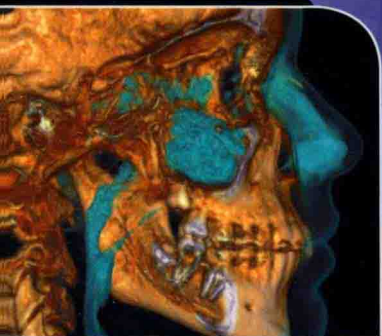


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Medical Diagnosis & Treatment



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MAXINE A. PAPADAKIS

STEPHEN J. McPHEE

ASSOCIATE EDITOR MICHAEL W. RABOW

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CURRENT

Medical Diagnosis & Treatment

FIFTY-FOURTH EDITION

Edited by

Maxine A. Papadakis, MD

Professor of Medicine
Associate Dean of Students
School of Medicine
University of California, San Francisco

Stephen J. McPhee, MD

Professor of Medicine, Emeritus
Division of General Internal Medicine
Department of Medicine
University of California, San Francisco

Associate Editor

Michael W. Rabow, MD

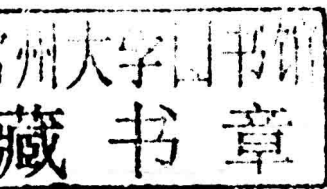
Professor of Medicine
Division of General Internal Medicine
Department of Medicine
University of California, San Francisco

With Associate Authors



Medical

New York Chicago San Francisco Athens London Madrid Mexico City
Milan New Delhi Singapore Sydney Toronto



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Authors

Michael J. Aminoff, MD, DSc, FRCP

Distinguished Professor and Executive Vice Chair,
Department of Neurology, University of California,
San Francisco; Attending Physician, University of
California Medical Center, San Francisco
aminoffm@neurology.ucsf.edu
Nervous System Disorders

Charalambos Babis Andreadis, MD, MSCE

Assistant Professor of Medicine, Division of Hematology/
Oncology, University of California, San Francisco
candreadis@medicine.ucsf.edu
Blood Disorders

Alicia Y. Armstrong, MD, MHSCR

Medical Monitor, Contraceptive and Reproductive Health
Branch, Eunice Kennedy Shriver National Institute for
Child Health and Human Development, National
Institutes for Health, Rockville, Maryland
ayba55@aol.com
Gynecologic Disorders

David M. Barbour, PharmD, BCPS

Pharmacist, Denver, Colorado
dbarbour99@gmail.com
Drug References

Robert B. Baron, MD, MS

Professor of Medicine; Associate Dean for Graduate and
Continuing Medical Education; Vice Chief, Division of
General Internal Medicine, University of California,
San Francisco
baron@medicine.ucsf.edu
Lipid Disorders; Nutritional Disorders

Kevin Barrows, MD

Associate Clinical Professor of Family and Community
Medicine, Medical Director, Osher Center for
Integrative Medicine; Department of Family and
Community Medicine, University of California,
San Francisco
barrowsk@ocim.ucsf.edu
CMDT Online—Integrative Medicine

Thomas M. Bashore, MD

Professor of Medicine; Clinical Chief, Division of
Cardiology, Duke University Medical Center, Durham,
North Carolina
thomas.bashore@duke.edu
Heart Disease

Timothy G. Berger, MD

Professor of Clinical Dermatology, Department of
Dermatology, University of California, San Francisco
bergert@derm.ucsf.edu
Dermatologic Disorders

Brook Calton, MD, MHS

Assistant Clinical Professor, Division of Geriatrics,
Department of Medicine, University of California,
San Francisco
References

Matt Cascino, MD

Chief Medical Resident, Department of Medicine,
University of California, San Francisco
References

Hugo Q. Cheng, MD

Clinical Professor of Medicine, University of California,
San Francisco
quinny@medicine.ucsf.edu
Preoperative Evaluation & Perioperative Management

Mark S. Chesnutt, MD

Clinical Professor, Pulmonary & Critical Care Medicine,
Dotter Interventional Institute, Oregon Health &
Science University, Portland, Oregon; Director, Critical
Care, Portland Veterans Affairs Medical Center
chesnutm@ohsu.edu
Pulmonary Disorders

Thomas D. Chi, MD

Assistant Professor, Department of Urology, University of
California, San Francisco
TChi@urology.ucsf.edu
Urologic Disorders

Peter V. Chin-Hong, MD

Associate Professor, Division of Infectious Diseases,
Department of Medicine, University of California,
San Francisco
peter.chin-hong@ucsf.edu
*Common Problems in Infectious Diseases & Antimicrobial
Therapy*

Kerry C. Cho, MD

Assistant Clinical Professor of Medicine, Division of
Nephrology, University of California, San Francisco
kerry.cho@ucsf.edu
Electrolyte & Acid-Base Disorders

Patricia A. Cornett, MD

Professor of Medicine, University of California, San
Francisco; Chief, Hematology/Oncology, San Francisco
Veterans Affairs Medical Center, San Francisco, California
patricia.cornett@va.gov
Cancer

Marisa L. Cruz, MD

Fellow, Division of Endocrinology and Metabolism,
University of California, San Francisco
References

Russ Cucina, MD, MS

Associate Professor of Hospital Medicine; Medical Director, Information Technology, UCSF Medical Center; University of California, San Francisco
 rcucina@medicine.ucsf.edu
CMDT Online—Information Technology in Patient Care

Lloyd E. Damon, MD

Professor of Clinical Medicine, Department of Medicine, Division of Hematology/Oncology; Director of Adult Hematologic Malignancies and Blood and Marrow Transplantation, University of California, San Francisco
 damonl@medicine.ucsf.edu
Blood Disorders

