis, cruris, pedis, versicolor **129**, 161
Tinidazole 95, 100, 113, 151, 162, 230, 239, 242, 244, 245
Tipranavir 98, 101, **189**, 195, 229, 240, 243, 244, 245
Tivicay 245
TMP-SMX 99, 146, 152
  desensitization 83
Tobramycin 88, 115, **118**, 120, 202, 229, 235, 242, 244, 245
Tonsillitis
  Diffuse erythema 48
  Exudative 48, 49
Torsades de pointes 110
Toxic shock syndrome (strep., staph., clostridia) 56, 65
Toxocariasis 159
Toxoplasma gondii, toxoplasmosis 6, 44, **132**, **156**, 210
Trachoma **13**
Transplantation, infection 127
Transrectal prostate biopsy 203
Traveler's diarrhea **20**, 72, 113
Trazodone 238
Trematodes (flukes) **159**, **160**, 164
Trench fever 57
Trench mouth 45
Trichinellosis **159**
Trichinosis **159**
Trichomoniasis (vaginitis) 23, **26**, 156
Trichostrongylus **158**
Trichuris 158
Triclabendazole 160, **164**
Tricuspid valve infection, S. aureus 29, 30
Trifluridine 170, **178**, 244
Trimethoprim 92, 99, 117, 242, 245
Trimethoprim-sulfamethoxazole 7, 81, 82, 92, 112, **113**, 116, 132, 145, 151, 152, 156, 163, 203, 210, 231, 240, 241, 242, 244, 245
Trumeq 181, 183
Tropheryma whipplei 71
Truvada 181, 184, 196
Trypanosomiasis **157**, 210
Tuberculosis 10, 33, 43, 44, 54, 131, **137**, **138**, **139**, **140**, **141**, **143**, 144, 145, 146, 149, 229
  Multidrug-resistant **139**, **140**, **141**
  Tuberculin skin test (TST) **137**
Tularemia (Francisella tularensis) 40, **42**, 44, 56, **60**, 70, 72
Tumor Necrosis Factor 8, 33, 43, 127, 172
Typhlitis—neutropenic enterocolitis—cecitis **20**
Typhoid 62
Typhoid fever 17, 19, 62, 72
Typhus group (louse-borne, murine, scrub) **60**, 109

PAGES (page numbers bold if major focus)

U

Ulcerative colitis 151
Ulcerative gingivitis 45
Uncomplicated/P. malariae 154
Urethral catheter, indwelling **112**
Urethritis, non-gonococcal 23, 25, 72
Urinary tract infection 65, 70, 71, 113

V

Vaccinia, contact 176
Vaginosis, bacterial 26, 70
Valacyclovir 96, 169, 170, 171, 172, **178**, 209, 244, 245
Valganciclovir 96, 168, **177**, **178**, 209, 237, 242, 244, 245
Vancomycin 28, 29, 31, 82, 91, 99, 104, **107**, 116, 118, 119, 200, 201, 202, 203, 230, 231, 235, 242, 244, 245
Varicella zoster 13, 15, 65, 171, 172
Ventilator-associated pneumonia 41
Vibrio cholerae, parahemolyticus, vulnificus **19**, **20**, 54, 71
Viekira Pak 245
Vincent's angina 45
Viral infections 181
Visceral larval migrans 159
Voriconazole 93, 99, 117, 121, 122, 127, 131, 132, **136**, 229, 230, 235, 238, 239, 240, 244, 245
VRE (vancomycin-resistant enterococci) 29, 36, 104

W

Warts 25, 180
West Nile virus 7, 65, 167, 176
Whipple's disease 10, **21**
Whipworm 158
Whirlpool
  Nail Salon **56**
Whirlpool folliculitis (hot tub folliculitis) **56**
Whitlow, herpetic **27**, 170
Whooping cough 37, 69
Wound infection, post-op, post-trauma 45, 55, 56
Wuchereria bancrofti 158

X

Xanthomonas (Stenotrophomonas) maltophilia 42, 71

Y

Yersinia enterocolitica & pestis **20**, 31, 36, **44**, 54, 71

Z

Zalcitabine (ddC) 236, 238, 242, 244, 245
Zanamivir **173** **180**, 244, 245
Zeftera 244
Zidovudine (ZDV, AZT) 177, 183, 184, 185, 192, 208, 235, 236, 237, 238, 240, 241, 242, 244, 245
Zidovudine (ZVD) 97
Zika Virus 176

The Sanford Guide to Antimicrobial Therapy 2016 (46th Edition)

Avalilable in a wide array of formats

Print Editions

Pocket Edition (4.5 x 6.5 in)
Spiral Bound Edition (5 x 8 in)
Library Edition (7.5 x 11 in)

Digital Editions

Web Edition
Mobile applications for iOS and Android Devices

The Sanford Guide to HIV/AIDS Therapy 2015 -2016 (print and Apps) (24th Edition)

The Sanford Guide to Hepatitis Therapy (App)

For more information or to purchase:

Antimicrobial Therapy, Inc.
Publisher of the Sanford Guides
P.O. Box 276
11771 Lee Hwy
Sperryville, VA 22740, USA

Tel –1 540 987 9480
Fax –1 540 987 9486

www.sanfordguide.com
info@sanfordguide.com

The Sanford Guide Web Edition

Available for Subscription at
http://webedition.sanfordguide.com

Mobile Apps

The Sanford Guide to Antimicrobial Therapy
The Sanford Guide to HIV/AIDS Therapy
The Sanford Guide to Hepatitis Therapy
The Sanford Guide Collection