Tiffany O. Dea, PharmD, BCOP

Oncology Pharmacist, Veterans Affairs Medical Center, San Francisco, California; Adjunct Professor, Thomas J. Long School of Pharmacy and Health Sciences, Stockton, California
 tiffany.dea@va.gov
Cancer

Charles DeBattista, DMH, MD

Professor of Psychiatry and Behavioral Sciences Director: Depression Clinic and Research Program Director of Medical Student Education in Psychiatry, Stanford University School of Medicine, Stanford, California
 debattista@stanford.edu
Psychiatric Disorders

Tonja Dirkx, MD

Assistant Professor of Medicine, Division of Nephrology, Department of Medicine, Oregon Health & Science University, Portland, Oregon; Renal Clinic Director, Portland Veterans Affairs Medical Center
 dirkxt@ohsu.edu
Kidney Disease

Stuart J. Eisendrath, MD

Professor of Psychiatry; Director of The UCSF Depression Center, Langley Porter Psychiatric Hospital and Clinics, University of California, San Francisco
 stuart.eisendrath@ucsf.edu
Psychiatric Disorders

Paul A. Fitzgerald, MD

Clinical Professor of Medicine, Department of Medicine, Division of Endocrinology, University of California, San Francisco
 paul.fitzgerald@ucsf.edu
Endocrine Disorders

Patrick F. Fogarty, MD

Assistant Professor of Medicine, Department of Medicine; Director, Penn Comprehensive Hemophilia and Thrombosis Program, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania
 patrick.fogarty@uphs.upenn.edu
Disorders of Hemostasis, Thrombosis, & Antithrombotic Therapy

Lawrence S. Friedman, MD

Professor of Medicine, Harvard Medical School; Professor of Medicine, Tufts University School of Medicine, Boston, Massachusetts; Chair, Department of Medicine, Newton-Wellesley Hospital, Newton, Massachusetts; Assistant Chief of Medicine, Massachusetts General Hospital, Boston, Massachusetts
 lfriedman@partners.org
Liver, Biliary Tract, & Pancreas Disorders; Hepatobiliary Cancers (in Chapter 39)

Warren J. Gasper, MD

Clinical Instructor of Surgery, Division of Vascular and Endovascular Surgery, Department of Surgery, University of California, San Francisco
 warren.gasper@ucsf.edu
Blood Vessel & Lymphatic Disorders

Armando E. Giuliano, MD, FACS, FRCSED

Executive Vice Chair of Surgery, Associate Director of Surgical Oncology, Cedars-Sinai Medical Center, Los Angeles, California
 armando.giuliano@cshs.org
Breast Disorders

Ralph Gonzales, MD, MSPH

Professor of Medicine; Professor of Epidemiology & Biostatistics, Division of General Internal Medicine, Department of Medicine, University of California, San Francisco
 ralphg@medicine.ucsf.edu
Common Symptoms

Christopher Bl Granger, MD

Professor of Medicine; Director, Cardiac Care Unit, Duke University Medical Center, Duke Clinical Research Institute, Durham, North Carolina
 christopher.granger@dm.duke.edu
Heart Disease

Blake Gregory, MD

Chief Resident, Department of Medicine, University of California, San Francisco
References; Illustrations

B. Joseph Guglielmo, PharmD

Professor and Dean, School of Pharmacy, University of California, San Francisco
 guglielmoj@pharmacy.ucsf.edu
Common Problems in Infectious Diseases & Antimicrobial Therapy; CMDT Online—Anti-infective Chemotherapeutic & Antibiotic Agents

David L. Hamel, Jr., MD

Chief Medical Resident, Department of Medicine, University of California, San Francisco
References

Sarah Lee, MD

Pediatric Neurology Resident, Department of Neurology & Neurological Sciences, Stanford Hospital and Clinics, Stanford, California

*References***Jonathan E. Lichtmacher, MD**

Health Sciences Clinical Professor of Psychiatry; Director, Adult Psychiatry Clinic, Langley Porter Hospitals and Clinics, University of California, San Francisco
jonathanl@lppi.ucsf.edu

*Psychiatric Disorders***Chuangyi Mark Lu, MD, PhD**

Associate Professor, Department of Laboratory Medicine, University of California, San Francisco; Chief, Hematology and Hematopathology, Laboratory Medicine Service, Veterans Affairs Medical Center, San Francisco, California

mark.lu@va.gov

Appendix: Therapeutic Drug Monitoring & Laboratory Reference Intervals (includes Pharmacogenetic Testing online); CMDT Online—Diagnostic Testing & Medical Decision Making

Anthony Luke, MD, MPH

Professor of Clinical Orthopaedics, Department of Orthopaedics; Director, UCSF Primary Care Sports Medicine; Director, Human Performance Center at the Orthopaedic Institute, University of California, San Francisco

LukeA@orthosurg.ucsf.edu

*Sports Medicine & Outpatient Orthopedics***Lawrence R. Lustig, MD**

Francis A. Sooy, MD Professor of Otolaryngology—Head & Neck Surgery; Division Chief of Otolaryngology & Neurotology, Department of Otolaryngology—Head & Neck Surgery, University of California, San Francisco

llustig@ohns.ucsf.edu

*Ear, Nose, & Throat Disorders***C. Benjamin Ma, MD**

Associate Professor, Department of Orthopaedic Surgery; Chief, Sports Medicine and Shoulder Service, University of California, San Francisco

MaBen@orthosurg.ucsf.edu

*Sports Medicine & Outpatient Orthopedics***H. Trent MacKay, MD, MPH**

Professor of Obstetrics and Gynecology, Uniformed Services University of the Health Sciences, Bethesda, Maryland; Staff Physician, Department of Obstetrics and Gynecology, Walter Reed National Military Medical Center, Bethesda, Maryland

mackayt@mail.nih.gov

*Gynecologic Disorders***Umesh Masharani, MB, BS, MRCP(UK)**

Professor of Medicine, Division of Endocrinology and Metabolism, Department of Medicine, University of California, San Francisco

umesh.masharani@ucsf.edu

*Diabetes Mellitus & Hypoglycemia***Megan McNamara, MD, MSc**

Assistant Professor of Medicine, Department of Medicine, Case Western Reserve University, Cleveland, Ohio; Director of the Center for the Advancement of Medical Learning, Case Western Reserve School of Medicine, Cleveland, Ohio

Megan.Mcnamara@va.gov

*Women's Health Issues***Kenneth R. McQuaid, MD**

Professor of Clinical Medicine, University of California, San Francisco; Chief, Gastroenterology Section, San Francisco Veterans Affairs Medical Center

kenneth.mcquaid@med.va.gov

*Gastrointestinal Disorders; Alimentary Tract Cancers (in Chapter 39)***Maxwell V. Meng, MD, FACS**

Associate Professor, Department of Urology, University of California, San Francisco

mmeng@urology.ucsf.edu

*Urologic Disorders; Cancers of the Genitourinary Tract (in Chapter 39)***Tracy Minichiello, MD**

Associate Professor of Medicine, University of California, San Francisco; Chief, Anticoagulation and Thrombosis Services, San Francisco Veterans Affairs Medical Center

minichie@medicine.ucsf.edu

*Disorders of Hemostasis, Thrombosis, & Antithrombotic Therapy***Paul L. Nadler, MD**

Clinical Professor of Medicine; Director, Screening and Acute Care Clinic, Division of General Internal Medicine, Department of Medicine, University of California, San Francisco

nadler@medicine.ucsf.edu

*Common Symptoms***Jacqueline A. Nemer, MD, FACEP**

Associate Professor of Emergency Medicine, Department of Emergency Medicine, University of California, San Francisco

jacqueline.nemer@ucsf.edu

*Disorders Related to Environmental Emergencies***Anna Neumeier, MD**

Chief Medical Resident, Department of Medicine, University of California, San Francisco

References

C. Diana Nicoll, MD, PhD, MPA

Clinical Professor and Vice Chair, Department of Laboratory Medicine; Associate Dean, University of California, San Francisco; Chief of Staff and Chief, Laboratory Medicine Service, San Francisco Veterans Affairs Medical Center

diana.nicoll@va.gov

Appendix: Therapeutic Drug Monitoring & Laboratory Reference Intervals (includes Pharmacogenetic Testing online); CMDT Online—Diagnostic Testing & Medical Decision Making

Kent R. Olson, MD

Clinical Professor of Medicine, Pediatrics, and Pharmacy, University of California, San Francisco; Medical Director, San Francisco Division, California Poison Control System

kent.olson@ucsf.edu

Poisoning

Christopher D. Owens, MD, MSc

Associate Professor of Surgery, Division of Vascular and Endovascular Surgery, Department of Surgery, University of California, San Francisco,

christopher.owens@ucsfmedctr.org

Blood Vessel & Lymphatic Disorders

Steven Z. Pantilat, MD

Professor of Clinical Medicine, Department of Medicine; Alan M. Kates and John M. Burnard Endowed Chair in Palliative Care; Director, Palliative Care Program, University of California, San Francisco

stevep@medicine.ucsf.edu

Palliative Care & Pain Management

Manesh R. Patel, MD

Assistant Professor of Medicine, Division of Cardiology, Department of Medicine, Duke University Medical Center, Durham, North Carolina

patel017@notes.duke.edu

Heart Disease

Susan S. Philip, MD, MPH

Assistant Clinical Professor, Division of Infectious Diseases, Department of Medicine, University of California, San Francisco; Director, STD Prevention and Control Section, San Francisco Department of Public Health, San Francisco, California

susan.philip@sfdph.org

Spirochetal Infections

Michael Pignone, MD, MPH

Professor of Medicine, Division of General Internal Medicine, Department of Medicine, University of North Carolina, Chapel Hill

pignone@med.unc.edu

Disease Prevention & Health Promotion; CMDT Online—Diagnostic Testing & Medical Decision Making

Thomas J. Prendergast, MD

Associate Professor of Medicine, Oregon Health & Science University; Pulmonary Critical Care Section Chief, Portland Veterans Affairs Medical Center, Portland, Oregon

thomas.prendergast@va.gov

Pulmonary Disorders

Reed E. Pyeritz, MD, PhD

Professor of Medicine and Genetics; Vice-Chair for Academic Affairs, Department of Medicine, Raymond and Ruth Perelman School of Medicine of the University of Pennsylvania, Philadelphia

reed.pyeritz@uphs.upenn.edu

Clinical Genetic Disorders; CMDT Online—Fundamentals of Human Genetics

Michael W. Rabow, MD, FAAHPM

Professor of Clinical Medicine, Division of General Internal Medicine, Department of Medicine; Director, Symptom Management Service, Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco

mrabow@medicine.ucsf.edu

Palliative Care & Pain Management

Joseph H. Rapp, MD

Professor of Surgery in Residence, University of California, San Francisco; Chief, Vascular Surgery Service, Veterans Affairs Medical Center, San Francisco, California

rappj@surgery.ucsf.edu

Blood Vessel & Lymphatic Disorders

Paul Riordan-Eva, FRCOphth

Consultant Ophthalmologist, King's College Hospital, London, United Kingdom

paul.riordan-eva@nhs.net

Disorders of the Eyes & Lids

Vanessa L. Rogers, MD

Associate Professor, Obstetrics and Gynecology, University of Texas Southwestern Medical Center, Dallas, Texas

vanessa.rogers@utsouthwestern.edu

Obstetrics & Obstetric Disorders

Philip J. Rosenthal, MD

Professor, Division of Infectious Diseases, Department of Medicine, University of California, San Francisco; San Francisco General Hospital

prosenthal@medsfgh.ucsf.edu

Protozoal & Helminthic Infections

René Salazar, MD

Associate Professor of Clinical Medicine, Division of General Internal Medicine, Department of Medicine, University of California, San Francisco

salazarr@medicine.ucsf.edu

Disease Prevention & Health Promotion

Joshua S. Schindler, MD

Assistant Professor, Department of Otolaryngology,
Oregon Health & Science University, Portland, Oregon;
Medical Director, OHSU-Northwest Clinic for Voice
and Swallowing
schindlj@ohsu.edu
Ear, Nose, & Throat Disorders

Brian S. Schwartz, MD

Assistant Clinical Professor, Division of Infectious
Diseases, Department of Medicine, University of
California, San Francisco
brian.schwartz@ucsf.edu
Bacterial & Chlamydial Infections

Wayne X. Shandera, MD

Assistant Professor, Department of Internal Medicine,
Baylor College of Medicine, Houston, Texas
shandera@bcm.tmc.edu
Viral & Rickettsial Infections

Samuel A. Shelburne, MD, PhD

Assistant Professor, Department of Infectious Diseases,
MD Anderson Cancer Center, Houston, Texas
sshelburne@mdanderson.org
Mycotic Infections

Scott Steiger, MD

Assistant Clinical Professor, Division of General Internal
Medicine, University of California, San Francisco
Opioids for Chronic, Noncancer Pain (in Chapter 5)

Michael Sutters, MD, MRCP(UK)

Attending Nephrologist, Virginia Mason Medical
Center, Seattle, Washington; Affiliate Assistant
Professor of Medicine, Division of Nephrology,
University of Washington School of Medicine, Seattle,
Washington
michael.sutters@vmmc.org
Systemic Hypertension

Philip Tiso

Principal Editor, Division of General Internal Medicine,
University of California, San Francisco
References

Shivani V. Tripathi, MD

Fellow, Department of Dermatology, University of
California, San Francisco
References

Julian Villar, MD, MPH

Chief Resident, Department of Emergency Medicine, San
Francisco General Hospital, University of California,
San Francisco
References

Judith Walsh, MD, MPH

Professor of Clinical Medicine, Division of General
Internal Medicine, Women's Health Center of
Excellence, University of California, San Francisco
Judith.Walsh@ucsf.edu
Women's Health Issues

Thomas J. Walsh, MD, MS

Assistant Professor, Department of Urology, University of
Washington School of Medicine, Seattle, Washington
walsht@u.washington.edu
Urologic Disorders

Sunny Wang, MD

Assistant Clinical Professor of Medicine, Division of
Hematology and Oncology, University of California,
San Francisco; San Francisco Veterans Affairs Medical
Center
sunny.wang@ucsf.edu
Lung Cancer (in Chapter 39)

Suzanne Watnick, MD

Associate Professor of Medicine, Division of Nephrology
and Hypertension, Oregon Health & Science
University, Portland; Portland Veterans Affairs Medical
Center, Portland, Oregon
watnicks@ohsu.edu
Kidney Disease

CAPT Jason Woo, MD, MPH, FACOG

Medical Monitor, Contraceptive and Reproductive Health
Branch, Eunice Kennedy Shriver National Institute for
Child Health and Human Development, National
Institutes for Health, Rockville, Maryland
jasonwoo@pol.net
Gynecologic Disorders

Kevin C. Worley, MD

Assistant Professor of Obstetrics and Gynecology,
Department of Obstetrics and Gynecology, Division of
Maternal-Fetal Medicine, University of Texas
Southwestern Medical Center, Dallas, Texas Kevin.
Worley@UTSouthwestern.edu
Obstetrics & Obstetric Disorders

Andrew R. Zolopa, MD

Professor of Medicine, Division of Infectious Diseases and
Geographic Medicine, Stanford University, Stanford,
California
azolopa@stanford.edu
HIV Infection & AIDS

Preface

Current Medical Diagnosis & Treatment 2015 (CMDT 2015) is the 54th edition of this single-source reference for practitioners in both hospital and ambulatory settings. The book emphasizes the practical features of clinical diagnosis and patient management in all fields of internal medicine and in specialties of interest to primary care practitioners and to subspecialists who provide general care.

INTENDED AUDIENCE FOR CMDT

House officers, medical students, and all other health professions students will find the descriptions of diagnostic and therapeutic modalities, with citations to the current literature, of everyday usefulness in patient care.

Internists, family physicians, hospitalists, nurse practitioners, physicians' assistants, and all primary care providers will appreciate *CMDT* as a ready reference and refresher text. Physicians in other specialties, pharmacists, and dentists will find the book a useful basic medical reference text. Nurses, nurse-practitioners, and physicians' assistants will welcome the format and scope of the book as a means of referencing medical diagnosis and treatment.

Patients and their family members who seek information about the nature of specific diseases and their diagnosis and treatment may also find this book to be a valuable resource.

NEW IN THIS EDITION OF CMDT

- The latest 2014 American Heart Association/American College of Cardiology/Heart Rhythm Society (AHA/ACC/HRS) guidelines for anticoagulation recommendations for atrial fibrillation
- New table comparing the features of dabigatran, rivaroxaban, and apixaban for stroke prevention in nonvalvular atrial fibrillation
- Updated information and algorithms incorporating the guidelines for treatment of valvular heart disease and indications for interventions based on the 2014 AHA/ACC guidelines
- Discussion about the four groups of patients who benefit from statin medications based on the 2014 AHA/ACC guidelines
- Indications for high intensity and moderate intensity statins based on the 2014 AHA/ACC guidelines
- New evidence suggesting a cardiovascular cause for palpitations
- Updates on target specific oral anticoagulants
- Inclusion of Juvenile Nephronophthisis-Medullary Cystic Disease
- Revised psychiatric diagnoses in accordance with the *Diagnostic Statistical Manual*, 5th edition (DSM-5), including the identification of obsessive-compulsive disorder (OCD) spectrum disorders as a separate category from the anxiety disorders and updating of terms such as the subtypes of schizophrenia, somatization disorder, hypochondriasis, and substance abuse and dependence
- Positive and negative likelihood ratios for history, physical examination, and laboratory findings in the diagnosis of pneumonia
- Information about contact dermatitis from cellphone covers
- Use of omalizumab for refractory chronic urticaria
- New discussion about electronic cigarettes and tobacco cigarette cessation
- The new US Preventive Services Task Force (USPSTF) recommendation for universal HIV screening
- Update on HIV/TB coinfection
- New section on Middle East Respiratory Syndrome
- Extensive update on Arbovirus Encephalitides, Dengue, and Influenza
- Update on chronic pelvic pain
- New information about breast cancer risk for women with a family history of *BRCA* mutation
- An update on mammography screening for breast cancer
- Current recommendations for Papanicolaou smear screening
- Updated guidelines for management of abnormal cervical cytology
- Update on management of women at risk for preterm delivery
- Recommendations for low-dose CT screening of the lung in high-risk patients in relatively good health who meet National Lung Screening Trial criteria
- Risk prediction tools identifying variables that predicted postoperative myocardial infarction and cardiac arrest as well as postoperative respiratory failure
- New section on opioids for chronic, noncancer pain
- Update on the epidemic of opioid-based prescription drug abuse, misuse, and overdose

- Alternatives for treatment of diabetic retinopathy, anterior ischemic optic neuropathy, and optic neuritis
- Guidelines regarding use of ambulatory and home blood pressure measurements
- Guidelines for initiating antihypertensive therapy based on the UK's 2013 National Institute of Health and Care Excellence (NICE) and for blood pressure targets from the 2013 US Joint National Committee Report (JNC8) and Kidney Disease Improving Global Outcomes (KDIGO)
- Updated classification of glucose-6-phosphate dehydrogenase (G6PD) isoenzyme activity
- Updated treatment options for *Helicobacter pylori*
- Clarification of the best tests for celiac disease
- Clarification of the best test for *Clostridium difficile* infection, and an update on when to consider "fecal microbiota transplantation" for its treatment
- Update on use of immunomodulators, anti-TNF agents, and anti-integrins in Crohn disease
- New antivirals for treatment of hepatitis C
- Scoring tools for assessing the severity of acute pancreatitis
- New information on the antiphospholipid syndrome
- Update on surgical treatment of spinal stenosis
- New sections on IgG4-related disease and Takayasu arteritis
- Update on HLA-B alleles and risk of serious drug-induced hypersensitivity reactions
- New information on functional hypopituitarism, isolated hypogonadotropic hypogonadism, diagnosis of growth hormone deficiency in adults, treatment of diabetes insipidus, classification of amiodarone-induced thyrotoxicosis, preoperative parathyroid imaging, adrenal incidentaloma
- Latest recommendations for vaccinations

OUTSTANDING FEATURES OF CMDT

- Medical advances up to time of annual publication
- Detailed presentation of all primary care topics, including gynecology, obstetrics, dermatology, ophthalmology, otolaryngology, psychiatry, neurology, toxicology, urology, geriatrics, orthopedics, women's health, preventive medicine, and palliative care
- Concise format, facilitating efficient use in any practice setting
- More than 1000 diseases and disorders
- Annual update on HIV infection and AIDS
- Specific disease prevention information
- Easy access to medication dosages, with trade names indexed and costs updated in each edition
- Recent references, with unique identifiers (PubMed, PMID numbers) for rapid downloading of article abstracts and, in some instances, full-text reference articles

CMDT Online (www.AccessMedicine.com) provides full electronic access to *CMDT 2015* plus expanded basic science information and five additional chapters. The five online-only chapters (Anti-infective Chemotherapeutic & Antibiotic Agents, Fundamentals of Human Genetics, Diagnostic Testing & Medical Decision Making, Information Technology in Patient Care, and Integrative Medicine) are available at www.AccessMedicine.com/CMDT. CMDT Online is updated throughout the year and includes an expanded, dedicated Media Gallery as well as links to related Web sites. Subscribers also receive access to *Diagnosaurus* with 1000+ differential diagnoses, *Pocket Guide to Diagnostic Tests*, *Quick Medical Diagnosis & Treatment*, and *CURRENT Practice Guidelines in Primary Care*.

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Many students and physicians also have contributed useful suggestions to this and previous editions, and we are grateful. We continue to welcome comments and recommendations for future editions in writing or via electronic mail. The editors' and authors' institutional and e-mail addresses are given in the Authors section.

Maxine A. Papadakis, MD
papadakM@medsch.ucsf.edu
Stephen J. McPhee, MD
smcphoe@medicine.ucsf.edu
Michael W. Rabow, MD
mrabow@medicine.ucsf.edu
San Francisco, California

From inability to let alone; from too much zeal for the new and contempt for what is old; from putting knowledge before wisdom, and science before art and cleverness before common sense; from treating patients as cases; and from making the cure of the disease more grievous than the endurance of the same, Good Lord, deliver us.

—Sir Robert Hutchison

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Disease Prevention & Health Promotion

Michael Pignone, MD, MPH
René Salazar, MD

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GENERAL APPROACH TO THE PATIENT

The medical interview serves several functions. It is used to collect information to assist in diagnosis (the “history” of the present illness), to understand patient values, to assess and communicate prognosis, to establish a therapeutic relationship, and to reach agreement with the patient about further diagnostic procedures and therapeutic options. It also serves as an opportunity to influence patient behavior, such as in motivational discussions about smoking cessation or medication adherence. Interviewing techniques that avoid domination by the clinician increase patient involvement in care and patient satisfaction. Effective clinician-patient communication and increased patient involvement can improve health outcomes.

▶ Patient Adherence

For many illnesses, treatment depends on difficult fundamental behavioral changes, including alterations in diet, taking up exercise, giving up smoking, cutting down drinking, and adhering to medication regimens that are often complex. Adherence is a problem in every practice; up to 50% of patients fail to achieve full adherence, and one-third never take their medicines. Many patients with medical problems, even those with access to care, do not seek appropriate care or may drop out of care prematurely. Adherence rates for short-term, self-administered therapies are higher than for long-term therapies and are inversely correlated with the number of interventions, their complexity and cost, and the patient's perception of overmedication.

As an example, in HIV-infected patients, adherence to antiretroviral therapy is a crucial determinant of treatment success. Studies have unequivocally demonstrated a close relationship between patient adherence and plasma HIV RNA levels, CD4 cell counts, and mortality. Adherence levels of > 95% are needed to maintain virologic suppression. However, studies show that over 60% of patients are < 90% adherent and that adherence tends to decrease over time.

Patient reasons for nonadherence include simple forgetfulness, being away from home, being busy, and changes in daily routine. Other reasons include psychiatric disorders (depression or substance abuse), uncertainty about the effectiveness of treatment, lack of knowledge about the

consequences of poor adherence, regimen complexity, and treatment side effects.

Patients seem better able to take prescribed medications than to adhere to recommendations to change their diet, exercise habits, or alcohol intake or to perform various self-care activities (such as monitoring blood glucose levels at home). For short-term regimens, adherence to medications can be improved by giving clear instructions. Writing out advice to patients, including changes in medication, may be helpful. Because low functional health literacy is common (almost half of English-speaking US patients are unable to read and understand standard health education materials), other forms of communication—such as illustrated simple text, videotapes, or oral instructions—may be more effective. For non-English-speaking patients, clinicians and health care delivery systems can work to provide culturally and linguistically appropriate health services.

To help improve adherence to long-term regimens, clinicians can work with patients to reach agreement on the goals for therapy, provide information about the regimen, ensure understanding by using the “teach-back” method, counsel about the importance of adherence and how to organize medication-taking, reinforce self-monitoring, provide more convenient care, prescribe a simple dosage regimen for all medications (preferably one or two doses daily), suggest ways to help in remembering to take doses (time of day, mealtime, alarms) and to keep appointments, and provide ways to simplify dosing (medication boxes). Single-unit doses supplied in foil wrappers can increase adherence but should be avoided for patients who have difficulty opening them. Medication boxes with compartments (eg, Medisets) that are filled weekly are useful. Microelectronic devices can provide feedback to show patients whether they have taken doses as scheduled or to notify patients within a day if doses are skipped. Reminders, including cell phone text messages, are another effective means of encouraging adherence. The clinician can also enlist social support from family and friends, recruit an adherence monitor, provide a more convenient care environment, and provide rewards and recognition for the patient's efforts to follow the regimen. Collaborative programs that utilize pharmacists to help ensure adherence are also effective.

Adherence is also improved when a trusting doctor-patient relationship has been established and when patients actively participate in their care. Clinicians can improve patient adherence by inquiring specifically about the behaviors in question. When asked, many patients admit to incomplete adherence with medication regimens, with advice about giving up cigarettes, or with engaging only in “safer sex” practices. Although difficult, sufficient time must be made available for communication of health messages.

Medication adherence can be assessed generally with a single question: “In the past month, how often did you take your medications as the doctor prescribed?” Other ways of assessing medication adherence include pill counts and refill records; monitoring serum, urine, or saliva levels of drugs or metabolites; watching for appointment nonattendance and treatment nonresponse; and assessing predictable drug effects such as weight changes with diuretics or bradycardia from beta-blockers. In some conditions, even partial adherence, as with drug treatment of hypertension and diabetes mellitus, improves outcomes compared with nonadherence; in other cases, such as HIV antiretroviral therapy or treatment of tuberculosis, partial adherence may be worse than complete nonadherence.

▶ Guiding Principles of Care

Ethical decisions are often called for in medical practice, at both the “micro” level of the individual patient-clinician relationship and at the “macro” level of the allocation of resources. Ethical principles that guide the successful approach to diagnosis and treatment are honesty, beneficence, justice, avoidance of conflict of interest, and the pledge to do no harm. Increasingly, Western medicine involves patients in important decisions about medical care, eg, which colorectal screening test to obtain or modality of therapy for breast cancer or how far to proceed with treatment of patients who have terminal illnesses (see Chapter 5).

The clinician’s role does not end with diagnosis and treatment. The importance of the empathic clinician in helping patients and their families bear the burden of serious illness and death cannot be overemphasized. “To cure sometimes, to relieve often, and to comfort always” is a French saying as apt today as it was five centuries ago—as is Francis Peabody’s admonition: “The secret of the care of the patient is in caring for the patient.” Training to improve mindfulness and enhance patient-centered communication increases patient satisfaction and may also improve clinician satisfaction.

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HEALTH MAINTENANCE & DISEASE PREVENTION

Preventive medicine can be categorized as primary, secondary, or tertiary. Primary prevention aims to remove or reduce disease risk factors (eg, immunization, giving up or not starting smoking). Secondary prevention techniques promote early detection of disease or precursor states (eg, routine cervical Papanicolaou screening to detect carcinoma or dysplasia of the cervix). Tertiary prevention measures are aimed at limiting the impact of established disease (eg, partial mastectomy and radiation therapy to remove and control localized breast cancer). Tables 1–1 and 1–2 give leading causes of death in the United States and estimates of deaths from preventable causes.

Many effective preventive services are underutilized, and few adults receive all of the most strongly recommended services. The three highest-ranking services in terms of potential health benefits and cost-effectiveness include discussing aspirin use with high-risk adults, tobacco-use screening and brief interventions, and immunizing children. Other high-ranking services with data indicating substantial room for improvement in utilization are screening adults aged 50 and older for colorectal cancer, immunizing adults aged 65 and older against pneumococcal disease, and screening young women for *Chlamydia*.

Several methods, including the use of provider or patient reminder systems (including interactive patient health records), reorganization of care environments, and possibly provision of financial incentives (though this remains controversial), can increase utilization of preventive services, but such methods have not been widely adopted.

Table 1–1. Leading causes of death in the United States, 2011.

Category	Estimate
All causes	2,437,163
1. Diseases of the heart	596,339
2. Malignant neoplasms	575,313
3. Chronic lower respiratory diseases	143,382
4. Cerebrovascular diseases	128,931
5. Accidents (unintentional injuries)	122,777
6. Alzheimer disease	84,691
7. Diabetes mellitus	73,282
8. Influenza and pneumonia	53,667
9. Nephritis, nephrotic syndrome, and nephrosis	45,731
10. Intentional self-harm (suicide)	38,285

Source: National Center for Health Statistics 2012.

Table 1–2. Deaths from all causes attributable to common preventable risk factors. (Numbers given in the thousands.)

Risk Factor	Male (95% CI)	Female (95% CI)	Both Sexes (95% CI)
Tobacco smoking	248 (226–269)	219 (196–244)	467 (436–500)
High blood pressure	164 (153–175)	231 (213–249)	395 (372–414)
Overweight–obesity (high BMI)	114 (95–128)	102 (80–119)	216 (188–237)
Physical inactivity	88 (72–105)	103 (80–128)	191 (164–222)
High blood glucose	102 (80–122)	89 (69–108)	190 (163–217)
High LDL cholesterol	60 (42–70)	53 (44–59)	113 (94–124)
High dietary salt (sodium)	49 (46–51)	54 (50–57)	102 (97–107)
Low dietary omega-3 fatty acids (seafood)	45 (37–52)	39 (31–47)	84 (72–96)
High dietary trans fatty acids	46 (33–58)	35 (23–46)	82 (63–97)
Alcohol use	45 (32–49)	20 (17–22)	64 (51–69)
Low intake of fruits and vegetables	33 (23–45)	24 (15–36)	58 (44–74)
Low dietary polyunsaturated fatty acids (in replacement of saturated fatty acids)	9 (6–12)	6 (3–9)	15 (11–20)

BMI, body mass index; CI, confidence interval; LDL, low-density lipoprotein.

Note: Numbers of deaths cannot be summed across categories.

Used, with permission, from Danaei G et al. The preventable causes of death in the United States: comparative risk assessment of dietary, lifestyle, and metabolic risk factors. *PLoS Med.* 2009 Apr 28;6(4):e1000058.

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PREVENTION OF INFECTIOUS DISEASES

Much of the decline in the incidence and fatality rates of infectious diseases is attributable to public health measures—especially immunization, improved sanitation, and better nutrition.

Immunization remains the best means of preventing many infectious diseases. Recommended immunization schedules for children and adolescents can be found online at <http://www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html> and the schedule for adults is outlined in Table 30–7. Substantial vaccine-preventable morbidity and mortality continue to occur among adults from vaccine-preventable diseases, such as hepatitis A, hepatitis B, influenza, and

pneumococcal infections. Strategies to improve vaccination rates include increasing community demand for vaccinations; enhancing access to vaccination services; provider- or system-based interventions, such as reminder systems; assigning vaccination responsibilities to non-physician personnel and interventions that activate patients through personal contact.

Evidence suggests annual **influenza vaccination** is safe and effective with potential benefit in all age groups, and the Advisory Committee on Immunization Practices (ACIP) recommends routine influenza vaccination for all persons aged 6 months and older, including all adults. When vaccine supply is limited, certain groups should be given priority, such as adults 50 years and older, individuals with chronic illness or immunosuppression, and pregnant women. An alternative high-dose inactivated vaccine is available for adults 65 years and older. Adults 65 years and older can receive either the standard dose or high-dose vaccine, whereas those younger than 65 years should receive a standard-dose preparation.

Increasing reports of **pertussis** among US adolescents, adults, and their infant contacts have stimulated vaccine development for older age groups. The ACIP recommends routine use of a single dose of tetanus, diphtheria, and 5-component acellular pertussis vaccine (Tdap) for adults aged 19–64 years to replace the next booster dose of tetanus and diphtheria toxoids vaccine (Td). Due to increasing reports of pertussis in the United States, clinicians may choose to give Tdap to persons aged 65 years and older (particularly to those who might risk transmission to at-risk infants who are most susceptible to complications, including death), despite limited published data on the safety and efficacy of the vaccine in this age group.

Both **hepatitis A vaccine** and immune globulin provide protection against hepatitis A; however, administration of immune globulin may provide a modest benefit over vaccination in some settings. A recombinant protein **hepatitis E vaccine** has been developed that has proven safe and efficacious in preventing hepatitis E among high-risk populations. Hepatitis B vaccine administered as a three-dose series is recommended for all children aged 0–18 years and high-risk individuals (ie, health care workers, injection drug users, people with end-stage renal disease). Adults with diabetes are also at increased risk for hepatitis B infection, and in October 2011, the ACIP recommended **vaccination for hepatitis B** in diabetic patients aged 19–59 years. In diabetic persons aged 60 and older, hepatitis B vaccination should be considered.

Human papillomavirus (HPV) virus-like particle (VLP) vaccines have demonstrated effectiveness in preventing persistent HPV infections, and thus may impact the rate of cervical intraepithelial neoplasia (CIN) II–III. The American Academy of Pediatrics (AAP) recommends routine HPV vaccination for girls aged 11–12 years. The AAP also recommends that all unvaccinated girls and women aged 13–26 years receive the HPV vaccine. In October 2011, the ACIP approved recommendations for routine vaccination of males 11 or 12 years of age with three doses of HPV4 (quadrivalent vaccine). Vaccination of males with HPV may lead to indirect protection of women by reducing transmission of HPV and may prevent anal intraepithelial neoplasia and squamous cell carcinoma in men who have sex with men. Despite the effectiveness of the vaccine, rates of immunization are low. Interventions addressing personal beliefs and system barriers to vaccinations may help address the slow adoption of this vaccine.

Persons traveling to countries where infections are endemic should take precautions described in Chapter 30 and at <http://wwwnc.cdc.gov/travel/destinations/list.htm>. Immunization registries—confidential, population-based, computerized information systems that collect vaccination data about all residents of a geographic area—can be used to increase and sustain high vaccination coverage.

The rate of tuberculosis in the United States has been declining since 1992. In 2011, the US tuberculosis rate was 3.4 cases per 100,000 population, a decrease of 6.4% from the 2010 rate. This represents the lowest recorded rate since national tuberculosis surveillance began in 1953. Skin testing for **tuberculosis** (see Table 9–13) and treating selected patients reduce the risk of reactivation tuberculosis. Two blood tests, which are not confounded by prior BCG (bacillus Calmette-Guérin) vaccination, have been developed to detect tuberculosis infection by measuring in vitro T-cell interferon-gamma release in response to two antigens (one, the enzyme-linked immunospot [ELISpot], [T-SPOT.TB] and the other, a quantitative ELISA [QuantiFERON-TBGold] test). These T-cell-based assays have an excellent specificity that is higher than tuberculin skin testing in BCG-vaccinated populations.

The Advisory Council for the Elimination of Tuberculosis has called for a renewed commitment to eliminating tuberculosis in the United States, and the Institute of

Medicine has published a detailed plan for achieving that goal. Patients with HIV infection are at an especially high risk for tuberculosis. In 2010, there were an estimated 1.1 million incident cases of tuberculosis among the 34 million people living with HIV. Early initiation of antiretroviral therapy may help control the HIV-associated tuberculosis syndemic.

Treatment of tuberculosis poses a risk of hepatotoxicity and thus requires close monitoring of liver transaminases. Alanine aminotransferase (ALT) monitoring during the treatment of latent tuberculosis infection is recommended for certain individuals (preexisting liver disease, pregnancy, chronic alcohol consumption). ALT should be monitored in HIV-infected patients during treatment of tuberculosis disease and should be considered in patients over the age of 35. Symptomatic patients with an ALT elevation three times the upper limit of normal or asymptomatic patients with an elevation five times the ULN should be treated with a modified or alternative regimen.

In 2010, the Centers for Disease Control and Prevention (CDC) updated guidelines for the prevention and treatment of **sexually transmitted diseases**. Highlights of these guidelines include updated treatments for bacterial vaginosis and genital warts as well as antibiotic-resistant *Neisseria gonorrhoeae*, the prevalence of which has risen (see Chapter 30).

HIV infection is a major infectious disease problem in the world. Since sexual contact is a common mode of transmission, primary prevention relies on eliminating unsafe sexual behavior by promoting abstinence, later onset of first sexual activity, decreased number of partners, and use of latex condoms. Unfortunately, as many as one-third of HIV-positive persons continue unprotected sexual practices after learning that they are HIV-infected. Preexposure prophylaxis with antiretroviral drugs in men who have sex with men could have a major impact on preventing HIV infection, and studies evaluating the impact in other groups are underway. Postexposure prophylaxis is widely used after occupational and nonoccupational contact, and it has been estimated to reduce the risk of transmission by approximately 80%.

The CDC recommends universal HIV screening of all patients age 13–64, and the US Preventive Services Task Force (USPSTF) recommends that clinicians screen adolescents and adults age 15 to 65 years. In addition to reducing sexual transmission of HIV, initiation of antiretroviral therapy reduces the risk for AIDS-defining events and death among patients with less immunologically advanced disease.

In immunocompromised patients, live vaccines are contraindicated but many killed or component vaccines are safe and recommended. *Asymptomatic* HIV-infected patients have not shown adverse consequences when given live MMR and influenza vaccinations as well as tetanus, hepatitis B, *H influenza* type b and pneumococcal vaccinations—all should be given. However, if poliomyelitis immunization is required, the inactivated poliomyelitis vaccine is indicated. In *symptomatic* HIV-infected patients, live virus vaccines such as MMR should generally be avoided, but annual influenza vaccination is safe.